HIV, viral hepatitis and STIs

a guide for primary care

ashm
Australasian Society for HIV Medicine

2008 Edition

ABOUT ASHM

The Australasian Society for HIV Medicine is a peak representative professional body for medical practitioners and other health care workers in Australasia who work in HIV, viral hepatitis and related disease areas.

It was formed in 1988 (as the Australian Society of AIDS Physicians). It changed its name in 1989 to reflect a broader membership base and was incorporated in New South Wales in 1990. ASHM became a registered charity in 2003.

ASHM is a key partner in the Australasian and regional response to HIV, viral hepatitis and related diseases. It works closely with government, advisory bodies, community agencies and other professional organisations in Australia and the Asia Pacific region. It conducts broad education programs in HIV and viral hepatitis for medical practitioners, health care providers and allied health workers and manages programs of continuing medical education.

ASHM is governed by an elected voluntary board and managed by a secretariat. It receives support from the Australian Government Department of Health & Ageing, the Australian Government's Agency for International Development (AusAID), State and Territory Departments of Health and the private sector, and has established the ASHM Foundation which raises funds in support of educational activities. ASHM works on a range of issues affecting its members, including education and training, resources, HIV treatment, viral hepatitis, international/development issues and professional affairs. ASHM conducts an annual medical scientific conference. In addition, the ASHM Conference Division provides professional conference organisation to third parties.

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Preface

In March 2005, ASHM arranged for an evaluation of the monograph *HIV/viral hepatitis: a guide for primary care*, which was first produced in 2001, with a Second Edition in 2004. A major recommendation emerging from the evaluation was that this resource be reviewed to include the management of sexually transmitted infections (STIs). Originally, ASHM intended the monograph as a resource to provide general practitioners and other interested clinicians and health care workers with an introduction to HIV and viral hepatitis. The aim with this latest edition of *HIV, viral hepatitis and STIs: a guide for primary care* has been to produce a practical manual for risk assessment, screening and testing, diagnosis and basic principles of management of HIV, viral hepatitis and STIs, by reviewing epidemiology, transmission, microbiology and virology, history-taking, signs and symptoms, assessment and primary care management of these conditions. We have included two new chapters, one on screening and one on primary care management of STIs. Clinicians who test for HIV and viral hepatitis and those who provide non-specialist care for infected patients make up the intended audience for this monograph, as well as primary care practitioners who see patients with STIs and those who screen for STIs in their day to day work. The monograph places due emphasis on opportunistic screening for STIs as a valuable measure for the wellbeing of patients and one which also has the potential for improving public health and reducing the spread of HIV in the community. Physicians, medical students, nurses, allied health professionals, as well as individuals with a specific interest in these conditions, may find this volume useful.

HIV, viral hepatitis and STIs elucidates key differences and similarities in the assessment, diagnosis and management of infections due to HIV, STIs, hepatitis B virus (HBV) and hepatitis C virus (HCV). Although the medical management of these infections is different and the causative microbiological and virological agents are diverse, it makes good sense to take this approach because aspects of human behaviour (in this case sexual, recreational and addictive) determine an individual patient's risk of acquiring and transmitting these agents. In all these conditions, the medical issues cannot be divorced from the sociobiological. The same types of behaviour put people at risk of HIV, all the STIs and the viral hepatitides. Clinicians find that because patterns of transmission overlap, they often need to conduct risk assessment and testing for HIV, STIs, HBV and HCV at the same time. There are also overlapping clinical issues, for example the synergy between STIs and HIV, the management of fatigue or other symptoms associated with chronic viral infections and the impact of drug and alcohol dependence on medical management. In addition, the stigma associated with infection with one or more of these infections often determines health seeking behaviour and has an important bearing on psychosocial and legal issues.

The incorporation of viral hepatitis and STIs within an ASHM publication is a substantial change of direction. It reflects the trend in public policy and medical practice towards locating HIV and AIDS within the broader public and sexual health context. It also utilises the partnership model established for the management of HIV infection within the context of hepatitis C. Maximising the health of infected people through a range of interventions at the primary care level is a key focus of HIV, viral hepatitis and STIs, in line with the priorities delineated in the National Hepatitis C Strategy, the National HIV/AIDS Strategy, the National Aboriginal and Torres Strait Islander Sexual Health and Blood Borne Virus Strategy and the National Sexually Transmissible Infections Strategy. The need for a collaborative, 'shared care' relationship between primary care clinicians and specialists is a central theme. With the increasing complexity of clinical management, a productive 'shared care' model of care ensures best practice for the patient while maintaining medical standards and legal requirements in relation to screening, diagnosis, management and referral of patients. It is hoped that *HIV, viral hepatitis and STIs* will facilitate closer working relationships between general practitioners, specialists, sexual health clinics and other health service providers in the areas of HIV, viral hepatitis and sexual health generally.

Many organisations and individuals have contributed to the production of this new edition and previous editions of this monograph. On behalf of ASHM, we would like to acknowledge the input of the Royal Australian College of General Practitioners, the Gastroenterological Society of Australia (GESA)/ Australian Liver Association, the Royal College of Physicians, the Australasian Chapter of Sexual Health Medicine, the Australian College of Rural and Remote Medicine, the Australian Federation of AIDS Organisations, the National Association of People Living with AIDS and Hepatitis Australia.

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Authors and reviewers gave time and energy to this project in the context of busy practices and heavy workloads, and their demonstrated commitment to medical education deserves considerable recognition. Thanks to the many other individuals who contributed ideas and information to the project.

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Sharon Lewin
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Melbourne, July 2007

HIV, HBV, HCV and STIs: similarities and differences

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Introduction

The three major blood-borne viruses, human immunodeficiency virus (HIV), hepatitis B virus (HBV) and hepatitis C virus (HCV), are members of different virus families but have one thing in common: their major mode of transmission is via blood or bodily fluids. Sexually transmitted infections (STIs) are a diverse group of infections caused by widely differing micro-organisms (viruses, protozoa, bacteria, yeasts, ectoparasites and even a nematode), whose common characteristic is that they are transmitted from person to person by sexual contact such as deep kissing, vaginal sex, anal sex, oral sex, oro-anal sex or just close intimate physical contact.

Table 1.1 provides a list, probably not exhaustive, of the causative agents and their accompanying infections which are capable of being sexually transmitted (i.e. sexually transmissible infections). The distinction between the terms 'sexually transmitted' and 'sexually transmissible' is a fine one and there is little consensus about the correct usage—in this monograph the terms will be used interchangeably, with 'sexually transmitted' being favoured.

Some infections (e.g. gonorrhoea, chlamydia and syphilis) are readily recognisable as being STIs while others (e.g. hepatitis A and the enteric infections) are only sexually transmitted under certain circumstances, namely where sexual activity facilitates oro-anal transmission (Table 1.1). The three major blood-borne viruses mentioned above are all capable of sexual transmission so can also be categorised as STIs, with HIV and HBV very readily sexually transmitted, but HCV only rarely sexually transmitted (see below). Despite their diversity, STIs share two other common characteristics which justify considering them as a group:

- Similar behavioural characteristics lead to people contracting, and being at risk of, STIs—so control strategies are similar for all of them
- Most STIs, in their early stages, are asymptomatic or so mildly symptomatic as to be easily overlooked, yet are infectious—screening at-risk people is essential for population management.

Key points

- Human immunodeficiency virus (HIV), hepatitis B virus (HBV) and hepatitis C virus (HCV) are distinct viruses with different epidemiological profiles, modes of transmission, natural histories and treatments.
- All three viruses lead to chronic infection in many infected individuals and are characterised by hypermutability and quasispecies.
- The microbiological and virological agents which cause STIs are highly diverse, having specific epidemiological profiles, varied modes of sexual transmission, different natural histories and individual treatment modalities.
- HIV is transmitted through sexual contact, blood-to-blood contact and mother-to-child transmission. Without treatment, most infected individuals develop severe immune deficiency within ten years. Combination antiretroviral therapy has transformed the course of the disease, extending the life expectancy of infected individuals by many years.
- STIs have a complex synergistic relationship with HIV. Most STIs play an enhancing role in the acquisition and transmission of HIV, while HIV may alter the natural history and response to treatment of some STIs.
- HBV is transmitted through mucous membrane contact (including unprotected sexual contact), blood-to-blood contact, mother-to-child transmission and intrafamilial transmission.
  A safe and effective vaccine against HBV is available. The age of infection is crucial in determining the natural history of HBV. For people who develop chronic active hepatitis B, treatment is effective in a substantial minority of patients. Chronic active hepatitis B may progress to cirrhosis and hepatocellular carcinoma.
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TABLE 1.1 Sexually *Transmissible* Infections (i.e. those *capable* of sexual transmission)

STI	Causative micro-organism	Mode of sexual transmission	Commonly found in:
BACTERIA			
bacterial vaginosis *(probably NOT a true STI)*	*Gardnerella vaginalis*, *Atopobium vaginae*, *Mobiluncus sp* and other anaerobic bacteria	unknown	WSW, but also any sexually active woman
chancroid	*Haemophilus ducreyi*	genital skin to skin and mm to mm contact	individuals who have unprotected sex in endemic areas
donovanosis	*Klebsiella granulomatis*	uncertain	remote Indigenous communities in Australia
enteric infections	*Campylobacter spp*	oral faecal contamination during sex	mostly MSM
	Shigella spp	oral faecal contamination during sex	mostly MSM
	Salmonella spp	oral faecal contamination during sex	mostly MSM
	Yersinia enterocolitica	oral faecal contamination during sex	mostly MSM
chlamydia infection	*Chlamydia trachomatis serovars D-K*	genital, rectal and oropharyngeal mm to mm contact	all sexually active people
lymphogranuloma venereum (LGV)	*Chlamydia trachomatis serovars L1-L3*	genital and rectal skin to skin and mm to mm contact	MSM and individuals who have unprotected sex in endemic areas
mycoplasma infection	*Mycoplasma genitalium*	genital mm to mm contact	probably all sexually active people
	Mycoplasma hominis	role uncertain	role in genital infection uncertain
Neisseria infection (gonorrhoea)	*Neisseria gonorrhoeae*	genital, rectal and oropharyngeal mm to mm contact	all sexually active people
urethritis, pharyngeal colonisation	*Neisseria meningitidis*	oropharyngeal mm to urethral mm (rarely)	mostly, but not exclusively MSM
ureaplasma infection	*Ureaplasma urealyticum (some subtypes)*	genital mm to mm contact	probably all sexually active people
syphilis	*Treponema pallidum*	genital, rectal and oropharyngeal mm to mm and skin to skin contact	all sexually active people
ECTOPARASITES			
pubic lice	*Pthirus pubis*	close body contact, sharing a bed	everyone
scabies	*Sarcoptes scabiei*	close body contact, sharing a bed, plus institution and household contact	everyone
NEMATODES			
thread worms	*Enterobius vermicularis*	oral faecal contamination during sex	predominantly MSM

TABLE 1.1 Sexually *Transmissible* Infections (i.e. those *capable* of sexual transmission) continued			
STI	**Causative micro-organism**	**Mode of sexual transmission**	**Commonly found in:**
PROTOZOA			
enteric infections	*Entamoeba spp*	oral faecal contamination during sex	MSM
	Giardia duodenale	oral faecal contamination during sex	MSM
trichomoniasis	*Trichomonas vaginalis*	mm to mm contact during peno-vaginal sex	heterosexually active people
VIRUSES			
adenoviral urethritis	*Adenoviruses*	genital and oropharyngeal mm to mm contact	all sexually active people
cytomegalovirus infection	*Cytomegalovirus (CMV)*	oral mm to mm contact, saliva exchange	all sexually active people
infectious mononucleosis	Epstein-Barr virus (EBV)	oral mm to mm contact, saliva exchange	all sexually active people
genital herpes	Herpes simplex virus types 1 and 2 (HSV-1 and HSV-2)	genital, rectal and oropharyngeal skin to skin and mm to mm contact	all sexually active people
genital human papillomavirus infection (genital warts and squamous intraepithelial lesions - SIL)	Human papillomavirus (HPV) (many types, but especially 6 and 11 for genital warts; and 16 and 18 for SIL)	genital, rectal, mouth and oropharyngeal skin to skin and mm to mm contact oral faecal contamination during sex	all sexually active people
hepatitis A	*Hepatitis A virus (HAV)*	oral faecal contamination during sex	predominantly MSM
hepatitis B	*Hepatitis B virus (HBV)*	exchange of body fluids during sex	all sexually active people
hepatitis C (rarely)	*Hepatitis C virus (HCV)*	blood exchange during sex	potentially all sexually active people, but rare*
human immunodeficiency virus infection	Human immunodeficiency virus types 1 and 2 (HIV-1 and HIV-2)	exchange of body fluids during sex	all sexually active people
Kaposi's sarcoma (KS)	Human herpes virus 8 (HHV-8)	uncertain, probably exchange of body fluids	predominantly MSM
molluscum contagiosum	*Molluscum contagiosum (pox) virus (MCV)*	direct skin to skin contact	all sexually active people
YEASTS			
candidiasis	*Candida spp* (ubiquitous commensals, only incidentally sexually transmitted)	genital mm to mm contact	all sexually active people

* There is increasing evidence for the sexual transmission of HCV in HIV-positive MSM[1]

mm = mucous membrane
MSM = men who have sex with men
WSW = women who have sex with women

Key points

Continued from page 9

- HCV is transmitted primarily through blood-to-blood contact. The sharing of equipment during injecting drug use is the most common mode of transmission in Australia. A minority of people clear HCV from the body but the majority develop a chronic infection. Some chronically infected individuals will develop symptoms such as fatigue and nausea. A small proportion of individuals will progress to liver failure or hepatocellular carcinoma. Combination therapy may be effective, although HCV genotype significantly influences response to treatment.
- Early diagnosis and treatment of non-viral STIs is an effective intervention for the population control of STIs generally, while suppressive anti-viral therapy for genital herpes decreases onward transmission of this virus and may indirectly assist in reducing the spread of HIV.

This chapter describes the blood-borne viral and sexually transmitted micro-organisms, specifically focusing on their biology, transmission, pathogenesis and natural history. It also provides an introduction to the principles of therapy and discusses the effects of therapy on the natural history of each of these infections. This chapter will discuss only the following STIs as representative of the group as a whole. These six infections are included because of their serious long-term sequelae or because they are common in Australia and New Zealand:

- Genital chlamydial infection (including lymphogranuloma venereum [LGV])
- Genital herpes (herpes simplex virus, or HSV)
- Genital warts (human papillomavirus, HPV)
- Gonorrhoea (*Neisseria gonorrhoeae*)
- Syphilis (*Treponema pallidum*)
- Trichomoniasis (*Trichomonas vaginalis*)

In addition, there will be a brief discussion about bacterial vaginosis because it is very common. Bacterial vaginosis may not be a true STI as it can occur in celibate women on rare occasions and treating the sexual partners of women with bacterial vaginosis has no effect on recurrence rates in index patients.

Biology (virology and microbiology)

HIV

The manifestations of HIV were first apparent in the early 1980s when an epidemic of unexplained cases of immunodeficiency was reported in the western world. Evidence suggested the cause to be a transmissible agent, and in 1984 the agent was confirmed to be a retrovirus now known as human immunodeficiency virus (HIV). Human infection may date back to the early part of the twentieth century and the virus may have originally been transmitted zoonotically to humans from primates in Africa.

HIV is a single-stranded ribonucleic acid (RNA) virus. It has an outer envelope that surrounds two copies of single-stranded RNA as well as a number of viral proteins. From its outer envelope protrudes the 120 glycoprotein (gp 120). The HIV replication cycle commences when gp 120 attaches to the CD4 receptor and the chemokine co-receptor CCR5. (These receptors are expressed on the surface of the CD4 lymphocyte, the cell that HIV predominantly infects.) Attachment precipitates the fusion of the membranes of virus and cell via the HIV envelope 41 glycoprotein (gp 41), allowing the virus to enter the cell. The RNA then undergoes reverse transcription, a process whereby RNA is converted to deoxyribonucleic acid, (DNA) using the viral-encoded reverse transcriptase. The resulting viral DNA, called the provirus, migrates to the nucleus and integrates into the host chromosome.

The provirus acts as a template to allow production of messenger RNA to produce the components of new virus particles, including the RNA genome of new virions. The viral proteins are processed and cleaved by another virus-specific enzyme known as HIV protease. Viral proteins and RNA are then assembled and bud from the cell membrane, forming mature HIV particles that can infect other cells. Some of the CD4 cells are irreparably damaged by HIV infection. Premature cell death of damaged CD4 cells in part contributes to the immunosuppression characteristic of advanced HIV disease.[2]

HBV

HBV is a non-cytopathic virus and contains a partially double-stranded DNA genome. This virus predominantly infects hepatocytes and belongs to the hepadnavirus family. HBV has an outer envelope containing hepatitis B surface antigen (HBsAg) and a core containing hepatitis B core antigen (HBcAg). Excess HBsAg is produced as sub-viral particles which circulate in the blood and permit serological diagnosis of HBV. The core contains the genomic DNA as well as the viral-encoded DNA polymerase, which is detected in liver tissue. HBV also produces hepatitis B 'e' antigen or HBeAg, which is secreted into the blood and is detected by serological assay. The presence of circulating HBeAg and serum HBV DNA is indicative of ongoing viral replication and increased infectivity. Resolution of HBV infection is accompanied by clearance of HBeAg and HBsAg and seroconversion to anti-HBe-positivity (anti-HBe+) and anti-HBs-positivity (anti-HBs+).

Soon after entering the hepatocyte, the genomic DNA is converted in the nucleus to a form known as supercoiled or covalently closed circular (ccc) DNA. This serves as a template to yield two types of RNA: a pregenomic RNA that ultimately undergoes reverse transcription to yield DNA for progeny virus and messenger RNA for structural proteins. The former is assembled into mature virions that are then released from the cell.

In long-term, chronic infection, HBV DNA may integrate into the host cell genome but integration is typically incomplete and a full life cycle cannot occur from these integrated sequences. Viral integration does play a role in the development of hepatocellular carcinoma, especially in the setting of cirrhosis. Supercoiled HBV DNA in the liver cell nucleus is long-lived and resistant to all current antiviral therapies, resulting in lifelong chronic infection.[3]

HCV

HCV is a single-stranded, enveloped RNA virus belonging to the flavivirus family. It causes most cases of what was previously known as non-A, non-B hepatitis. HCV was discovered when infected serum was injected into a number of chimpanzees, whose sera were then used to identify a clone that reacted with an infected serum panel from patients with non-A, non-B hepatitis. This finding ultimately formed the basis of the first antibody test for detection of HCV. The virus has only recently been cultivated in cell culture systems.

The HCV replication cycle has been partially elucidated. The viral receptor has not been conclusively demonstrated on the hepatocyte. Following infection of the hepatocyte and internalisation of the virus, HCV RNA is translated by the host cell ribosomes to produce a large viral polyprotein, which is cleaved and processed by both host cellular and virus-specific (NS-2 and NS-3) enzymes. The viral polymerase/replicase (NS-5B) copies the viral RNA in the cytoplasm and, as soon as a pool of progeny RNA molecules and core proteins is present, assembly of the nucleocapsids occurs. Mature HCV virions then develop and bud through the plasma membrane.

Chlamydia trachomatis

Chlamydia trachomatis is a common human pathogen divided into 15 different serovars. Serovars A, B, Ba and C cause trachoma; serovars D to K cause genital (and sometimes conjunctival) infection; serovars L1-L3 are associated with lymphogranuloma venereum (LGV) and tend to be more virulent and invasive showing a predilection for lymphatic vessels and tissue. *C. trachomatis* is a bacterium, but an obligate intracellular one, so can only be isolated and grown in suitable host cells. There are two main structures in the life cycle of *C. trachomatis*, the elementary body (EB) and the reticulate body (RB). The EB is a rigid-walled structure packed with DNA and is the infectious particle. It infects a potential host cell by adhering to its surface.

The EBs enter the cell by endocytosis and soon begin the second phase of their life cycle as metabolically active reticulate bodies. The RBs use adenosine triphosphate (ATP) derived from the host cell to replicate by binary fission, each producing several hundred progeny. The RBs become larger and form inclusions in the cytoplasm of infected cells which can be detected by staining (e.g. with iodine). A microscopist can see these intracytoplasmic inclusions in some infected cells draped around the nucleus like a cloak; the word 'chlamys' is Greek for 'cloak', so this gave the micro-organism its name. After about 20 hours some of the RBs undergo reorganisation to form new EBs that with cell lysis, burst out of the old cell ready to infect other susceptible cells. The whole life cycle takes about 72 hours. Chlamydial disease confined to epithelial surfaces tends to produce only a mild immune response, whereas more serious sequelae (e.g. salpingitis) and systemic disease such as LGV, elicit a vigorous antibody reaction.[4]

Herpes simplex virus–types 1 and 2 (HSV-1 and HSV-2)

The herpes simplex viruses are double-stranded DNA viruses, members of the human herpesvirus family and are exceptionally successful human pathogens. Like the varicella-zoster virus, HSV-1 and HSV-2 are neurotropic viruses but have the ability to cause infection in many other cell types. HSV-1 and HSV-2 are widely prevalent and tend to cause only mild and self-limited disease. A characteristic which they share with other members of the human herpesvirus family is the ability to establish latent infection, so that they are able to persist throughout the life of the host. During latency, the genome of the invading virus is maintained in stable form in the infected neural cell with no production of progeny virus for variable periods of time and no apparent cytotoxic effects. Periodically, reactivation of virus replication occurs with virus migrating back down axons to surface sites. The clinical severity of herpes simplex infections and the host's capacity to control viral replication depends very much on cell-mediated immunity, although humoral immune mechanisms also play an important part.[5]

Human papillomavirus (HPV)

The human papillomaviruses (HPV) are small DNA viruses which induce proliferation of epithelial cells with the production of papillomas. More than 35 HPV types infect genital skin and mucous membrane. So far HPV has not been grown in tissue culture and typing is dependent on detection of the genome by molecular cloning and sequencing. Genital HPV types are divided into high-risk and low-risk depending on their potential to promote the development of squamous cell cancers in infected cells. Types 6 and 11 are low-risk types as they are rarely associated with cancers and tend to cause typical genital warts.

Types 16, 18, 31, 33, 35 and 45 are high-risk types. About 50% of invasive squamous cell cancers of the cervix carry the HPV DNA of type 16. HPV has a highly significant role in the development of ano-genital cancers whether they be cervical, vulval, penile or anal cancers.[6] Genital HPV is ubiquitous in the community; an American study published in 2006 found that in women aged 18 to 25 years, the overall HPV frequency of detection was 26.9% and there was detectable high-risk HPV DNA in 20%[7], while another recent study from a very broad cross-section of the population in the USA found that the prevalence of HPV DNA in young women aged 14 to 24 years was 33.8%.[8] Infection usually occurs in adolescence and young adulthood soon after the beginning of sexual activity. Because of the asymptomatic nature of much HPV genital infection and the lack of any specific antiviral treatment, up until now control of high-risk HPV type infection in the community has depended entirely on cervical cancer screening and follow-up with surgical ablation of high grade squamous intraepithelial lesions. The recent development and licensing in Australia of two prophylactic vaccines (Gardasil and Cervarix) for girls and young women against the commonest high-risk and low-risk genital HPV types is therefore a considerable step forward, although it should be noted that only one of the vaccines (Gardasil) is active against HPV types causing genital warts.[9] Studies of the vaccine in young gay men will now proceed to inform possible future use of the vaccine to prevent anal cancer in this group.

Neisseria gonorrhoeae

Neisseria gonorrhoeae, or the gonococcus, the causative agent of gonorrhoea, is perhaps the best known sexually transmitted agent and has caused considerable morbidity in human beings since the earliest recorded history. Gonococci are gram-negative bacteria which characteristically grow in pairs as diplococci. Under the light microscope they are indistinguishable from meningococci and indeed meningococci, on occasions, have been demonstrated to cause urethritis—hence the need for accurate microbiological identification of urethral isolates. Like *C. trachomatis*, gonococci have a predilection for the mucous membrane surfaces of the urethra, endocervical canal, rectum, pharynx and conjunctiva. Sequelae of untreated infections can be serious and severe. Some uncommon strains of gonococci cause little inflammatory response on mucosal surfaces but have the ability to invade, leading to bacteraemia and more systemic disease.

Gonococci possess surface molecules called pili which are largely responsible for adhesion to mucosal surfaces and also for invasion into the submucosa. Pili also serve as targets for host defences but have an amazing ability to undergo swift antigenic change. This accounts for the almost complete absence of acquired natural immunity against attacks of mucosal gonorrhoea. A person can be successfully treated for gonococcal urethritis or cervicitis today and if exposed to infection again tomorrow is completely susceptible to re-infection. A great deal is known now about the pathogenicity of *N. gonorrhoeae* and associated host-bacterial interactions. Despite all this accumulated knowledge, gonorrhoea remains a considerable problem around the world. There has been a notable lack of progress towards vaccine development and the gonococcus has an extraordinary capacity to acquire resistance to antibiotics very rapidly. This ability continues to present a formidable challenge. Medical science always seems to be only one step ahead of this doughty Darwinian survivor.[10]

Treponema pallidum

Treponema pallidum is the bacterial agent which causes syphilis, another well known and once feared STI. *T. pallidum* is a spirochaetal organism related to Borrelia and Leptospira. It is a long, thin, tightly coiled bacterium, just beyond the resolution of the light microscope, although it can be demonstrated in a microscope with a dark field condenser. Here, in a wet preparation, it distinguishes itself from other spirochaetes by its regular tight spirals and its characteristic motility. Both the corkscrew shape and the mobility of the organism play important roles in its invasion and dissemination. The body mounts an immune response against invading treponemes, both humoral and cell-mediated, and many of the unique clinical features of syphilis are due to the immune response. Bacteria are able to establish latency in lymphatic and splenic tissue and during this period of latency, which may last for many years in untreated patients, the infected person will be resistant to reinfection from a new challenge with *T. pallidum*.[11]

Trichomonas vaginalis

Trichomonas vaginalis is a flagellated protozoan which lives only in the human genitourinary tract. As long ago as 1836 Donné demonstrated trichomonads as motile organisms in a preparation of fresh vaginal discharge, and for the next hundred years *T. vaginalis* was regarded as a harmless inhabitant of the vagina. It causes symptomatic infection (vaginitis in women and urethritis in men) but more often is carried asymptomatically in both sexes. It is highly infectious and almost invariably sexually transmitted.[12]

Bacterial vaginosis

Bacterial vaginosis is a common, complex, clinical syndrome of which the characteristic feature is an alteration in the normal vaginal flora. Normal lactobacilli are absent or greatly reduced and a swarm of gram-variable, small, mostly anaerobic micro-organisms including *Gardnerella vaginalis*, *Atopobium vaginae*, *Mobiluncus sp*, and *Prevotella sp* replace them. Some of these organisms are highly motile and tend to cluster around shed epithelial cells in vaginal fluid. Microscopists describe such cells as 'clue cells' and they are a hallmark of bacterial vaginosis. The normal

acidic milieu of the vagina is lost with the pH rising to 7 or above. The cause of this curious condition is still unknown and while it has some features in common with other STIs, namely strong association with sexual activity, the lack of any similar condition or conjunction of micro-organisms in males, whether symptomatic or not, makes its classification as an STI suspect in our present state of ignorance. However, the condition is very common in women who have sex with women (WSW) and in this group bacterial vaginosis certainly seems to be acting like an STI.[13]

Quasispecies and hypermutability of blood-borne viruses

The replicase enzymes of all three blood-borne viruses, the HIV reverse transcriptase, the HBV DNA polymerase and the HCV RNA polymerase, are hypermutatable. Mutation, particularly under immunological and therapeutic pressure, leads to the presence in a given individual of a number of closely related, but genetically distinct, viral variants known as quasispecies. The emergence of quasispecies is the likely reason why infection with these viruses results in chronic infection in most individuals despite a host immune response. Each one of the virus-specific enzymes previously discussed is the focus of intense research to develop potent and selective inhibitors of key viral functions, which could result in significant gains in managing the health of people persistently infected with these viruses.[14]

Transmission

While each blood-borne virus has distinct transmission patterns, HIV, HBV and HCV can all be transmitted parenterally through the sharing of injecting equipment, needle-stick injuries, or piercing and tattooing with contaminated equipment. On the other hand, efficiency of sexual transmission differs markedly between viruses. STIs are by definition transmitted through sexual contact but the precise mode of transmission varies from infection to infection—different sexual activities favour the transmission of different sexually transmissible agents: individuals don't acquire pubic lice and gonorrhoea in quite the same way (see Table 1.1).

HIV

HIV is predominantly transmitted sexually, with efficiency being greatest through receptive anal intercourse. In Australia, transmission is most commonly seen in homosexual men, whereas in developing countries, especially in Africa, HIV is predominantly acquired through vaginal intercourse. Transmission through injecting drug use is uncommon in Australia, accounting for 4% of HIV cases, but is particularly prevalent in parts of Europe and Asia (including countries of the former Soviet Union) and the USA. Transmission by blood products largely occurred before the introduction of antibody screening in 1985 in Australia and was responsible for the high incidence of HIV among multiply-transfused people, such as those with haemophilia. It is now exceedingly rare in countries where blood is screened. Transmission by needle-stick injury occurs in 0.3% of exposures from HIV-infected individuals. Perinatal transmission occurs in 20–45% of infants born to infected mothers, but this rate can be reduced to 1–2% with the administration of antiretroviral therapy during pregnancy, labour and after delivery, and other interventions, such as caesarean section and avoidance of breast-feeding.[15] In Australia there have been 22,785 new diagnoses of HIV infection, with 9,827 cases of AIDS to the end of June 2006 and 6,621 AIDS-related deaths.[16]

HBV

Most HBV cases result from perinatal transmission, which accounts for high prevalence in people from endemic countries, particularly China and South East Asian and Pacific nations. Transmission is effectively prevented by HBV vaccination and administration of hepatitis B immunoglobulin (HBIG) to newborns of hepatitis B surface antigen positive women, but such programs are not currently available in many developing countries where most cases occur.

Among adults, HBV transmission is predominantly via sexual contact and injecting drug use. In Australia, the overall prevalence of HBV infection has been estimated to be 90,000 to 160,000.[17] The risk of transmission by percutaneous exposure such as a needle-stick injury is approximately 30% if the person with HBV infection has replicative disease (defined as HBV DNA+ by hybridisation assay or HBsAg+ and HBeAg+), compared with 3% for those with HBV infection with non-replicative disease (that is, people without HBeAg or HBV DNA but with HBsAg+).[3]

HCV

HCV transmission is predominantly parenteral. The most common mode of transmission in Australia remains injecting drug use, which is responsible for approximately 80% of the estimated 225,000 prevalent cases nationally and is reported as the predominant risk factor in over 90% of the estimated 16,000 annual incident cases.[18] Among particular immigrant populations, poor infection-control practices during procedures such as vaccination (European and Asian) and chemoprophylaxis programs for schistosomiasis (Egyptian) may have been responsible for many cases. The role of sexual transmission is still controversial. If sexual transmission of HCV does occur, it is at a very low level that makes it inappropriate to routinely recommend safe sex among long-term monogamous couples.

Sexual transmission is likely to be more efficient, however, where there is HIV co-infection and high HCV viral load.[19] Risk of sexual transmission may also be increased when blood is present in the genital tract, such as during menstruation. Perinatal transmission

occurs in approximately 5% of deliveries, although this may be higher in women who have HIV co-infection or high levels of viraemia. Elective caesarean section in women with HIV/HCV co-infection is usually advocated, although its role in reducing perinatal transmission in women with HCV mono-infection is unclear and is generally not recommended as routine in this context.[21]

Chlamydia trachomatis

Chlamydia trachomatis tends to infect columnar epithelium rather than squamous epithelium. Direct mucous membrane-to-mucous membrane contact facilitates transmission and chlamydial elementary bodies in infected genital secretions and discharges readily seed uninfected mucous membrane and cause infection in columnar cells. During birth, transmission occurs from a mother with cervical chlamydial infection to the child very efficiently (overall risk is 50–75%).

Indirect transmission of chlamydial infection by fomites appears to be extremely uncommon. Lymphogranuloma venereum (LGV) serovars are transmitted similarly by direct surface to surface contact or contamination of susceptible genital surfaces by contaminated secretions. The recent LGV outbreak in men who have sex with men (MSM) appears to be predominantly via anal intercourse with multiple partners, fisting and use of contaminated sex toys. For all practical purposes, transmission of the genital serovars of *C. trachomatis* is sexual and vertical only, and conjunctival infection in the adult results from auto-inoculation with infected secretions from genitals to eye by the patient's own fingers.[22]

HSV-1 and HSV-2

Sexual transmission is a highly significant method of transmission of these viruses.[23] However, most people with oral and labial cold sores are infected with HSV-1 in childhood usually by being kissed on or near the mouth by family or relatives. Once they grow up and become sexually active, they can pass HSV-1 on to various anatomical sites in one or other of their sexual partners by kissing or by oro-vulval, oro-penile or oro-anal sex. A significant proportion of anogenital herpes is due to HSV-1 infection (30% or more in many studies).[25]

All that is required for transmission of HSV-1 or HSV-2 is for the virus from an infected person to come in contact with a mucosal surface (vaginal, cervical, rectal, pharyngeal, buccal, labial, conjunctival) or a slightly abraded skin surface anywhere on the body of a susceptible person.

People never exposed to either virus are most susceptible and may develop a severe primary attack when infected; those with antibodies to one or other HSV, demonstrating previous exposure, are still capable of being infected by the alternative virus but have some degree of protection and may suffer a less severe infection. The two viruses exhibit different tropism for anatomic sites; HSV-1 can infect both oral and genital sites but tends to thrive better in the mouth area, in that it reactivates more commonly there with viral shedding and sometimes with clinically obvious recurrences; HSV-2 can also infect both oral and genital sites but thrives better in the genital region.

However, surprisingly, a study published in 2006 of men seropositive for HSV-2 (about half of whom were also HIV positive), showed that 40% of the men shed HSV-2 from both genital and oral sites. Oral shedding was always asymptomatic, it usually occurred at the same time as genital shedding and it occurred more commonly in HIV-positive men.[26]

All these facts explain why HSV infection is so common in sexually active people and why control of the spread of infection in communities presents such a challenge. Transmission rates can be reduced with careful and consistent condom use, and suppressive therapy with antiviral drugs for those who suffer frequent recurrences. Only an effective vaccine will make a significant impact on the problem of herpes simplex virus infection at population level.

All forms of sexual contact can lead to transmission of HSV-1 or HSV-2 and mother-to-child transmission can occur at the time of birth. Neonatally acquired herpes can be a devastating and life-threatening disease. Fortunately mothers who are already infected with herpes provide their own antibodies transplacentally which substantially protect the infant from infection, even if HSV is shed by the mother around the time of delivery. However, if a pregnant woman is infected in the anogenital region with HSV-1 or HSV-2 in the last trimester of pregnancy and fails to develop significant HSV antibody levels (as shown by testing prior to delivery), the baby is at significant risk of acquiring neonatal herpes. In this situation obstetricians recommend a caesarean section birth.[4]

Human papillomavirus

Sexual contact of all types accounts for all genital HPV infection. This includes the low-risk HPV types which result in the growth of genital warts and the high-risk HPV types that are associated with ano-genital cancers. Genital HPV is a sexually transmitted infection demonstrated by the now well established fact that women without a present or prior sex partner tend to have a very low yield of HPV DNA in cervico-vaginal secretions, women with only one sex partner have a slightly higher yield and women with a history of more than one partner have a substantially higher yield.

Each time a person acquires a new sex partner, that person's risk of acquiring genital HPV increases considerably. The consequence is that most sexually active adults have acquired one or more of the plethora of genital HPV types by the time they reach their fourth decade. Direct skin-to-skin, skin-

to-mucous membrane and mucous membrane-to-mucous membrane contact is all that is required for transmission to occur. HPV infection with one or more genital types of HPV does occur around the mouth and lips as a result of oral sex but is only a problem in an immunosuppressed patient. Similarly mother-to-child transmission of HPV at the time of birth sometimes does occur resulting in genital or laryngeal infection in the infant, but fortunately these infections rarely cause clinical problems.[6] *Laryngeal papillomatosis*, while extremely rare, can be a very significant clinical problem in young children.

Neiserria gonorrhoeae

The gonococcus is highly infectious but is a fragile organism outside the human body, being poorly resistant to environmental changes such as heat and drying. Transmission is therefore almost exclusively by sexual contact or from mother to infant at the time of birth. Transmission by fomites is extremely unlikely. Gonorrhoea transmission is fairly efficient, with a prevalence of infection of 50–90% in female sex contacts of a man with urethral gonorrhoea.

Transmission is by direct mucous membrane-to-mucous membrane contact or via infected genital secretions on a susceptible mucosal surface. Transmission from male to female via vaginal sex is slightly more efficient than from female to male and, similarly, transmission from the male partner to the receptive partner in anal sex is more efficient than vice versa. The pharyngeal mucosa is readily infected from an infected urethral meatus via oral sex while transmission from infected pharynx to urethra is less common but well documented, especially among MSM. Adult gonococcal conjunctivitis (a sight-threatening infection) is almost always acquired by auto-inoculation via the person's own fingers from his or her infected genitals, while neonatal conjunctivitis is acquired by direct inoculation of the baby's conjunctivae during transit through the infected maternal endocervical canal.[10]

Treponema pallidum

Syphilis is only acquired by sexual contact or by transplacental transmission of *Treponema pallidum*, i.e. from an infected mother to her foetus in utero. An old study suggested that the risk of acquiring syphilis from an infectious partner was about 30% per sexual exposure.[26] A woman infected with syphilis has a potential risk of transmitting syphilis transplacentally during many years of untreated infection (8–10 years at least, although the risk decreases with every passing year). However, people with syphilis seem only able to transmit it to sexual partners during the first two years of untreated infection. This suggests that for sexual transmission to occur, moist mucosal or cutaneous lesions (i.e. those that appear in primary and secondary syphilis) must be present, so that active treponemes on those surfaces of an infected person have an opportunity of reaching and penetrating moist mucosal or cutaneous surfaces of the sexual partner. Infectious lesions include the primary chancre and all the mucosal manifestations of secondary syphilis, e.g. snail track ulcers, condylomata lata, mucous patches, and split papules. Even microscopic and non-clinically obvious mucosal lesions, as may occur in the vagina, the mouth, under the foreskin and perianally, in early latent syphilis, are infectious to sexual partners and probably account for most of the transmission that occurs in areas where syphilis is endemic.[26]

Trichomonas vaginalis

Trichomonas vaginalis is transmitted almost exclusively by sexual contact. There has been a long debate about the possibility of transmission by contaminated fomites such as face cloths, towels, and toilet seats. While it is true that the organism is hardier than *T. pallidum* and *N. gonorrhoeae* and may survive 45 minutes or so outside the body, epidemiological evidence to support non venereal transmission is slim. *T. vaginalis* is not known to infect rectal mucosa, the conjunctiva or the pharynx. In this respect it differs from the gonococcus and *C. trachomatis*. Vaginal intercourse appears to be the main way trichomoniasis is spread, with oral sex and anal sex having no part to play.[12]

Bacterial vaginosis

The aetiology of this condition is unknown. It remains uncertain whether sexual transmission of agents (known and unknown) plays a part in its aetiology.

Natural history

HIV

Following inoculation with HIV, there is a period of high-level viraemia associated with a reduction in the CD4 cell count. A host immune response then develops, partially controlling viral replication, but is unable to clear HIV from the body. A substantial proportion of patients (proportions in recent reports range from 50–92%) suffer a mononucleosis-like seroconversion illness characterised by fever, pharyngitis, lymphadenopathy, rash, splenomegaly and aseptic meningitis. Other HIV-infected patients are asymptomatic or suffer a more non-specific illness. These acute-phase effects then resolve as the immune system mounts an antiviral response that causes the viral load to decrease markedly. Simultaneously, there is a rebound increase in CD4 cell count to near baseline levels and the patient enters a period of clinical latency, although very high levels of viral replication continue, especially in the lymphoid compartment. The plasma HIV RNA plateaus to a constant level of viraemia known as the virological set point. If left untreated, the patient experiences a gradual decline in CD4 cell count, with a median loss of 80 cells per year. Progression to AIDS (the development of opportunistic infections or specific malignancies) occurs a median of 10 years after initial infection with HIV. At this time the CD4 cell count has usually fallen below 200 cells/µl and the patient is severely immunocompromised (Figure 1.1).[2,27]

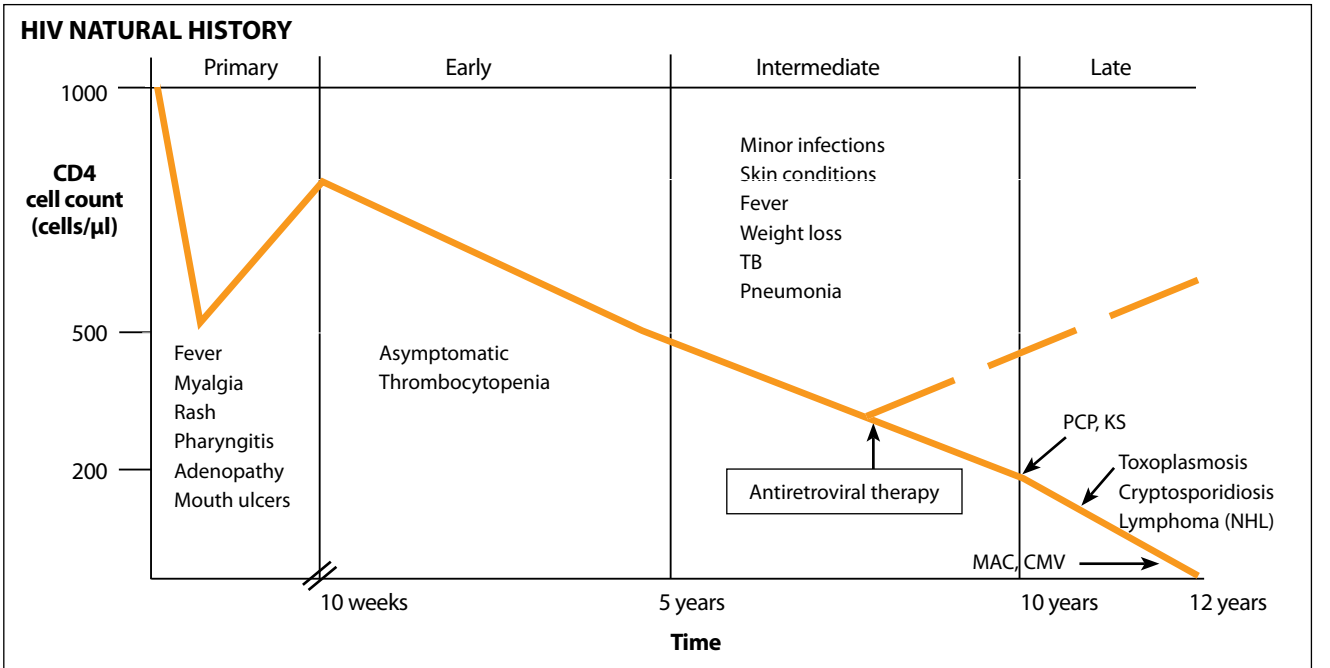

FIGURE 1.1 The various stages of HIV infection depicting the development of different opportunistic infections with advanced immunodeficiency and the impact of antiretroviral therapy on CD4 cell count recovery.

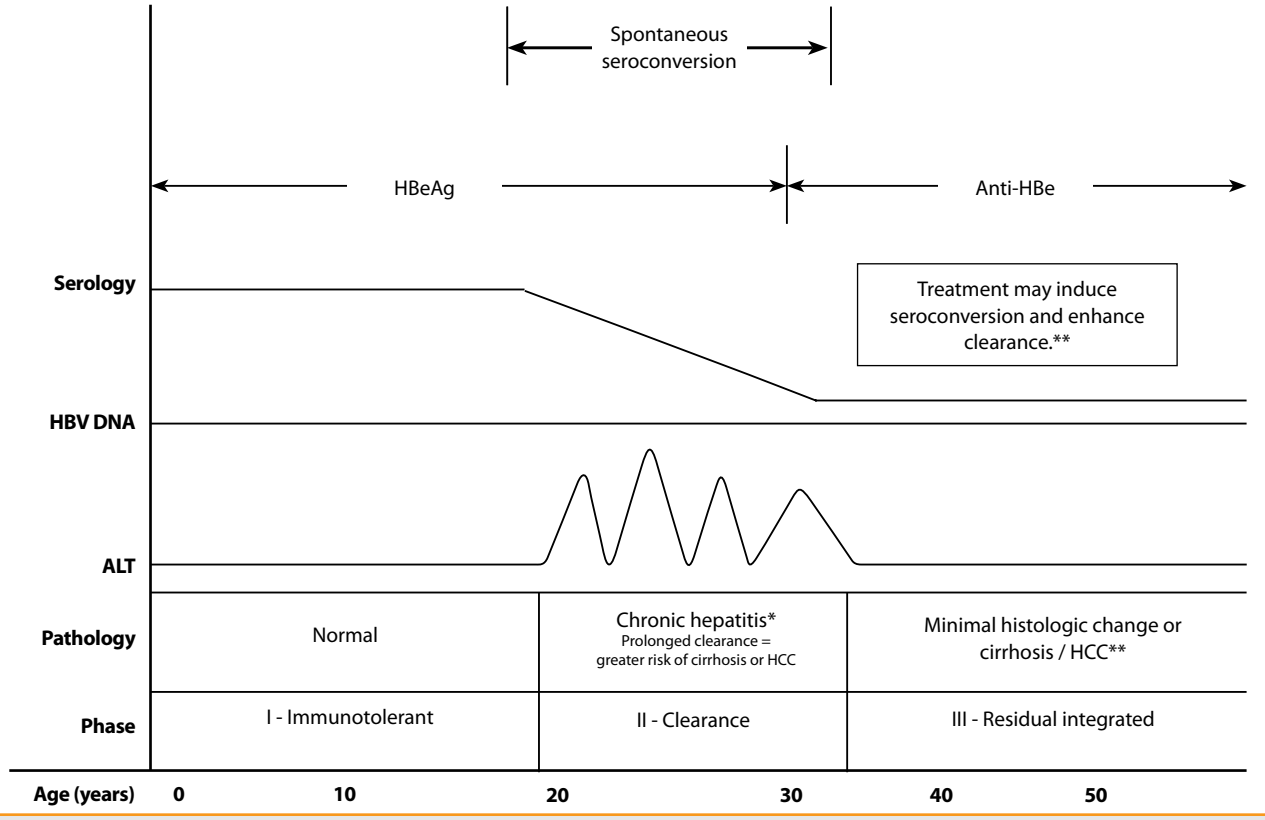

FIGURE 1.2 Demonstrates the three phases of infection in a person from an endemic area.

* Cirrhosis may develop during the period of attempted immune clearance.

** Antiviral therapy increases the likelihood of HBeAg to anti-HBe seroconversion. Active disease may occur despite loss of HBeAg.

HBV

HBV, by contrast, is almost exclusively an immune-mediated disease. The outcome of infection is largely determined by the age at which infection is acquired, which relates to the maturity of the immune response. In endemic countries where infection occurs during birth (perinatal infection) or in early childhood (early horizontal infection), over 90% of HBV transmissions will become chronic (as defined by a persistence of HBsAg for more than six months), and clinical acute hepatitis rarely occurs. If, however, an individual is infected as an adult, chronic infection will occur in less than 5% of people, although almost half will manifest clinical features of acute hepatitis.

The natural history of chronic HBV infection has been defined by stages of immune response. Initially patients have no immune response to the virus and are said to be in the immunotolerant phase. At this time, they have normal liver function despite high levels of HBV DNA and detectable HBeAg, indicating active viral replication.

Later in life, usually in the second to fourth decades, the immune system is triggered to attack the virus-infected hepatocyte and a period of immune clearance ensues, whereby patients demonstrate flares of elevated serum aminotransferase levels with histological evidence of active hepatitis.

If these flares persist for too long or are substantial, the patient may ultimately develop cirrhosis and liver failure. About 25–40% of people with long-term infection will die of cirrhosis or hepatocellular carcinoma (HCC) (Figure 1.2). However, if these immune-based clearances are successful, the patient will demonstrate an HBeAg seroconversion to anti-HBe, have undetectable HBV DNA by hybridisation assay and show normalisation of serum aminotransferase levels with associated improvement of liver histology. The person with HBV infection then enters into the latent phase with an improved long-term prognosis (Figure 1.2).

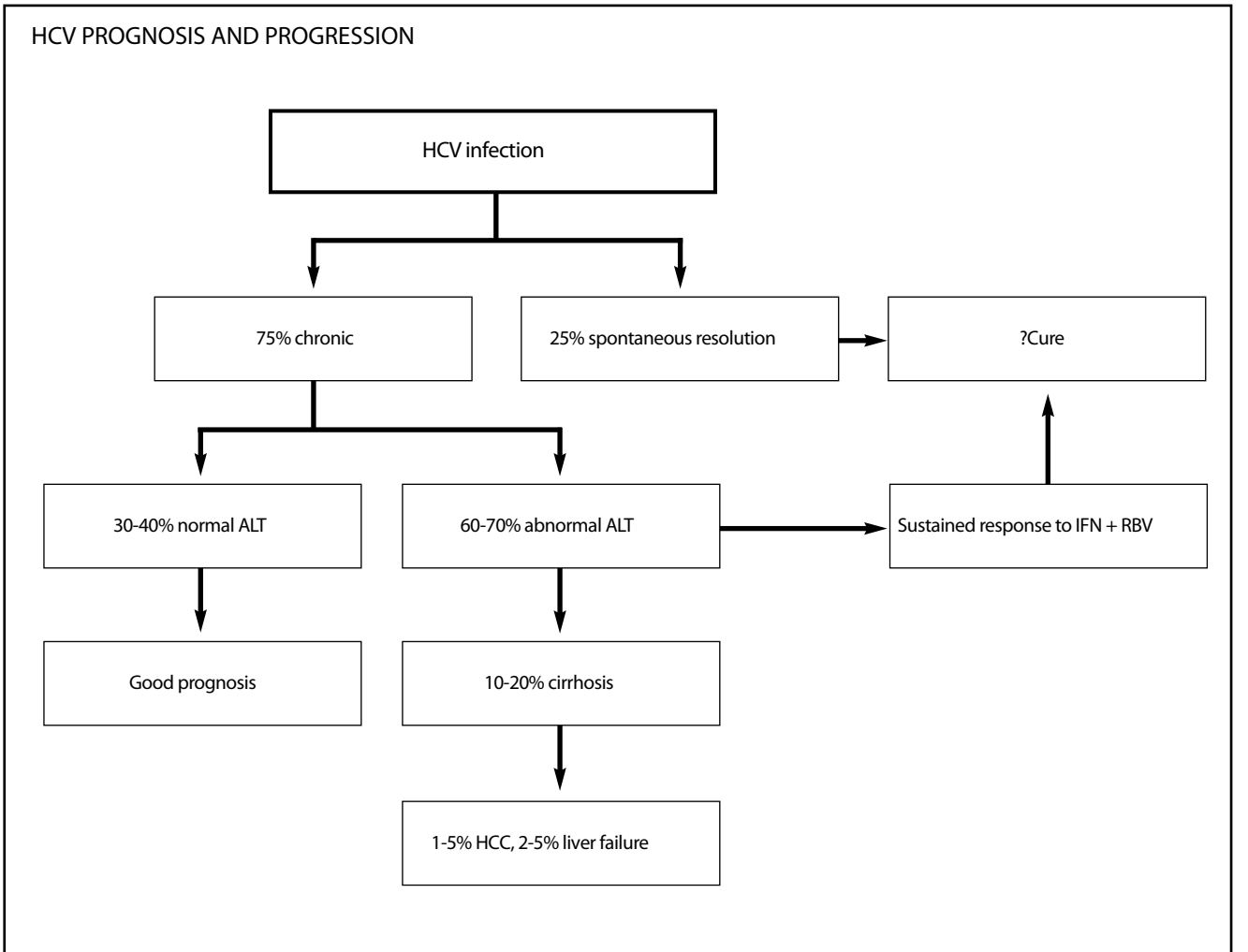

FIGURE 1.3 The natural history of hepatitis C infection and the impact of successful therapy on infection

Occasionally, under the pressure of immune-mediated flares, HBV mutants are selected. These so-called precore (or HBeAg-negative) mutants fail to secrete HBeAg protein but still replicate, as evidenced by detectable HBV DNA in serum and elevated serum aminotransferase levels. HBeAg-negative infection is particularly prevalent in certain geographical areas, such as around the Mediterranean basin and in South East and northern Asia. In Australia, migrants from these regions are frequently infected with such variants.[3]

HCV

Unlike HBV, the immune response generated in adults newly infected with hepatitis C is usually inadequate to effectively control viral replication. As a consequence, the majority of acute infections progress to chronic infection, defined as a positive HCV RNA in serum six months after the estimated date of infection. The proportion of people estimated to clear acute hepatitis C varies between 25% and 40%, and clearance occurs more frequently in patients who are symptomatic or who become jaundiced. Understanding of the natural history of chronic hepatitis C infection has improved in recent years with the realisation that fewer people progress to cirrhosis than was originally estimated (Figure 1.3). Models based on large longitudinal community-based cohorts estimate the risk of progression to cirrhosis to be 7% at 20 years and 20% at 40 years of infection.[27] Estimates of hepatitis C-related mortality are 1% at 20 years and 4% at 40 years.[28] Despite this, an increasing burden of advanced liver disease is anticipated within Australia in future years, with between 15,000 and 20,000 cases of cirrhosis by the year 2010.

Factors associated with an accelerated risk of progression include older age at infection, male gender, heavy alcohol intake, co-infection with HBV and HIV and possibly obesity, linked to the presence of steatosis (fatty liver) on biopsy. The risk of liver failure in people with compensated cirrhosis is around 4–5% per year and the risk of hepatoma around 1–3% per year in Australia.

People who have chronic hepatitis C and normal liver function tests generally have very low rates of fibrosis progression. At present the majority of these patients are not routinely offered HCV therapy and are treated only in the context of clinical trials.

Co-infection with HIV, HBV or HCV

Multiple blood-borne viral infections in the same individual can markedly alter the natural history of disease. For example, HBV has no adverse effect on HIV or the development of AIDS, but HIV does influence HBV and can be associated with accelerated development of cirrhosis and liver failure. The exact mechanism(s) of the pathogenesis of this co-infection are presently unknown but are probably due to virological (higher HBV viral load in co-infection) and host immunological (dysregulated immune responses) factors.

Individuals with HIV and HCV co-infection have higher HCV viral loads and a more rapid course to end-stage liver disease. This has been demonstrated by the correlation between declining CD4 cell counts and the increasing percentage of HCV-related hospital admissions and deaths among people with HIV and HCV co-infection.[29]

Chlamydia trachomatis

The natural history of genital chlamydia infection varies depending on whether infection is caused by the D to K serovars, or the L1 to L3 serovars.

D to K serovars

Primary sites of genital infection with D to K serovars of *C. trachomatis* in adults are mucosal surfaces lined by columnar epithelium, hence urethritis, endocervicitis, proctitis and pharyngitis can result, depending on the type of sexual activity. Most of these infections are mild and it is more likely that infected people remain asymptomatic for a considerable time rather than developing obvious symptoms and signs. In infants following mother-to-child transmission, primary sites of infection are the naso-pharynx, the conjunctivae and, more rarely, the vagina or urethra.

Genital D to K chlamydia infections can spread from their site of original infection. In women, cervical infection tends to spread upwards through the endometrium causing a mild endometritis with onward spread to the mucosal lining of the fallopian tubes with resulting salpingitis.

Infection can spread from the surface of the fallopian tubes into the surrounding peritoneum and supporting ligaments resulting in pelvic inflammatory disease (PID). Sometimes transcoelomic spread can result in perihepatitis (the Fitz-Hugh Curtis syndrome). In men, ascending infection can result in epididymo-orchitis. In adults, both PID and epididymo-orchitis caused by *C. trachomatis* tend to be milder than similar gonococcal disease, but the potential for long-term damage in women (pelvic sepsis, tubo-ovarian abscess, infertility and increased risk of ectopic pregnancy) is equivalent in both infections: chlamydia PID is a more silent and insidious infection than the gonococcal variety. In infants, naso-pharyngeal infection is often a precursor to the development of pneumonitis.[22]

L1–L3 serovars (LGV)

Until quite recently lymphogranuloma venereum (LGV) remained an uncommon infection mostly seen in tropical and sub-tropical resource-poor countries. It was exceedingly rare in Australia, New Zealand and other Western countries. Tropical LGV has three stages:

- A primary ulcer on the genitals, usually of short term duration
- A secondary stage characterised by systemic symptoms, inguinal lymphadenitis and sometimes a moderately severe proctitis

- A third stage with chronic sequelae: bubo formation often with rupture and discharging inguinal sinuses, lymphatic obstruction with genital elephantiasis and rectal stricture and fistula formation

In 2003 and 2004 the first cases of rectal infection with an L2 serovar in MSM were identified in the Netherlands and subsequently more cases have been detected in most other Western countries with significant populations of homosexually active men, including in major Australian cities.

The vast majority of these cases have been characterised by moderately severe to severe rectal proctitis with systemic symptoms (fever and malaise) and little or (more often) no involvement of inguinal lymph nodes.[30]

Herpes simplex virus – types 1 and 2 (HSV-I and HSV-2)

Both HSV-1 and HSV-2 can cause genital herpetic infection. The most common scenario for genital infection with either of the herpes simplex viruses is for a person, during a sexual contact, to acquire the virus on a genital mucous membrane or cutaneous surface with either extremely mild symptoms or no symptoms at all marking the event. In the case of a person with no previous exposure to HSV-1 or HSV-2, and where a large dose of virus is acquired, within a few days of acquisition painful vesicles or blisters develop which rapidly break down to form shallow tender ulcerations. At the same time, draining lymph nodes become enlarged and tender and there may be systemic symptoms of fever and malaise. This is called primary genital herpes infection. It is distressing and uncomfortable in both men and women and may last up to three weeks before spontaneously remitting. There is a third group of people whose first contact with genital HSV (the initial attack) lies somewhere between the extremes of the severe primary outbreak and the entirely asymptomatic group.

The virus establishes latent infection in sensory nerve ganglia in the vicinity of the spinal cord and periodically reactivates with migration down the nerve fibres and intermittent release of infectious virions onto the surface—this is called 'viral shedding' and is the cause of most onward transmission of HSV. All people infected with genital HSV undergo the same pattern of recurrent reactivation of latent virus and intermittent reappearance of infectious virions at a surface site. For some people, recognisable symptoms of blistering and ulceration accompany this reactivation; for others asymptomatic reactivation is the rule. Genital infection with HSV-2 is more likely to result in symptomatic recurrences than genital infection with HSV-1.

Neonatal HSV infection can manifest as lesions localised to the skin, eyes or mouth; an encephalitis; or a severe disseminated life-threatening infection.[5]

Human papillomavirus

There are still substantial gaps in knowledge about the natural history of genital HPV infection. Most infections are acquired in adolescence and early adult life and HPV infection shares characteristics with other STIs, namely: it is more common in those who commence sexual activity early; those who have frequent partner changes or multiple partners; and those whose partner has or has had frequent partner changes. However, few sexually active people avoid acquiring one or more of the genital HPV types during their lifetime. The outcomes of anogenital infection with HPV include:

- 'Invisible infection' where the only indication that infection has occurred is the presence of HPV DNA in epithelial cells, as detected by an appropriate test
- Cytological signs of infection as seen in a cytological smear or in material taken by biopsy (e.g. at colposcopy). Such cytological changes are in the form of low-grade or high-grade squamous intraepithelial lesions (LSIL or HSIL)
- Typical exophytic warts

In general, HPV infections tend to resolve over time in immunocompetent people presumably reflecting increasing immune control over the virus, although local immune mechanisms in epithelium are still poorly understood. Genital HPV infection may persist for many years despite apparent complete clinical resolution and it is not uncommon for people who become immunosuppressed later in life to develop recurrences of anogenital warts which had troubled them in their early adult life. In time many exophytic warts disappear even without treatment and most low-grade and even high-grade squamous intraepithelial lesions regress. However, a small percentage of squamous intraepithelial lesions do develop into anogenital cancers. This is much more likely to occur if the HPV types causing the lesions are high-risk types, the most common being types 16 and 18. On the other hand, exophytic warts caused by HPV types 6 or 11 appear to have virtually no potential to develop into cancer.[6]

Neisseria gonorrhoeae

Neisseria gonorrhoeae targets exactly the same columnar cells in the mucous membrane of urethra, endocervix, rectum, pharynx and conjunctiva as does *Chlamydia trachomatis*. Within a few days the infection elicits a vigorous local immune response with the production of cytokines and the influx of large numbers of polymorphonuclear lymphocytes. Thus, most strains of gonorrhoea tend to produce visible signs of inflammation, i.e. meatitis, urethritis, and cervicitis, although it is only the infection in the male urethra which usually results in early detectable symptoms of dysuria and purulent discharge. Infection at other sites is much less likely to cause readily recognisable symptoms, at least in the first few weeks. A small percentage of men seems to acquire urethral gonorrhoea asymptomatically, probably

reflecting infection with less virulent strains or strains less well equipped to elicit a mucosal immune response; some of these strains are more likely to cause epididymo-orchitis than clinically obvious mucosal infection. Untreated, *N. gonorrhoeae* invades the submucosa sometimes causing submucosal abscesses, spreads into adjoining glandular structures such as Bartholin's, Skene's and Littré's glands with the potential for further abscess formation. A mild lymphadenitis in draining lymph nodes often accompanies acute infection. Gonorrhoea initiates an inexorable ascending infection to the fallopian tubes, surrounding ligaments and adjoining organs in women, causing an acute pelvic inflammatory disease. Less commonly, infection spreads to the epididymis and testis in men, causing an acute epididymo-orchitis. The infection eventually resolves, but, in the absence of early treatment, healing occurs with damaging scar tissue formation and fibrosis. In the urethra and the fallopian tubes such scarring can permanently interfere with normal function. A small number of gonococcal strains has the potential to invade the blood stream causing bacteraemia with systemic symptoms and disseminated skin and joint manifestations (disseminated gonococcal infection).

In the neonate, infected by its mother at birth, gonorrhoea characteristically produces an acute sight-threatening conjunctivitis which is recognised two or three days after birth.[31]

Treponema pallidum

The natural history of syphilis in an adult is divided into three stages—primary, secondary and tertiary.

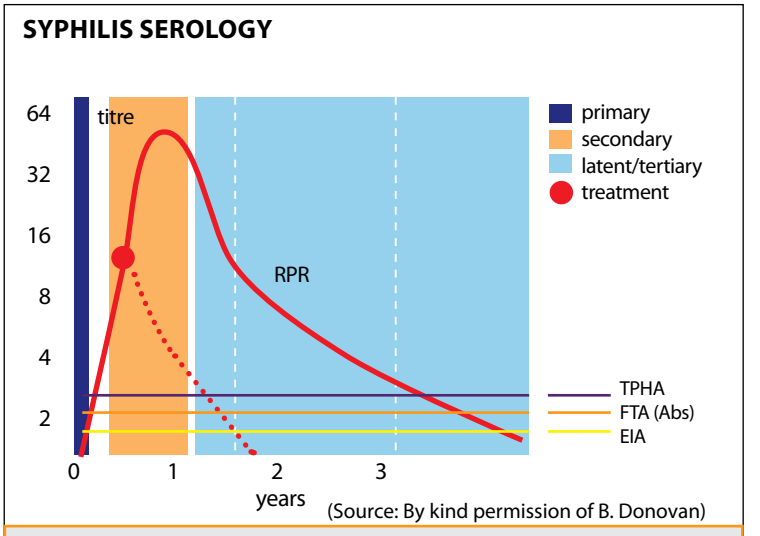

FIGURE 1.4

Someone without clinical signs or symptoms of syphilis, but having positive syphilis serology and no history of having been treated for syphilis, is said to have latent syphilis. By convention in Australia and the UK, primary and secondary syphilis and the first two years of latent infection are called 'early' syphilis (i.e. the period during which syphilis is infectious by sexual contact), while tertiary, cardiovascular, neurosyphilis and latent infection beyond two years is called 'late' syphilis. In the USA 'early' syphilis refers only to the first twelve months of infection. Table 1.2 and Figure 1.4 describe the stages of syphilis in adults with a guide to accompanying serology results.

TABLE 1.2 Stages of syphilis in Adults

INFECTIOUS			NON-INFECTIOUS except vertically		
EARLY (<2 years) Early latent (asymptomatic)	**RPR** 1:8 or greater	**SPECIFIC TEST** Reactive	**LATE (>2 YEARS)** LATE LATENT (asymptomatic)	**RPR** Very variable, usually 1:4 or less – sometimes becomes non-reactive eventually	**SPECIFIC TEST** Reactive
Primary (chancre)	May be non-reactive, but then increasing titre with time	Reactive (except very early in infection)	Tertiary (skin lesions, gummata)	Usually less than 1:16	Reactive
Secondary (rash, mucous membrane lesions, alopecia, lymphadenopathy)	1:8 or greater (i.e. 1:16, 1:32, 1:64)	Reactive	Cardiovascular (aortitis)	Usually less than 1:16	Reactive
Specific test = TPPA or TPHA, FTA ABS, EIA			Neurosyphilis (may be asymptomatic – only abnormal CSF being demonstrated)	1:8 or greater	Reactive

Primary syphilis (the chancre) is a self-limiting condition, with ulceration healing within a few weeks in untreated patients. Secondary syphilis is also self-limiting with clinical manifestations resolving over several weeks, although, in at least 25% of untreated people, relapses of secondary syphilis continue to occur over the first two years after infection. Tertiary syphilis, cardiovascular and neurosyphilis occur at a variable period of time after infection, from as short as one year through to forty years later. Historical studies done on untreated patients indicate that only about 30% of those with syphilis develop these late manifestations of disease. In the other 70%, immune responses manage to control the infection. Co-infection with HIV may alter the natural history of syphilis.[26]

Trichomonas vaginalis

Trichomonal infection occurs in vaginal epithelium and the lining of the urethra of men and women. It can also infect the cervix; acute trichomonal inflammation at this site causes the clinical appearance called 'strawberry cervix'. Sometimes infection spreads to associated glands (e.g. Bartholin's and Skene's). The organism has been isolated from the prostate gland and from epididymal aspirates, but its role in prostatitis and epididymitis is uncertain; if it does occur it is rare. Trichomonal infection in pregnancy has been associated with an increased risk of pre-term delivery, preterm rupture of membranes and maternal puerperal infection.[12]

Bacterial vaginosis

The natural history of bacterial vaginosis remains largely a mystery. There is an association with pelvic inflammatory disease but the significance of this is uncertain. The presence of bacterial vaginosis in pregnancy (both symptomatic and asymptomatic) may lead to low birth-weight in babies, premature delivery and post-partum endometritis but the results of studies of therapeutic interventions against bacterial vaginosis in early pregnancy have been surprisingly variable. There is no clear consensus on how best to manage bacterial vaginosis in pregnancy as yet, but some experts recommend screening and treatment of high-risk mothers (especially those with a previous history of premature delivery).[13]

HIV and STIs—co-infection and the cofactor effect

There is a complex interaction between HIV and STIs. Very early in the HIV epidemic, studies in sub-Saharan Africa showed that STIs causing ano-genital ulcerative disease (GUD) substantially increased the risk of people acquiring HIV.[32] This finding was not surprising, as any breach in genital skin or mucous membrane was likely to increase ease of entry for HIV. Subsequently, studies showed it was possible to recover HIV from genital ulcers (including herpetic ulcers) in HIV-positive people. In other words, the presence of GUD made it more likely that HIV-positive people could transmit the infection to a sexual partner. Successfully treating the STI responsible for GUD stopped the shedding of HIV and decreased the risk of HIV transmission. The synergy between HIV and genital HSV-2 infection is especially worrying because HSV-2 is the most common cause of genital ulceration around the world and both symptomatic and asymptomatic shedding of HSV-2 occur relatively frequently in patients with the infection. Studies have shown that HSV-2 sero-positivity itself is a risk factor in both the acquisition and transmission of HIV.[33] While suppressive therapy with antiviral drugs (e.g. acyclovir, valaciclovir, famciclovir) may decrease the risk of transmission of HSV-2 and so decrease the risk of transmission of HIV in patients with co-infection, routine use of these drugs in every HSV-2 sero-positive person is not a realistic option globally.

HIV shedding also substantially increases from genital sites during infection with other STIs. Gonococcal urethritis and cervicitis in men and women with HIV infection lead to substantially higher HIV viral loads in genital secretions than when people do not have gonorrhoea. Appropriate treatment for gonorrhoea causes a precipitate fall in such high HIV viral loads.[34] Any STI associated with local inflammation increases the risk of acquiring HIV for a person without infection and enhances the risk of passing on HIV from a person with the infection to sexual partners.[35] Even in bacterial vaginosis, a condition not characterised by local inflammation, but where the vaginal alkalinity is raised, there is an enhanced risk of a woman acquiring HIV infection, perhaps because the usual protective acid environment of the vagina is lost.

In addition, HIV alters the natural history of many STIs (especially syphilis and genital herpes, but also HPV) and some STIs appear to have an influence on the natural history of HIV (again syphilis and herpes). In summary, the interaction of STIs with HIV is a synergistic one which considerably enhances the transmission of HIV in populations and cumulatively increases the burden of morbidity and mortality of all STIs around the world.[36]

Therapy

HIV

The course of HIV has been drastically altered by the introduction of highly active antiretroviral therapy (HAART or combination antiretroviral therapy). This therapy usually consists of a combination of at least three drugs from two or three of the different classes of antiretroviral drugs: the nucleoside analogue reverse transcriptase inhibitors (NRTIs), the non-nucleoside reverse transcriptase inhibitors (NNRTIs) and protease inhibitors (PIs). A combination of three agents, usually two NRTIs combined with either an NNRTI or PI, is administered when the CD4 cell count falls below a certain threshold. Although the optimal time to commence therapy has not been established, Australian and international guidelines recommend that treatment should be considered when the CD4

cell count falls below 350 cells/mm3, with some suggesting intervention around 350 cells/mm3, or when the HIV viral load is above 55,000 copies/mL. Individualised decisions should take into account the patient's readiness to start therapy, the baseline CD4 cell count and HIV RNA level and the potential risks and benefits of treatment. Combination antiretroviral therapy is very potent in reducing viral load and delaying drug resistance, and has resulted in a dramatic reduction in mortality and increased life expectancy in people with HIV infection. This success has meant that HIV infection is becoming a chronic manageable disease for many people in many industrialised countries. Immune-based therapies, such as interleukin-2 and therapeutic vaccination, are also under investigation.

The aim of therapy for HIV infection is to sustain an undetectable viral load, which is achievable in approximately 50–60% of patients, and to produce immune reconstitution. Immunological benefit may be modest (CD4 cell counts frequently remain below normal levels) but may still occur in those who fail to achieve full virological suppression.

At present we do not know the long-term durability of the response in those who achieve virological control or whether drug resistance and loss of efficacy will ultimately emerge. Many of the antiretroviral drugs have significant side effects and some have complex dosing schedules, making adherence (a major determinant of the development of resistance) an issue for concern. However, fixed dose combination drugs are now available and most of the newer antiretroviral agents are administered once or twice daily, making adherence to combination regimens easier. Long-term survival of these people also has unmasked chronic drug toxicities, particularly metabolic problems such as lipodystrophy and lipoatrophy, hyperlipidaemia, insulin resistance and hepatic mitochondrial toxicity.[37]

HBV

The goal of HBV treatment is to prevent the development of hepatocellular failure and hepatocellular carcinoma (HCC). This is achieved through suppression of viral replication with resolution of hepatic inflammation, as viral eradication with loss of HBsAg is rare. Treatment is usually initiated in people with elevated HBV DNA >104-5 IU/mL and/or evidence of hepatitis with raised alanine aminotransferase (ALT) or fibrosis or inflammation on liver biopsy. Response to treatment can be assessed biochemically (ALT), virologically (HBV serology and DNA) or histologically (liver fibrosis). Currently, a number of different agents are available, including immunomodulators (interferon-a and pegylated (PEG) interferon-a) and antiviral nucleos(t)ide analogues (lamivudine, adefovir and entecavir). In HBeAg-positive people, the aim of treatment is HBeAg seroconversion which is associated with a durable suppression of HBV DNA off treatment in 50–90% of people. Treatment with interferon-a is a four to six months finite course associated with HBeAg seroconversion rates of around 20%, with higher rates (30%) using the longer acting pegylated interferon-a. As interferon is an immunomodulator, it is not associated with viral resistance. It does have significant systemic side effects, however, which often means that patients prefer the oral nucleos(t)ide analogues.

Lamivudine was the first nucleoside analogue found to effectively reduce HBV DNA, with HBeAg seroconversion rates of 17–32%, usually in those with raised ALT. However, at four years, over 60% develop viral resistance to lamivudine. Recently, entecavir was licensed for first-line HBV treatment. This agent appears to be more effective than lamivudine, with 67% undetectable HBV DNA and 21% HBeAg seroconversion at 48 weeks.[38,39] HBV resistance has been estimated to be approximately 3% by three years, but is significantly higher in those with previous lamivudine resistance. As a second-line agent, adefovir is a nucleotide analogue that effectively suppresses HBV DNA but is also associated with resistance rates of 15% at four years. There is also the risk of nephrotoxicity and hypophosphataemia, which requires monitoring. The treatment of HBeAg-negative infection is problematic and therapy is probably needed lifelong to achieve viral suppression. Newer agents such as tenofovir and telbivudine will become available in the near future. Combination therapy may offer a future strategy for some patients if studies demonstrate this to be effective.[29,37,40] Finally, development of end-stage liver disease may mandate liver transplantation, the outcomes of which have been significantly improved with the use of these antiviral therapies and HBV immunoglobulin to prevent graft re-infection.[41,42]

HCV

Similar to HBV, HCV is treated to prevent the development of cirrhosis, which is associated with hepatocellular failure and hepatocellular cancer. However, unlike HBV, the aim of treatment is viral eradication. The combination of pegylated interferon-a and ribavirin is now the standard of care for chronic HCV. Pegylated interferon is produced through the attachment of a polyethylene glycol (PEG) molecule to standard interferon. This improves the pharmacokinetic properties of interferon and allows for once-weekly administration. Not only is this new formulation more convenient to administer but response rates are enhanced. Sustained virological remission (SVR) is defined as the absence of HCV RNA from serum six months after completion of therapy and is influenced by both HCV genotype and HCV viral load. SVRs with standard interferon and ribavirin combination therapy were in the region of 35% for genotype 1 and 80% for genotype 2 and 3.

With pegylated interferon there is a significant improvement in genotype 1 response rates by approximately 10% to between 42% and 52%.[35-45] The anticipated SVR rate for genotype 2 and 3 patients

remains very high at around 80%. The duration of therapy required is also genotype dependent, with genotype 2 and 3 patients requiring only six months of therapy compared to 12 months for genotype 1 patients. Response rates in cirrhotic patients are also markedly improved with pegylated interferon therapy compared to standard interferon therapy (SVR 43% versus 33%). Once SVR has been achieved it is highly durable, with almost all patients (more than 95%) remaining clear of the virus with extended follow-up.

End-stage liver disease due to HCV is now the most common indication for liver transplantation in Australia. Graft re-infection is almost universal, although disease progression is still relatively slow in most cases.[14,46]

Until recently, access to treatment was dependent upon the demonstration of liver fibrosis on biopsy. However, with the improvement in treatment outcomes and a better understanding of the pathogenesis of HCV, treatment is now accessible for most patients with chronic HCV without biopsy. Furthermore, there has been significant progress in the development of the non-invasive assessment of liver fibrosis (eg fibroscan and fibrotest) which will become available in the future.

STIs

The general principles of therapy for STIs are three, namely:

- To cure patients of their infection, if possible; if not, to relieve symptoms and to stop progression of disease
- To render individuals non-infectious as soon as possible to prevent ongoing transmission in the community
- To treat all sexual partners

Sexual health and public health physicians favour simple, single-dose treatments, capable of being taken immediately.[47] These are obviously ideal principles rarely met in practice, but they need to be kept at the forefront of the minds of all practitioners treating patients with STIs. Except for the viral STIs, simple, single-dose treatments now exist for almost all the common uncomplicated STIs. The development of azithromycin in the mid-1990s truly revolutionised therapy for genital chlamydia infection—prior to that time, treatment for chlamydia depended on doxycycline which had to be given for a minimum of seven days. Many patients failed to complete the course, failed to be cured and so remained potentially infectious.

Antiviral therapies are readily available in Australasia for genital herpes and, although not curative, they will relieve the symptoms of troublesome outbreaks (especially primary attacks) and substantially reduce viral shedding, thus reducing the risk of further transmission. Ongoing clinical trials are currently assessing the public health effectiveness and practical utility of this chemotherapeutic intervention in high-risk groups (e.g. people with HIV infection and MSM with herpes).[48]

There is no antiviral therapy for HPV infection and none in development, clearance of clinical manifestations of this virus being mediated by the immune response in immunocompetent people.

Public health objectives inevitably link closely with treatment goals in STI management. Where effective treatment is available, the aim is to treat all sexual partners of patients diagnosed with an STI and, where there is no effective treatment, the lesser aim is to provide information, education and counselling for sexual partners. Contact tracing (partner notification) meets these aims. Because of the complex and synergistic interactions between STIs and HIV, especially in communities at high risk for both types of infection, clinicians must make a new commitment to contact tracing. ASHM's manual on contact tracing discusses this important aspect of STI management and is a great resource for busy practitioners.[49]

Prevention

There is an effective and safe vaccine for HBV which is provided universally for babies and adolescents in Australia through the National Immunisation Program. It is important to offer vaccination to high-risk patients who have not been previously immunised. Unfortunately, technical difficulties associated with vaccine development suggest that effective vaccines for HIV and HCV are at least five to 10 years away.

There is also an effective and safe vaccine for hepatitis A virus. To prevent infection through sexual transmission of this virus, clinicians should encourage vaccination in all individuals who engage in sexual activities where any degree of faecal contamination of fingers or mouth could occur. This includes all MSM.

There are now two effective and safe vaccines against HPV licensed for use in Australia. There are several differences between them. Gardasil provides protection against HPV types 6, 11, 16 and 18 and is recommended for use in young women aged between nine and 26. There is a funded vaccination program for school girls and a two year catch up program for young women. Based on immunogenicity studies, Gardasil is also licensed in Australia for use in boys aged between nine and 15, but there are no data as yet on its effectiveness in preventing infection and disease in males. Cervarix, the other HPV vaccine is designed to protect against infection with HPV types 16 and 18, but also has activity against types 31 and 45. It is licensed for women and girls aged between 10 and 45 in Australia. Health practitioners should be offering HPV vaccine to all young women, preferably before they commence sexual activity. If Gardasil is used, it should protect women from the common genital wart viruses and the most common high-risk types of HPV. It should not be a substitute for regular

Papanicolaou smears as other high-risk HPV types exist and circulate in the community.

Prevention strategies for the blood-borne viruses based on public health behaviour modification and harm minimisation approaches have been effective in Australia and elsewhere and remain the foundation of prevention for individuals at risk of these viral infections. All people should be given clear messages about the risks of STIs, the asymptomatic nature of most early STIs in men and women, the enhancing effects of STIs on the risk of acquiring HIV, the need for regular sexual health check-ups for those with multiple sexual partners or frequent changes of partner, and the reliability of male (or if preferred, female) condoms in substantially reducing the risk of transmitting and acquiring almost all the STIs.

References

1 Danta M, Brown D, Bhagani S, et al. Recent epidemic of acute hepatitis C virus in HIV-positive men who have sex with men linked to high-risk sexual behaviours. AIDS 2007;21(8):983–91.

2 Stewart G, (ed). Managing HIV. North Sydney: Australasian Medical Publishing Company Ltd; 1997.

3 Lee WM. Hepatitis B infection. N Engl J Med 1997;337:1733–45.

4 Schacter J. Biology of Chlamydia trachomatis. In: Holmes KK, Sparling PF. Mardh P-A, Lemon SM, Stamm WE, Piot P, Wasserheit JN editors. Sexually Transmitted Diseases. 3rd ed. New York: McGraw-Hill; 1999: 391–406.

5 Corey L, Wald A. Genital herpes. In Holmes KK, Sparling PF. Mardh P-A, Lemon SM, Stamm WE, Piot P, Wasserheit JN editors. Sexually Transmitted Diseases. 3rd ed. New York: McGraw-Hill, 1999: 285–312.

6 Koutsky LA, Kiviar NB. Genital human papillomaviruses. In Holmes KK, Sparling PF. Mardh P-A, Lemon SM, Stamm WE, Piot P, Wasserheit JN, editors. Sexually Transmitted Diseases. 3rd ed. New York: McGraw-Hill, 1999: 347–60.

7 Manhart LE, Holmes KK, Koutsky LA, Wood TR, Kenney DL, Feng Q, Kiviat NB. Human papillomavirus infection among sexually active young women in the United States: implications for developing a vaccination strategy. Sex Transm Dis 2006; 33: 502–8.

8 Dunne EF, Unger ER, Sternberg M, McQuillan G, Swan DC, Patel SS et al. Prevalence of HPV Infection amongst females in the United States. J Am Med Assoc 2007; 297: 813–9.

9 Bauer HM, Ault K. Human papillomavirus: current prevalence and future protection. [editorial]. Sex Transm Dis 2006; 33: 509–11.

10 Sparling FP. Biology of Neisseria gonorrhoeae. In Holmes KK, Sparling PF. Mardh P-A, Lemon SM, Stamm WE, Piot P, Wasserheit JN editors. Sexually Transmitted Diseases. 3rd ed. New York: McGraw-Hill; 1999: 433–50.

11 Stamm LV. Biology of Treponema pallidum. In Holmes KK, Sparling PF. Mardh P-A, Lemon SM, Stamm WE, Piot P, Wasserheit JN editors. Sexually Transmitted Diseases. 3rd ed. New York: McGraw-Hill; 1999: 467–72.

12 Krieger JN, Alderete JF. Trichomonas vaginalis and trichomoniasis. In Holmes KK, Sparling PF. Mardh P-A, Lemon SM, Stamm WE, Piot P, Wasserheit JN editors. Sexually Transmitted Diseases. 3rd ed. New York: McGraw-Hill; 1999: 587–604.

13 O'Brien RF. Bacterial vaginosis: many questions–any answers? Curr Opin Pediatr 2005; 17: 473–8.

14 The National Institutes of Health. Consensus Development Conference: Management of hepatitis C. Hepatology (supplement 1) 1997.

15 Gibb DM, Tess BH. Interventions to reduce mother to child transmission of HIV infection: new developments and current controversies. AIDS 1999;13(suppl A):S93–S102.

16 National Centre in HIV Epidemiology and Clinical Research. HIV/AIDS, viral hepatitis and sexually transmissible infections in Australia, Australian HIV Surveillance Report. 2006; 22: 4.

17 O'Sullivan BG, Gidding HF, Law M, Kaldor JM, Gilbert GL, Dore GJ. Estimates of chronic hepatitis B virus infection in Australia. Australian & New Zealand Journal of Public Health 2000; 28:212–6.

18 Law MG, Dore GJ, Bath N, Thompson S, Crofts N, Dolan K, et al. Modelling hepatitis C virus incidence, prevalence and long-term sequelae in Australia, 2001. Int J Epidemiol 2003; 32:717–724.

19 Serpaggi J, Chaix M-L, Batisse D, Dupont C, Vallet-Pichard A, Fontaine H et al. Sexually transmitted acute infection with a clustered genotype 4 hepatitis C virus in HIV-1-infected men and inefficacy of early antiviral therapy. AIDS 2006; 20: 233–40.

20 MacDonald M, Crofts N, Kaldor J. Transmission of hepatitis C virus: rates, routes, and cofactors. Epidemiol Rev 1996;18:137–46.

21 Crofts N, Jolley D, Kaldor J, van Beek I, Wodak A. Epidemiology of hepatitis C virus infection among injecting drug users in Australia. J Epidemiol Community Health 1997;51:692–7.

22 Stamm WE. Chlamydia trachomatis infections in the adult. In Holmes KK, Sparling PF. Mardh P-A, Lemon SM, Stamm WE, Piot P, Wasserheit JN editors. Sexually Transmitted Diseases. 3rd ed. New York:McGraw-Hill; 1999: 407–22.

23 King A, Nicol C, Rodin P. Herpes Genitalis and Hepatitis B Infections. In Venereal Diseases. 4th ed. London: Balliere Tindall 1980: 325–6.

24 Corey L, Adams HG, Brown ZA, Holmes KK. Genital herpes simplex virus infections: clinical manifestations, course, and complications. Ann Intern Med 1983; 98: 958–72.

25 Kim HN, Meier A, Huang M-L, Kuntz S, Selke S, Celum C et al. Oral herpes simplex virus type 2 reactivation in HIV-positive and –negative men. J Infect Dis 2006; 194: 420–7.

26 Sparling PF. Natural history of syphilis. In Holmes KK, Sparling PF. Mardh P-A, Lemon SM, Stamm WE, Piot P, Wasserheit JN editors. Sexually Transmitted Diseases. 3rd ed. New York:McGraw-Hill; 1999: 473–8.

27 Chakraborty R and Rowland-Jones S. The pathogenesis of HIV disease. J HIV Ther 1999;4:2–8.

28 Dore GJ, Freemen AJ, Law M, Kaldor JM Is severe liver disease a common outcome for people with chronic hepatitis C? Journal of Gastroenterology and Hepatology 2002;17, 423–30.

29 Dieterich D. Hepatitis C virus and human immmunodeficiency virus: clinical issues in co-infection. Am J Med 1999;107:79S–84S.

30 Simms I, Ward H, Martin I, Sarah A, Ison C. Lymphogranuloma venereum in Australia. Sex Health 2006;3: 131–3.

31 Hook EW III, Hunter Handsfield H. Gonococcal infections in the adult. In Holmes KK, Sparling PF. Mardh P-A, Lemon SM, Stamm WE, Piot P, Wasserheit JN, editors. Sexually Transmitted Diseases. 3rd ed. New York: McGraw-Hill; 1999: 451–466.

32 Cameron DW, Simonsen JN, D'Costa LJ, Ronald AR, Maitha GM, Gakinya MN et al. Female to male transmission of human immunodeficiency virus type 1: risk factors for seroconversion in men. Lancet 1989;2(8660);403–7.

33 Wald A, Link K. Risk of human immunodeficiency virus infection in herpes simplex virus type 2-seropositive persons: a meta-analysis. J Infect Dis 2002; 185:45–52.

34 Cohen MS, Hoffman IF, Royce RA, Kazembe P, Dyer JR, Costello DC et al. Reduction in concentration of HIV-1 in semen after treatment of urethritis: implications for prevention of sexual transmission of HIV-1. Lancet 1997; 349: 1868–73.

35 Laga M, Manoka A, Kivuvu M, Malele B, Tuliza M, Nizilla N et al. Non-ulcerative sexually transmitted diseases as risk factors for HIV-1 transmission in women: results from a cohort study. AIDS 1993; 7: 95–102.

36 Robinson NJ, Mulder DW, Auvert B, Hayes RJ. Proportion of HIV infections attributable to other sexually transmitted diseases in a rural Ugandan population: simulation model estimates. Intl J Epidemiol 1997; 26: 180–189.

37 International AIDS Society-USA Panel. Antiretroviral therapy in adults: Updated recommendations of the International AIDS Society-USA Panel. J Am Med Assoc 2000;283:381–90.

38 Chang TT, Gish RG, de Man R, Gadano A, Sollano J, Chao YC, et al for the BEHoLD AI463022 Study Group. A comparison of entecavir and lamivudine for HBeAg-positive chronic hepatitis B. N Engl J Med 2006;354(10):1001–10.

39 Lai CL, Shouval D, Lok AS, Chang TT, Cheinquer H, Goodman Z, et al for the BEHoLD AI463027 Study Group. Entecavir versus lamivudine for patients with HBeAg-negative chronic hepatitis B. N Engl J Med 2006;354(10):1011–20.

40 Hoofnagle JH and Di Bisceglie AM. The treatment of chronic viral hepatitis. N Engl J Med 1997;336:347–356.

41 Torresi J and Locarnini S. Antiviral chemotherapy for the treatment of hepatitis B virus infection. Gastroenterol 2000;118 (suppl):S83–S103.

42 Shaw T and Locarnini S. Combination chemotherapy for hepatitis B virus: the final solution? Hepatology 2000;32:430–2.

43 Manns MP, McHutchison JG, Gordon SC, Rustgi VK, Shiffman M, Reindollar R, et al. Peginterferon alfa-2b plus ribavirin compared with interferon alfa-2b plus ribavirin for initial treatment of chronic hepatitis C: a randomized trial. Lancet 2001, 358: 958–65

44 Fried MW, Shiffman ML, Reddy KR, Smith C, Marinos G, Goncales FL, et al. Peginterferon alfa-2a plus ribavirin for chronic hepatitis C virus infection. N Engl J Med 2002, 347: 975–82

45 Hadziyannis SJ, Sette H, Morgan TR, Balan V, Diago M, Marcellin P, et al for the PEGASYS International Study Group. Peginterferon-alfa 2a and ribavirin combination therapy in chronic hepatitis C. A randomized study of treatment duration and ribavirin dose. Annals of Internal Medicine, 2004;140: 346–55

46 Pianko S and McHutchison JG. Treatment of hepatitis C with interferon and ribavirin. J Gastroenterol Hepatol 2000;15:581–6.

47 Hunter Handsfield H. Principles of treatment of sexually transmitted diseases. In Holmes KK, Sparling PF. Mardh P-A, Lemon SM, Stamm WE, Piot P, Wasserheit JN editors. Sexually Transmitted Diseases. 3rd ed. New York:McGraw-Hill; 1999: 711–21.

48 Russell DB. Herpes and HIV infection-has the time come to act? Sex Health 2006; 3: 67–71.

49 Australasian Society for HIV Medicine (ASHM). Australasian contact tracing manual. 3rd edn. Sydney: ASHM; 2003.

Blood-borne viruses and STIs: might this patient be positive? Epidemiology and transmission

2

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Introduction

Early diagnosis is important for all treatable conditions. Early identification of sexually transmitted infections (STIs) and blood-borne viral infections (BBVs) in particular can facilitate both treatment and prevention. Therapy for human immunodeficiency virus (HIV) infection can postpone immune damage and thereby prevent development of opportunistic infections and malignancies, treatment of treatable STIs prevents sequelae and reduces transmission, while improved therapies for hepatitis B virus (HBV) and hepatitis C virus (HCV) can clear the virus and improve clinical outcomes in some individuals. In addition to providing the benefits of treatment, early diagnosis, accompanied by relevant education, can help to reduce the rate of ongoing transmission of STIs, HIV, HBV and HCV.

Diagnosis of each of these infections generally requires simple tests. However, indications for testing are frequently overlooked and opportunities for early diagnosis are missed. The decision to test should be based on a detailed history of risk behaviour as well as a physical examination of the patient. It should always be borne in mind that people may prefer to conceal a history of risk taking especially when it concerns sex, drugs or both. Consequently, a low threshold for testing should be maintained. Individuals infected with a blood-borne virus who do not report high-risk behaviours are more likely to present with advanced disease. Late presentation has been associated with poor clinical outcomes, particularly in relation to HBV and HIV.

An understanding of the epidemiology and transmission of both blood-borne viruses and other STIs, along with a detailed behavioural history, will help make an accurate assessment of the likely risk of infection, and guide appropriate testing.

Blood-borne viruses (HIV/HBV/HCV): prevalence and risk factors for transmission

Although HIV, HBV and HCV are all blood-borne viruses, the efficiency of transmission in different settings varies enormously (Table 2.1). Transmission will depend on many factors, including the infectivity of the source (e.g. the viral load of HIV, HBV or HCV) and the type of exposure.

The clearest example of the differences in transmissibility of these three viruses is sexual contact. Unprotected anal or vaginal sex with a person who has the infection carries a high-risk of transmission for both HIV and HBV but a very low risk of transmission for HCV (Table 2.1).[1]

Key points

- HIV and HBV are transmitted through sexual contact, as well as blood-to-blood contact and from mother to child. HCV is transmitted by blood-to-blood contact.
- STIs are transmitted through various forms of sexual contact including all oral sexual activities.
- In Australia, the prevalence of HIV, HBV and HCV is high among particular groups. However, risk exposure, rather than group membership, should be the basis for risk assessment.
- In Australia and New Zealand, the prevalence of genital chlamydial infection is high in young sexually active people. Most early infection is asymptomatic so screening for chlamydia in primary care practice is vital.
- The decision to test should be based on an assessment of risk as well as physical examination. Some people may prefer not to reveal a history of risk behaviour, and a low threshold for testing should be maintained.
- People with a blood-borne virus infection who do not report high-risk behaviours are more likely to present late and to suffer resultant poor clinical outcomes.

TABLE 2.1 Risk of HIV, HBV and HCV transmission (from a known positive source)

	HIV	HBV[a]	HCV[b]
Sexual contact			
Unprotected anal (receptive)	very high	very high	very low[c]
Unprotected anal (insertive)	high	very high	very low[c]
Unprotected vaginal	high[d]	very high	very low[c]
Unprotected oral (cunnilingus and fellatio, receptive and insertive)	very low	low-moderate	negligible
Mother to child (perinatal)			
No intervention	20-45%	30-90%	5%[e]
With intervention	<5%[f]	<5%[g]	NA[h]
Occupational exposure (needle-stick)	0.3%	20-40%	2-10%
Sharing injecting equipment among IDUs	very high	very high	extremely high[i]
Unsterile tattooing and piercing	high	very high	very high
Unsterile medical and other procedures	high	high	high

a Refers to chronic hepatitis B (HBsAg+), with higher risk where source is HBeAg+ and/or HBV DNA+.
b Refers to chronic hepatitis C (HCV RNA+).
c Higher risk may be associated with certain practices or circumstances where there is the possibility of blood-to-blood contact (e.g. traumatic sexual practices, sex during menstruation) or high HCV viral load (e.g. HIV co-infection).
d Some evidence of higher risk for male-to-female than female-to-male transmission.
e Higher risk (15–20%) in presence of HIV/HCV co-infection, related to higher HCV viral load.
f Proven interventions include antiretroviral therapy, caesarean section and avoidance of breastfeeding.
g Intervention includes HBV immunoglobulin and vaccination.
h There is no currently proven intervention for perinatal HCV transmission.
i Some evidence of HCV transmission when sharing injecting equipment other than needles (e.g. spoons, tourniquets).

The explanation for this disparity is the absence (or extremely low concentration) of HCV found in semen or vaginal secretions, in contrast to the high levels of both HIV and HBV in these bodily fluids.[2]

There are also differences in perinatal transmissibility of HIV, HCV and HBV. HCV has a relatively low efficiency of transmission in the perinatal setting; only 5% of infants born to women with HCV will become infected, with factors such as maternal viral load and duration of labour affecting risk of transmission. Without intervention, mother-to-child transmission of HIV and HBV is common. In the absence of prophylaxis, rates of mother-to-child transmission of hepatitis B are very high, particularly from HBeAg-positive mothers with high viral load (more than 85% transmission). Thus, routine HBsAg testing is recommended in all pregnant women, and both passive (hepatitis B immunoglobulin) and active (hepatitis B vaccination) is given to the baby within 12 to 24 hours of birth.

This strategy is thought to be over 95% effective in preventing neonatal infection. The rate of HIV mother-to-child transmission without intervention is 25%. However, proven interventions can reduce the risk of perinatal transmission of HIV to 1–2%[3] and HBV to less than 5%.[3-5]

In contrast to the lower efficiency of HCV transmission through sexual contact, HCV is more efficiently transmitted than HIV or HBV through blood-to-blood contact where injecting equipment (including swabs, spoons, water, tourniquets, needles and syringes) is shared.[6]

The likelihood of transmission after a specific exposure is also related to the risk of infection in the source. Although transmission of blood-borne viruses is associated with certain risk behaviours, prevalence rates are higher in specific groups in Australia: HIV in men who have sex with men (MSM); HBV and HCV among injecting drug users; HBV in Indigenous Australians and Asian-born populations; and all three viruses in people with haemophilia treated with clotting factor replacement therapy prior to 1990 (Table 2.2). The low prevalence of HIV in people other than homosexual men in Australia accounts for the relatively low risk of HIV infection after unprotected heterosexual exposure and sexual assault.

The prevalence of HCV is very high among persons who have ever injected drugs, and use of injecting equipment that has been contaminated with HCV-infected blood carries a very high risk of transmission. Consequently, infection is common after even a small number of exposures, such as the occasional sharing of injecting equipment.

The global HIV epidemic and its implications for Australia

Outside Australia, the patterns of HIV transmission are extraordinarily diverse. Many countries in Europe and North America are seeing extensions of the HIV epidemic into ethnic and social minorities, immigrant groups and the socially disadvantaged. HIV infection levels in injecting drug users are often very high. In much of sub-Saharan Africa, HIV is extremely prevalent, reaching 30–40% in young adults in some countries. High rates of genital ulceration and poor access to medical services and preventative education account, in part, for high-prevalence rates. In some communities in Australia (particularly remote Aboriginal communities) and in some of our nearest neighbours (including Papua New Guinea), the same combination of factors exists (poverty, marginalised populations, high rates of STIs) that have allowed such explosive epidemics in other countries.

In Asia, four countries (Thailand, Myanmar, Indonesia and Cambodia) have adult prevalence rates over 1% and within these countries there are certain populations, particularly injecting drug users and sex workers, with much higher HIV prevalence. In addition, expanding HIV epidemics in India and China are of increasing concern. Travellers to regions of high-prevalence of HBV or HIV should be informed of the risks of acquiring these infections through sexual or accidental exposure.

The global pattern of HIV infection is beginning to be reflected in the pattern of heterosexual HIV transmission in Australia. Immigrants from high-prevalence countries and their partners feature prominently among those newly diagnosed, as do visitors to high-prevalence regions. During 2001 to 2005, 57% of people who acquired HIV through heterosexual contact were from a high-prevalence country or had reported heterosexual contact with a partner from a high-prevalence country.[18]

CASE STUDY 1

Clinical assessment: cough and fever may indicate a HIV-related illness

Cough and fever

Jessica is a 37-year-old secretary who presents to her GP with a recent onset of cough and fever. Brief chest examination is unremarkable and she is prescribed five days of amoxycillin. She re-presents three weeks later with marked shortness of breath, weakness and fatigue. Chest X-ray shows signs consistent with a diffuse pneumonitis and she is admitted to hospital. Jessica's HIV antibody test is positive (ELISA and Western Blot) and she has a CD4 cell count of 25 cells/µl and a HIV viral load of 500 000 copies/mL. Upon presumptive treatment for *Pneumocystis jiroveci* pneumonia (PCP), the cough resolves and chest X-ray normalises. Jessica is commenced on triple combination antiretroviral therapy that she tolerates well. One year after presentation, she remains well on antiretroviral therapy and PCP prophylaxis.

CASE STUDY 2

Risk assessment: non-disclosure of high-risk sexual activity

Sexual risk activity

A 29-year-old garage mechanic visits his GP complaining of a purulent urethral discharge. He seems open, personable and readily admits to having many sexual partners in the past—mostly casual 'one-night stands'—with whom he usually uses condoms. However, at the time of presentation, he has been with his current girlfriend for over a year and the couple no longer use condoms. The man reports that while his girlfriend was away last weekend, he went to a nightclub and met a woman with whom he had sex. He was very drunk and is unsure whether a condom was used. He tested negative to an HIV antibody test two years ago in another city. He denies any same-sex partners or injecting drug use.

The GP conducts a screening for STIs, including urethral swabs, and suggests blood tests for HIV, syphilis and HBV. The man seems a bit resistant to the idea at first, but then agrees. He accepts a script for ciprofloxacin and azithromycin and agrees to return in one week for his results.

The man's urethral swab grows *Neisseria gonorrhoeae,* as expected, but his HIV antibody test is also positive. All other tests are negative. The young man is shocked at the news. He admits that he did not tell the full truth on his previous visit; in fact, most of his casual partners have been male. He reports both insertive and receptive anal sex without condoms and says he is most likely to seek casual sex when he has been drinking heavily.

TABLE 2.2 Seroprevalence estimates for HIV, HBV and HCV in Australia[a]

	HIV	HBV[b]	HCV
Injecting drug users	1-2%[c]	40-50%[d]	50-60%[c]
Sexual orientation			
Homosexual/bisexual men	5-10%[e]	40-50%[d]	5-7%[f]
Homosexual/bisexual women	<1%	2-5%[f]	2-5%[f]
Heterosexual men	<1%	1-2%	1-2%
Heterosexual women	<1%	1-2%	1%
Ethnicity			
Indigenous Australian	<1%[g]	20-30%[h]	2-5%[i]
Asian	<1%	20-30%[h]	2-5%[j]
Other	<1%	1-2%	1-2%
Health care workers[k]	<1%	1-2%	1-2%
Recipients of blood products[l]			
People with clotting disorders[m]	20-30%	50-60%[g]	0-80%
Other	1%	1-2%	2-5%

a) Some of these estimates are based on limited data, and should be considered as guides to levels of infection rather than true prevalence values.
b) Based on prevalence of anti-HBc, indicating previous exposure. Approximately 95% of people exposed to HBV as adolescents and adults clear HBV infection (HBsAg- and anti-HBs+) and are immune to re-infection.
c) Based on HCV antibody prevalance from the National Needle and Syringe Program Survey Report 2002-2006.[7]
d) Prevalence of chronic hepatitis B (HBsAg+) estimated to be 2–3%.[8,9]
e) Based on self-reported HIV status among gay men at gay community fair days in Australian capitals.[10]
f) Higher prevalence estimates than heterosexual groups due to higher prevalence of injecting drug use.[11,12]
g) Despite higher rates of other STIs, HIV prevalence is similar among indigenous and non-indigenous Australians.[13]
h) The majority of transmission occurs during the perinatal period or early childhood, therefore the estimate for chronic hepatitis B (5–10%)[14] is higher than for other high-risk groups (2–3% for IDU, homosexual men).
i) Higher estimate due to increased prevalence of injecting drug use and incarceration.[15]
j) Higher estimate due to probable increased exposure through non-sterile medical, dental and other skin penetration procedures in non-Australian born Asians. Higher estimated prevalence in people born in other selected, high prevalence countries (e.g. Italy, Egypt).
k) Although cases of occupational transmission of blood-borne viruses have been reported, including five cases of HIV[16], prevalence of HIV, HBV and HCV is estimated to be similar to the general population.
l) In Australia, screening for HBV was introduced in the early 1970s, HIV in 1985, and HCV in 1990.
m) Includes people with haemophilia A, haemophilia B, and von Willebrand's disease. In general, prevalence rates increase with severity of clotting disorder and age (due to introduction of screening).[17]

Other STIs: prevalence and transmission

Genital chlamydial infection

The rate of chlamydia infections has been steadily rising over the last decade. Increased testing and the availability of nucleic acid amplification tests (NAATs) such as polymerase chain reaction (PCR), that are easier to perform, and have greater sensitivity than the culture of the organism, could account for some of the increase, but it is not thought to be the sole reason. We are not winning the battle against genital chlamydial infection. The common form of genital chlamydial infection is due to *Chlamydia trachomatis* serovars D to K causing urethral, cervical and rectal infections. The Australia-wide notification rate of infections per 100,000 population has doubled in five years from 109 in 2001 to 217 in 2005. In 2006 in Victoria alone there were 10,000 infections notified. This is a disease of younger people aged 15 to 39 years (more sexual activity, more partners), but is most commonly diagnosed in the 20 to 29 year groups—females more than males.[19,20]

Lymphogranuloma venereum (LGV) is caused by *Chlamydia trachomatis* serovars L1, L2 and L3. It is very uncommon in Australia, however, in recent years, there has been a small cluster of cases in very sexually active men who have sex with men (MSM). It is prudent, therefore, to consider the possibility of LGV in an MSM patient who has symptomatic chlamydial proctitis or where *C. trachomatis* is detected by NAAT on routine rectal screening in an MSM (see Chapter 12: Primary Care Management of STIs). Clinicians will need to discuss with their local laboratory the issue of specific testing for LGV, should the need arise.

Genital herpes

Genital herpes is not a notifiable disease. The general population prevalence in Australasia is 12–20%. It is higher in MSM and sex workers. The majority of people with genital herpes are unaware that they have the infection. They have either sub-clinical infection, i.e. they have mild recurring symptoms that they do not recognise as herpes, or they have truly asymptomatic infection.

HSV-2 normally has its latent phase in the sacral ganglia. The cause of genital herpetic infection has changed, with approximately 50% of genital herpes diagnosed today caused by HSV-1 (the virus commonly associated with oral herpes which normally has its latent stage in the trigeminal ganglia).[21,22]

Genital warts and human papillomavirus (HPV)

Human papillomavirus (HPV) infection is so common in the community that acquiring one of the many genital types of HPV is virtually synonymous with having sex. The point prevalence in the 15 to 25-year-old group is approximately 25% for genital HPV. There are many types of HPV with approximately 40 types site-specific to the genitals. The HPV types 6 and 11 are the causative viruses for the majority (90%) of genital warts. Ten to 15% of adults will get genital warts in their lifetime, causing much anxiety and stress. HPV can be carried asymptomatically, an important fact to explain to patients when they are concerned where their infection might have come from. There are approximately 15 types of HPV which are associated with dysplastic changes in the genital region, especially at the transformation zones of the cervix and the anal canal. Types 16 and 18 cause 70–80% of cervical cancer in Australia and are implicated in the development of anal squamous carcinoma as well. In Australia a vaccine for types 6, 11, 16 and 18 is now on the immunisation schedule for young women. It is also licensed on the basis of immunogenicity for young boys aged nine to 15, but is not available free on the immunisation schedule for men as there are not yet any clinical trial data on its efficacy in preventing infection or disease in men. This new vaccine should reduce the rate of infection with these four HPV types in years to come, and reduce the incidence of cervical cancer. Vaccinated women should continue screening for cervical cancer

CASE STUDY 3

Sexual health context: an STI indicates the need for HIV testing

STIs

A young, openly gay man in a regional city presents to a GP with a four-day history of a very painful anus, which he assumes to be haemorrhoids, as he has suffered them previously. He says he has never had anal sex. On examination, there are extensive perianal ulcers and the GP takes swabs for herpes, gonorrhoea and chlamydia. The young man is appalled that he could have an STI, and the GP encourages him to talk about his sexual history. The patient states that he only ever has safe sex and has never had an STI. He reports a negative HIV antibody test about two years ago and he has been vaccinated successfully against HBV. He averages about three different sexual partners a month at the local beat and he has never injected. Upon further questioning about his sexual behaviour, the patient reports that he and his most recent partner had done 'just about everything two guys can do, short of fucking'. When questioned, he agrees that there had been some oral-anal contact 'both ways'. The GP suggests pharyngeal and anal swabs and raises the issue of HIV testing. The patient readily agrees. The anal swab returns positive for Herpes Simplex Virus (HSV) type 1 but cultures for gonorrhoea and the HIV antibody test are negative.

CASE STUDY 4

HCV prevalence and transmission: past injecting drug use may have caused infection

Past injecting drug use

Angeli is a 29-year-old solicitor who is four-months pregnant. Upon routine testing, her GP discovers that Angeli has abnormal liver function tests (ALT 68 IU). She is otherwise in perfect health. She presents with her husband and reports no risk factors for HBV or HCV infection and is unvaccinated for HBV. She describes herself as 'healthy and clean-living'. Upon investigation, it is discovered that Angeli is anti-HBc-negative but HCV antibody positive. When seen on her own, Angeli reports that she injected amphetamines on 'one or two occasions' at age 19, while a university student. Although she does not recall sharing injecting equipment, she admits that the memories are very hazy as she had been drinking on those occasions and had allowed a friend to inject her. She has told no one about this past drug use, not even her husband, whom she fears will not understand. She is deeply upset that this brief experimentation has come back to haunt her current life and health, and she has fears that it could affect her husband's and baby's health. She initially requires HCV RNA PCR testing to confirm that her abnormal liver function tests do represent active hepatitis C infection. She is much relieved to hear, however, that even if her HCV RNA test is positive the risk of transmission to her baby is quite low and that transmission to her partner very unlikely.

with regular Papanicolaou smears, as the vaccine does not cover all cancer associated types of HPV. It is not currently recommended for men in the prevention of anal cancer. Further studies using the vaccine in MSM are awaited.[21,22]

Gonorrhoea

Gonorrhoea has been slowly increasing over the last decade. It is mainly seen in MSM, Indigenous people, overseas people particularly from South East Asia, and in recently returned travellers who have had sex (either heterosexual or homosexual) with a local person in a country where gonorrhoea is endemic. The overall rate of infection in Australia in 2006 was 42 per 100,000, representing a rise of 27% for both men and women between 2002 and 2006. The rate of gonorrhea in men has been consistently a little more than double that in women over the past five years, a reflection of the substantial contribution MSM make to gonococcal infection rates in Australia.[20] The majority of gonorrhoea diagnosed is urethral and rectal.[19,20]

Syphilis

Syphilis is another infection that has been steadily on the rise. Syphilis has for a long time been prevalent in Australia's Indigenous population. It is now often seen in MSM as well and, in recent years, the rates of syphilis in Victoria and Queensland have risen, entirely due to homosexually acquired infection, while in NSW syphilis rates have actually slightly declined. In the Northern Territory, after a welcome reduction in the syphilis rate since the beginning of the new century (while rates in the non-Indigenous population have continued to decline in the past three years), there has been a rise in infectious syphilis in the Northern Territory's Indigenous population.[20]

Due to the chronicity of untreated infection and the often long latent periods characteristic of syphilis, this is an infection which can be diagnosed in any age. Indeed, it remains in the differential diagnosis for dementia.[19,20]

Trichomoniasis

Trichomoniasis is not a notifiable infection in any state in Australia. Infection due to *Trichomonas vaginalis* is most prevalent in the Indigenous population or in returned travellers from higher prevalence countries. Infection is often asymptomatic in both sexes. Symptomatic infection may occur in women but is very rare in men. It is still essential to treat both partners when a woman is diagnosed with trichomonal infection.[19-21,23]

Risk assessment: Might this patient be positive for an STI or a blood-borne virus?

Risk assessment is based on a thorough history of the patient's sexual practices, drug use, tattoos and piercings, medical history relating to vaccination, use of blood products in Australia (prior to 1985 for HIV and 1990 for HCV) and possible medical exposure overseas. The history should be taken in a manner that enables the patient to discuss recent and remote risks and exposures (see Chapter 3).

While taking a complete history may not be an option at every general practice consultation, it may be possible to accrue this information over a period of time. Alternatively, the patient could be offered a follow-up appointment to allow risk assessment to be completed.

When faced with a person who is identifiably at high risk, e.g. an openly gay man or an opiate-dependent drug user, the possibility of infection with a blood-borne virus is a possibility. For sexually active homosexual men, national guidelines recommend at least annual screening for gonorrhoea and chlamydia, syphilis and HIV, and screening and vaccination for hepatitis A and B.[24] However, as transmission is linked to risk behaviours rather than group membership, considering the possibility of infection with STIs or blood-borne viruses only in persons from 'high-risk groups' is likely to lead to undetected infections.

Many people who are from 'high-risk groups' remain at very low risk because of the nature of their sexual or drug-use practices, while those from perceived 'low-risk groups' may undertake high-risk behaviours.

A person may not provide truthful or accurate information regarding risk behaviours for several reasons including:

- Experience of discrimination within the health system and from health care workers on the basis of drug use or sexual behaviour
- Non-acceptance of his or her own behaviours and an inability to discuss these behaviours with any other person, even a health professional
- The desire to disassociate from past risk behaviours
- Cultural shame and language barriers
- Fear that confidentiality will be breached

A minority of people may not report high-risk behaviour at all. They may simply have had an unprotected heterosexual encounter (which has transmitted HIV) with someone whose own previous high-risk behaviour is unrecognised. Many HIV-infected women fall into this category. Making the diagnosis in these situations is dependent on retaining an open mind about the possibility of infection.

Risk assessment for STIs

In assessing any patient, it is important to consider whether they could have an STI and to maintain a low threshold for screening for STIs. The reasons are as follows:

- STIs are often asymptomatic in both sexes
- Infections with other STIs increase the risk of acquisition and transmission of HIV. This is particularly so for ano-genital ulcer disease (GUD)
- Unlike HIV, STIs can be transmitted through means other than unprotected anal and vaginal sex, e.g. by oral sexual activities and by genital skin to skin contact

- A person can contract more than one STI at a time. If patients are diagnosed with one STI it is prudent to screen them for others
- STIs can be debilitating for a patient's health as well as causing psycho-social and relationship issues. Some STIs and the complications they manifest, such as chronic pain syndromes, abscesses, infertility or life threatening problems such as ectopic pregnancy, have broad ranging sequelae
- Diagnosing an unexpected STI in an index patient indirectly has potential health benefits for their sexual partner(s)

It is helpful to know about the epidemiology of particular STIs, as the risk of some STIs is more common amongst some groups than others. It is beneficial to the patient and the public purse to know when to investigate and when not to carry out unnecessary tests just for the sake of completeness. This section explores some of the common STIs that patients should be tested for if the person is symptomatic.[21-23,25] How to manage the symptomatic patient is discussed in Chapter 12.

A history from the patient should be thorough (Table 2.3). Some of these issues will need to be discussed each time the patient comes to see you; others will be part of the past history and will need to be followed up as information is collected during subsequent visits.

TABLE 2.3 Issues raised in a consultation that may cause a clinician to think further investigation for STIs is warranted

• Diagnosis of another STI: HIV, Hepatitis B, chlamydia, gonorrhoea, HSV, trichomoniasis, syphilis
• Sexual history: multiple partners, unprotected sexual intercourse whether anal, oral or vaginal, recent change of partner (in the last year), high-risk partners (IDU; from a high prevalence country for HIV and other STIs; bisexual), multiple partners
• Sex workers: particularly working in an environment where regular medical check ups are not encouraged or regulated, e.g. street sex workers will be at much higher risk of STIs
• Victims of sexual assault: although in Australia the risk of HIV is low in this situation, for other STIs (especially chlamydia) the risk is higher. If a patient is seen directly after a sexual assault, think of prophylactic azithromycin and emergency contraception if a female has been vaginally assaulted by a male. There may be some instances where post-exposure prophylaxis against HIV is recommended, e.g. a male rape of a male
• Pregnancy: especially unwanted or in an adolescent—by definition they have had unprotected sex
• Infertility: previous pelvic inflammatory disease is always a possible cause of infertility; often too late by this stage but check especially for chlamydia
• Symptomatic patient (i.e. a patient with genital symptoms) – see Chapter 12: Primary care management of STIs

Clinical assessment: Might this patient have a blood-borne virus or an STI?

Many patients with STIs or with chronic HIV, HBV or HCV infection are asymptomatic. The diagnosis relies on the clinician retaining an index of suspicion in all clinical situations, and on a thorough assessment of risk.

Patients with acute HIV, HCV, HBV, and hepatitis A virus (HAV), disseminated gonococcal infection, primary herpes infection and secondary syphilis may present with systemic symptoms (Chapters 4 and 5). HIV, secondary syphilis or viral hepatitis should be considered in any patient with a febrile illness, particularly if there is a possibility of recent exposure to one of these pathogens. When symptoms of chronic infection with blood-borne viruses occur, they are often non-specific (e.g. fatigue, myalgia and fevers).

Symptoms and signs of moderately advanced HIV infection include weight loss, chronic diarrhoea, fevers, lymphadenopathy, oral candidiasis, seborrheic dermatitis, herpes zoster, frequent or severe recurrent oral or genital herpes and oral hairy leukoplakia (Chapter 6).

Symptoms and signs of early chronic viral HBV and HCV infection are more non-specific and include intermittent or chronic fatigue, abdominal discomfort and headaches. Symptoms and signs of more advanced chronic viral hepatitis include the exanthemata of chronic liver disease (palmar erythema, spider naevi), while decompensated cirrhosis (liver failure) is associated with the development of ascites, splenomegaly and abdominal venous distension (Chapters 6 and 7).

Some early STIs are usually asymptomatic, while symptoms and signs of complications of STIs vary depending on the clinical condition (see Chapter 12: Primary care management of STIs).

Testing of patients: when should you think to test?

This section contains a check list which provides a rough guide for testing for specific STIs.[21-23,25,26] For sexually active MSM, national guidelines recommend at least annual testing for chlamydia, gonorrhoea, syphilis, HIV, and an initial screen and vaccination if necessary for hepatitis A and B.[24] The reader should consult Chapter 8 for testing methods and appropriate anatomical testing sites.

Chlamydia

- Pregnancy – especially if unplanned or unwanted (or if having a termination of pregnancy)
- Sexually active patient under 25 years old – screen at least annually
- Change of partner
- Multiple partners
- Report of unprotected sexual intercourse
- Diagnosed with another STI
- Indigenous person, if not screened in the past 12 months
- MSM – think of testing for chlamydia in all MSM as it is a common anogenital infection in homosexually active men. LGV strains of chlamydia (L1 to L3) can cause a moderate to severe proctitis in MSM. Clinicians will need to discuss with their local laboratory the issue of specific testing for LGV should the need arise
- Sexual assault
- Sex workers (required as part of issuing a certificate); especially street sex workers

Gonorrhoea

- MSM: this group is at substantially higher risk of gonorrhea than the rest of the general Australian community
- History of sex with someone recently arrived from a high-prevalence country (e.g. India, South East Asia)
- Patient recently arrived from a high-prevalence country (e.g. India, South East Asia)
- Indigenous person, if not screened in the past 12 months
- Sex workers (required as part of issuing a certificate); especially street sex workers.

Herpes

- Symptomatic: nucleic acid amplification test (NAAT) testing from any suspicious lesions
- HIV-positive patients: type specific serology (see Chapter 8)
- Some specific clinical situations: type specific serology, e.g. discordant couples, especially if heterosexual – female with no history of herpes, male with a past history of genital herpes and couple are wanting a pregnancy

Genital warts and human papillomavirus

- Clinical diagnosis only: there is no screening available for genital warts
- Papanicolaou smears important in all women (see NHMRC guidelines): yearly for HIV-positive women
- HPV DNA testing for high-risk HPV subtypes is expensive and is used by specialist gynaecology hospital units in the management of cervical pathology. HPV DNA testing is recommended by the NHMRC and funded through the MBS as a 'test of cure' following treatment of high-grade squamous epithelial lesions (HSIL) of the cervix. It is not recommended as a primary screening test for HPV infection or cervical cancer.

Trichomoniasis

- Sex workers
- Women with a vaginal discharge
- Indigenous women
- History of sex with someone from a high-prevalence country
- Patient is recently returned from a high-prevalence country and had unprotected sexual intercourse with a local person in that country

Syphilis

- MSM
- HIV-positive patients
- Sex workers
- Indigenous persons
- Pregnant or if planning a pregnancy

HIV and the sexual health context

A person diagnosed with an STI is likely to be at increased risk of HIV infection. An STI can be a marker of recent or past risk and genital inflammation itself may have put the individual at higher risk of HIV infection. A full assessment of a person with an STI includes HIV, HBV and often HCV antibody testing.

HIV risk should be considered in all patients who present with an STI. Although the diagnosis of a heterosexually acquired STI is unlikely to be accompanied by HIV infection in Australia, the presence of an STI calls at least for careful clinical assessment of the actual risk with the informed cooperation of the person. There is a medical and legal imperative to fully investigate any patient diagnosed with an STI or blood-borne viral infection (Chapter 14). Failure to diagnose an STI can lead to ongoing transmission as well as clinical progression.

More than 20 years into the HIV epidemic, there is some evidence that 100% consistent use of condoms is becoming less common among gay men in Australia.[10] Since the mid 1990s, surveys have reported increasing levels of unprotected anal intercourse with casual

CASE STUDY 5

HBV transmission: perinatally acquired infection

HBV prevalence and transmission

Aaron is an 18-year-old student who consults his GP for hepatitis B vaccination. Pre-vaccination screening reveals that he is anti-HBc+ and HBsAg+. Aaron was born in Australia and his parents are university academics who arrived in Australia from south-eastern China in the mid-1970s. He is not aware of any hepatitis in the immediate family but his grandmother died of liver problems at a very old age. Due to Aaron's potential infectivity, his GP advises him to discuss his HBV-positive status with his girlfriend and housemates. He is also advised to discuss his HBV status with his family, with a view to their subsequent HBV testing. Due to the possibility of perinatally acquired infection, his GP stresses the particular importance of HBV testing for his mother.

partners among MSM, and surveillance data reveal increasing rates of gonorrhoea and syphilis in these populations.[7] Over the past five years, the rates of diagnosis of HIV infection have increased substantially in Victoria, Queensland, South Australia and Western Australia, but not in New South Wales.[27] Regular testing for gonorrhoea and other STIs in MSM who have casual sexual partners should be a routine part of clinical care. All gay and bisexual men should be assessed for HAV and HBV immunity and vaccinated if necessary. As well, clinicians looking after people living with HIV should recommend regular STI screening for their sexually active patients with HIV infection.

In addition to triggering consideration of HIV and HBV infection, the presence of an STI provides the primary care clinician with the opportunity to take a sexual history and promote safer sex practices (Chapter 3).

Prevention strategies

There are several proven means of reducing the efficiency of transmission of STIs, HIV, HBV and HCV (Table 2.4). The use of condoms for anal or vaginal sex and the use of clean injecting equipment remain the most effective means of prevention of transmission of HIV (Chapter 3). Similarly the use of condoms for anal and vaginal sex will significantly reduce the risk of most STIs. Because STIs may be transmitted through oral sex and because condoms are not 100% effective, however, clinicians should recommend regular sexual health check-ups for their sexually active patients, including screening for common STIs (see Chapter 8). The use of sterile injecting equipment is the most effective means of preventing HCV transmission.

Other interventions such as post-exposure prophylaxis may also have a role in prevention, particularly for HIV (Chapter 4). Antiretroviral therapy, caesarean section and avoidance of breast-feeding have reduced the risk of perinatal transmission of HIV to 1–2%.[3] Antenatal testing of women for common STIs and STIs with significant infant morbidity (e.g. syphilis) is an important measure for reducing risk of vertical transmission. HBV vaccination is safe and extremely effective. Nevertheless, many people at risk of infection remain unvaccinated in Australia. The search is currently underway for effective HIV and HCV vaccines, but these may be many years away. A vaccine against herpes simplex virus infection is urgently needed because of the synergistic effect of this infection on HIV transmission. Development of vaccines against other common STIs has unfortunately never been accorded high priority, no doubt a reflection of the ongoing stigmatised nature of these conditions.

Summary

STIs, HIV, HBV and HCV are different and distinct infections in terms of epidemiology and risk factors for transmission, although there are some similarities in the modes of transmission. The recommendation to test for common and significant STIs, HIV, HBV and HCV should be based on reported risk factors for transmission or the presence of clinical signs. A low threshold for testing is advised due to the reluctance of some people to disclose risk behaviours or their failure to identify risks.

TABLE 2.4 Factors associated with increased or decreased transmission of HIV, HBV, HCV

	Increased transmission	Decreased transmission
HIV	**Any** High viral load in index case	**Any** Low viral load (possibly through therapy) Post-exposure prophylaxis (antiretroviral therapy)
	Sexual Sexually transmitted infections in either partner Genital inflammation (includes STIs and non-infectious vaginal inflammation)	**Sexual** Condoms and safe sexual practices Treatment of sexually transmitted infections
	Occupational Deep penetrating injury Hollow-bore needle	**Occupational** Universal (standard) precautions
	Perinatal Vaginal delivery Breast-feeding	**Perinatal** Antiretroviral therapy Caesarean section Bottle-feeding
HBV	**Any** Unvaccinated status HBeAg+ or HBV DNA+ in index	**Any** Vaccination Post-exposure prophylaxis (immunoglobulin and vaccination)
HCV	**Any** HCV RNA+ index case High HCV viral load in index case	**Any** Negligible risk of transmission if source HCV RNA-negative Use of sterile, unused, injecting equipment in a safe environment

References

1 Royce RA, Sena A, Cates W, Cohen MS. Sexual transmission of HIV [published erratum appears in N Engl J Med 1997;337:799]. N Engl J Med 1997;336;1072–8.

2 Dore GJ, Kaldor JM. Detection of HCV RNA in semen (letter). Lancet 2000;356:1520.

3 Gibb DM, Tess BH. Interventions to reduce mother-to-child transmission of HIV infection: new developments and current controversies. AIDS 1999;13(suppl A):S93–S102.

4 Dore GJ, Kaldor JM, McCaughan GW. Systematic review of role of polymerase chain reaction in defining infectiousness among people infected with hepatitis C virus. Br Med J 1997;315:333–7.

5 Mandelbrot L, Landreau-Mascaro A, Rekacewicz, Berrebi A, Benifla JL, Burgard M, et al. Lamivudine-zidovudine combination for prevention of maternal-infant transmission of HIV-1. J Am Med Assoc2001;285:2083–93.

6 MacDonald M, Crofts N, Kaldor J. Transmission of hepatitis C virus: rates, routes, and cofactors. Epidemiol Rev 1996;18(2):137–48.

7 National Centre in HIV Epidemiology and Clinical Research (NCHECR). HIV/AIDS, viral hepatitis and sexually transmissible infections in Australia. Australian HIV Surveillance Report. Sydney; NCHECR; 2002-2006. Available at www.med.unsw.edu.au/nchecr

8 Anderson B, Bodsworth NJ, Rohrsheim RA, Donovan BJ. Hepatitis B virus infection and vaccination status of high-risk people in Sydney: 1982 and 1991. Med J Aust 1994;161(6):368–71.

9 Crofts N, Hopper JL, Milner R, Breschkin AM, Bowden DS, Locarnini SA. Blood-borne virus infections among Australian injecting drug users: Implications for spread of HIV. Eur J Epidemiol 1994;10(6):687–94.

10 Prestage G, Van de Ven P, Knox S, Grulich A, Kippax S, Crawford J. The Sydney Gay Community Periodic Surveys 1996 – 1999: Changes over time. Sydney: National Centre in HIV Social Research (NCHSR), 1999.

11 Bodsworth NJ, Cunningham P, Kaldor J, Donovan B. Hepatitis C virus infection in a large cohort of homosexually active men: independent associations with HIV-1 infection and injecting drug use but not sexual behaviour. Genitourin Med 1996;72:118–22.

12 Fethers K, Marks C, Mindel A, Estcourt CS. Sexually transmitted infections and risk behaviours in women who have sex with women. Sex Transm Inf 2000;76:345-9.

13 Guthrie JA, Dore GJ, McDonald AM, Kaldor JM, for the National HIV Surveillance Committee. HIV and AIDS in Aboriginal and Torres Strait Islander Australians. Med J Aust 2000;172:266–9.

14 Gust ID. Epidemiology of hepatitis B infection in the Western Pacific and South East Asia. Gut 1996;38(Suppl 2):S18–S23.

15 Correll P, MacDonald M, Dore G. Hepatitis C infection in indigenous communities in Australia. Hepatitis C: informing Australia's national response. Canberra: Department of Health and Aged Care; 2000:47–60.

16 National Centre in HIV Epidemiology and Clinical Research (NCHECR). Australian HIV Surveillance Report 11(3). Sydney: NCHECR, 1995.

17 Leslie DE, Rann S, Nicholson S, Fairley CK, Gust ID. Prevalence of hepatitis C antibodies in patients with clotting disorders in Victoria: relationship with other blood borne viruses and liver disease. Med J Aust 1992;156:789–92.

18 National Centre in HIV Epidemiology and Clinical research (NCHECR). HIV/AIDS, viral hepatitis and sexually transmissible infections in Australia. Australian HIV Surveillance Report. Sydney; NCHECR; 2006. (Available at www.med.unsw.edu.au/nchecr)

19 Department of Health and Ageing, Nationally Notifiable Diseases Surveillance System Data (NNDSS). [Online] [access April 2007]. Available from http://www.health.gov.au/internet/wcms/publishing.nsf/Content/Nationally+notifiable+diseases+%28NNDSS%29-2

20 National Centre in HIV Epidemiology and Clinical Research. HIV/AIDS, viral hepatitis and sexually transmissible infections in Australia, Australian HIV Surveillance Report. 2006. [Online] [access April 2007 April]. Available from http://www.nchecr.unsw.edu.au/NCHECRweb.nsf/resources/Quart_10/$file/jan06survrpt.pdf

21 Russell D, Bradford D, Fairley C, editors. Sexual Health Medicine. Melbourne: IP Communications, 2005.

22 Temple-Smith M, Gifford S, editors. Sexual Health, Melbourne: IP Communications, 2005.

23 Queensland Management Guidelines for the Detection and Treatment of Sexually Transmissible and other Genital Infections. Version III. Brisbane: Queensland Health, 2006.

24 STIGMA. Sexually transmitted infection testing guidelines for men who have sex with men. Sydney: STIGMA, 2005. Available at www.racp.edu.au/public/sexualhealth.htm

25 World Health Organization. Guidelines for the management of sexually transmitted infections. Geneva: World Health Organization., 2003.

26 Australasian Chapter of Sexual Health Medicine RACP 2004. Clinical guidelines for the management of sexually transmissible infections among priority populations. [Online] [access April 2007]. Available from URL http://www.racp.edu.au/public/SH_clinical_guidelines.pdf

27 Guy RJ, McDonald AM, Bartlett MJ, Murray JC, Giele CM, Davey TM, et al. HIV diagnoses in Australia: diverging epidemics within a low-prevalence country. Med J Aust 2007;187:1–4.

Talking with the patient: risk assessment and history-taking

3

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Introduction

Rapport, trust and effective communication are vital components of the doctor-patient relationship and contribute significantly to a clinician's ability to take a comprehensive history, particularly in the context of the sensitive issues around human immunodeficiency virus (HIV), sexually transmissible infections (STIs) and viral hepatitis. A thorough sexual and drug-use history is required to identify specific risk factors and behaviours regarding HIV, STIs and viral hepatitis, to establish a diagnosis and to provide a setting for targeted prevention and harm reduction messages and strategies.

Effective communication skills permit and encourage patient involvement in decision-making processes. This participation is associated with greater patient satisfaction, increased compliance with treatment and the creation of a relationship in which the patient feels comfortable raising issues such as death, grief and relationship or sexual problems.[1,2]

Key points

- Sexual and/or drug history-taking begins with general issues and progresses to more detailed and specific questioning regarding risk behaviours
- Factors that will assist effective communication during sexual and drug history-taking include:
  - A comfortable space and adequate time
  - Privacy and the absence of interruptions
  - Assurance and explanation of confidentiality
  - A non-judgemental attitude
  - Knowledge about alternative lifestyles and a willingness to learn
  - A willingness to discuss sexual and drug-use behaviour in detail
  - Listening carefully to the patient
  - A focus on the goals of the interview
- The cultural appropriateness of sexual history-taking may require consideration, particularly with regard to the gender of the clinician

General issues

Taking a sexual and drug-use history helps to ascertain the patient's risk of blood-borne viruses and STIs. To be effective, the process needs to be thorough and several factors should be considered before starting the interview.

The physical environment needs to be conducive to private discussion and adequate time must be set aside. If one appointment is not sufficient, allow for further discussion when the patient returns for his or her test results or follow-up, or suggest that the patient return another day to complete the interview.

Key elements of effective communication are listening carefully and being interested, non-judgemental and observant. Taking notice of the patient's unspoken cues and reflecting together on the most salient points may assist communication. Reflection is a very simple technique that gives the patient the opportunity to correct any misunderstandings and allows the clinician to check that he or she is on the right track.

One approach is to introduce the topic and explain to the patient the reasons for such detailed and private questioning. An opening statement that normalises the discussion may be useful. For example: 'Do you have any concerns about your risk of exposure to hepatitis C, HIV or other sexually transmitted infections?' The clinician may then state that it is important to raise these issues with all patients. Initial, open-ended questions should be followed by more detailed questioning. The clinician may begin by addressing the least confronting issues, followed by specific questions when the patient appears comfortable.

Communication style and language will vary depending on the clinician and the patient. The clinician is advised to use language with which he or she feels comfortable and familiar, and that takes account of the language used by individual patients. If the clinician doesn't understand a word or phrase the patient has used, an explanation should be requested. This helps to develop trust and a sense of engagement, as well as clarity of information.

The clinician should assure clients that confidentiality will apply to all information obtained in the context of clinical service delivery. Confidentiality issues may be especially important for adolescents and those living in smaller communities. While reassuring the patient, make clear early on that there are limitations to confidentiality in every jurisdiction, such as the requirement to report individuals who deliberately and repeatedly put others at risk of HIV infection, or to notify authorities where there is evidence of child abuse.

A major barrier to effective communication is awkwardness and embarrassment of patient and clinician when discussing sexual practices or recreational/injecting drug use. In particular, a clinician who has a long-standing relationship with a patient may be unable to broach certain topics. Alternatively, he or she may have difficulty raising sexual matters with patients of the opposite gender or of a different sexual orientation or age group. Lack of training, time constraints and limited knowledge of cultural and lifestyle issues can result in a reluctance by the clinician to persevere with these interviews.[3,4] A simple lack of practice also may impede a clinician in successfully taking a sexual and drug-use history. For issues that challenge the values or beliefs of the clinician, discussion with a colleague may help to familiarise him or her with unusual or challenging language or concepts.

Patients are often reluctant to report behaviour that is stigmatised and they may feel unable to discuss their behaviour with friends or family. If they feel they can trust the doctor, they may be happy to talk about their risk behaviours in the clinical setting, but the clinician may need to initiate this discussion.

It is useful to consider strategies for managing conversations that become awkward or difficult (Table 3.1). Breakdown in communication is very common and may result in a change of topic. If the interview is progressing poorly, it may be helpful for the clinician to consider his or her own responses to the content of the discussion. It is vital to be aware of the cues the patient is giving and to try to ensure his or her needs are met by the consultation. Empathy, humour and digression may help to dissipate anxiety. Clarifying or redirecting statements, such as 'Could I ask another question about HIV?' can help to structure the interview.

Despite knowledge and experience, interviews don't always go well. It's important to remember that 'Rome wasn't built in a day', and obtaining a full sexual and drug-taking history will often require several visits and gradual development of respect and trust between patient and clinician. Striving to ensure that the patient goes away from the initial consultation with the feeling that it was a positive experience and that the prospect of a return visit is not too onerous is far more important than pushing on with unfruitful lines of enquiry. Sometimes, however, referral to another clinician or service may be appropriate.

TABLE 3.1 What prevents effective communication?

• Inadequate physical environment (lack of privacy, lack of time, interruptions)
• Uncertainty about confidentiality
• Insufficient language skills or lack of a satisfactory interpreter
• Inability to persevere through awkward times in the interview
• Assumptions about sexuality and behaviour
• A judgemental attitude (displaying prejudice or lack of interest)
• Not listening to the patient
• Inappropriate use of open and closed questions
• Interrupting the patient excessively
• Ignorance and prejudice about alternative lifestyles

Risk assessment

General medical history

It is less threatening to discuss general medical history first and then lead into a more specific sexual and drug-use history. Early in the interview, non-threatening questions relating to HIV, STIs, hepatitis B and hepatitis C may be asked. These questions may address:

- A history and dates of blood transfusions (including major trauma or surgery, during which the patient may have been unaware of blood transfusion)
- Tattoos (including where, when and whether done professionally)
- Country of birth and residence
- Cultural practices (such as initiation ceremonies)
- Family history
- Vaccination history
- Piercing and other body modification
- Current baseline knowledge about HIV, STIs, hepatitis B virus (HBV) and hepatitis C virus (HCV)

TABLE 3.2 Drug history checklist

• Drug use (past and present)
• Type of drugs used (prescription, alcohol and tobacco, illegal)
• Routes of administration
• Sharing of injecting equipment (including swabs, filters, water, etc.)
• Associated harms and evidence of dependence
• Motivation to cease drug use or use non-injecting routes of administration

Drug-use history

Table 3.2 provides a checklist of information to gather when taking a drug-use history. General questioning may address the use of prescription medications, tobacco and alcohol, followed by use of non-prescription and illicit drugs. High levels of alcohol consumption

TABLE 3.3 Injecting drug use equipment and language

Common injecting equipment

The drug(s); water; spoon; filter; swab; tourniquet; syringe; needle; disposal container.

Language

The mix (drug and water); mixing; jacking back (obtaining a blood flashback in the syringe); pick (needle or needle and syringe); fit (needle and syringe); whack (either needle and syringe or the drug or the injection); whacked or hit (an injection of drugs); user (person who injects drugs); works (equipment); smack (heroin); gear (illicit drugs generally); ice, goey, whiz, speed, meth, d-meth, crystal, crystal meth, shabu, batu, tina and glass (amphetamines).

TABLE 3.4 Safe injecting procedures[7]

1. Preparation

- Choose a safe place to inject—avoid injecting alone
- Clean the area where you will be mixing
- Have everything you need within reach
- Wash hands (with soap and water or swabs)

2. Mixing up

- Clean the spoon with a swab
- Put the drugs into the spoon
- Use a new sterile fit to draw up water from new ampoule of water (or cooled boiled water in a clean glass)
- Do not put a used syringe into a group mix
- Add water to the spoon with the drugs; mix
- Add filter to mix
- Draw solution up through filter to remove impurities
- Remove air bubbles

3. Injecting

- Wipe injection site with swab
- Place tourniquet around arm above injection site (don't leave it on too long)
- Put the needle into your arm at 45° angle
- Pull back the plunger; blood should appear in the needle. If no blood appears, remove needle, stop blood flow and try again
- When you are sure the needle is in a vein, loosen tourniquet and depress the plunger, injecting solution
- Remove needle and apply pressure to site to stop blood flow

4. Clean up

- Rinse your fit with cold water (reduces contamination risk and gets rid of some blood in case fit is to be used again. See Appendix 4)
- Dispose of rinsing water
- Dispose of fit (recap your own, never recap another person's syringe)
- Wipe down the area where you have mixed up
- Wash hands and arms with soapy water (if not possible use swabs) Appendix 4 provides instructions on cleaning injecting equipment.

can play a significant role in sexual risk-taking and may be a target for discussion about risk reduction. Non-prescription drugs may also alter judgement and be a factor in the assessment of sexual risk. In addition, the sharing of straws or other equipment used to snort drugs has some risk of HCV transmission.

Injecting drug-use history

Important information to obtain about injecting drug-use includes:

- Whether and when any needles or other drug injecting equipment (such as swabs, waters or filters) were shared
- The types of drugs injected
- The frequency of drug use
- The duration of drug use
- The most recent occasion of use

Interviews about drug-use should be informed by a basic knowledge of common injecting drug-use equipment and practice, and the potential for HCV transmission at all stages of the injecting process. Table 3.3 contains a summary of drug-use language and equipment and Table 3.4 has a summary of safer injecting practices. Chapter 15 provides details of some relevant referral and information services.

Gathering detailed information will assist the clinician to assess the patient's risk of acquiring and transmitting infections, as well as the possible duration of infection. Drugs that may be injected include performance-enhancing substances such as steroids, as well as amphetamines, ecstasy, benzodiazepines and opiates such as heroin. Frequency and duration of use vary considerably; risk behaviour may consist of a few episodes of sharing injecting equipment many years ago, which the patient may be reluctant to disclose. It may be useful to suggest: 'Many people have indicated that they have injected only one or two times many years ago—could this be the case with you?'[1] Other useful questions regarding drug history are outlined in Table 3.5.

Health promotion about harm or risk reduction with regard to injecting drug use requires the clinician to have knowledge of safe procedures and information about local services, such as needle and syringe programs (Table 3.4 and Chapter 15). It is appropriate to discuss whether the patient wishes to reduce or cease drug use, and whether he or she would like a referral to an appropriate treatment service. Alternatively, non-injecting routes of drug administration, such as snorting and swallowing drugs, may reduce risk. If the patient is drinking alcohol at hazardous or harmful levels you should discuss strategies such as alternating their alcoholic drinks with either water or a soft drink. Patients and clinicians can access a range of agencies and resources providing information, advice and support for minimising harmful substance use. These include: Alcohol and Drug Information Service (ADIS), Alcoholics Anonymous (AA), Reachout, NHMRC Alcohol Guidelines[5], and Lifescripts.[6] Details for ADIS, AA and Reachout are included in Chapter 15.

TABLE 3.5 Useful questions about injecting drug use

• Have you ever injected?
• What do you inject?
• How often do you inject?
• Do you inject alone, or with other people?
• Have you shared needles or other injecting equipment?
• Do you know how to inject safely?
• Have you ever overdosed?
• Do you binge on drugs at certain times?
• Do you know how hepatitis C is transmitted?
• Are you concerned about your drug use?

Sexual history

The purpose of taking a sexual history is to assess and limit the risk of acquiring an infection with HIV or another STI. Sexual orientation or identity does not always equate with particular behaviour, therefore information about sexual practices, barrier and condom use and the risk behaviours of sexual partners is more specific and useful than the patient's stated sexual orientation and marital or partnership status. Common and often incorrect assumptions are related to heterosexuality, monogamy and preferred sexual practice.

The clinician should ascertain whether vaginal or anal penetration has taken place. Questions about anal sex should be asked of both men and women and, in the case of male-to-male sex, it should be determined whether penetration was receptive, insertive or both, e.g. was the patient a 'top', a 'bottom' or was he 'versatile'? Oral sex confers a lower risk of HIV transmission, but several STIs including herpes simplex virus (HSV), syphilis, gonorrhoea and chlamydia are readily transmitted by oral sex, which may take the form of oro-penile (fellatio), oro-vulval (cunnilingus) and oro-anal (rimming/anilingus) sex.

Penetration of the vagina or anus with sex toys, fingers and hands, or a full fist and forearm ('fisting') is generally considered low risk for HIV. However, this type of penetration may result in trauma that can provide a portal of entry for infection. As well, even without trauma, STIs can be transferred via contaminated fingers from anogenital sites of an infected partner even if no actual penile penetration occurs. The clinician may need to establish the precise nature of non-penetrative practices. Some non-penetrative practices such as mutual or non-shared masturbation are low-risk

TABLE 3.6 Risk assessment – useful questions

Sexual practice	Condom usage
• Do you consider that you might be at risk of HIV or another sexually transmitted infection? (Detail what activities may put someone at risk if necessary)	• Do you or your partner/s use condoms? Always, or how often?
• Do you have any concerns about HIV or other STIs (e.g. chlamydia, herpes)?	• Do you know about female condoms? Have you ever used them?
• When did you have sex last? (An important question for women if there is any chance of pregnancy)	• When did you start using condoms?
• Who was it with – someone you knew well, or a casual contact?	• When don't you use condoms?
• How many sexual partners have you had over the last three months? Since the last STI screen?	• What are your reasons for not using condoms?
• When did you last have a regular sexual partner?	• Do you have any problems using condoms?
• Have you had any other sexual partners?	• Do they fit well?
• Are your sexual partners male, female or both?	• Do you use a water-based lubricant?
• What types of sexual activity do you engage in with your partner? Vaginal? Oral? Anal? (Clarification may be needed)	• Have any condoms broken?
• Have you ever had an STI (e.g. chlamydia, herpes, gonorrhoea) or a check-up for STIs?	• When do you put the condom on? When the penis is erect?
• Do you know whether your sexual partners have been at risk for HIV or STIs? Have your male partner/s had sex with other men? Have your sexual partner/s ever injected drugs? Have your sexual partner/s lived in an area where many people have HIV?	• Do you (or does your sexual partner) sometimes only put a condom on when he is near to climaxing (coming)? (This practice is known as 'dipping' and can obviously be risky)
• Have you ever been a sex worker?	**Other transmission risks**
• Have you ever been the client of a sex worker?	• Did you have a blood transfusion or use blood products before 1990 in Australia?
• For MSM – do you use 'beats'; do you go to saunas or sex clubs? How frequently? What sexual activities do you take part in there?	• Have you had a medical procedure or blood transfusion overseas? Where and when?
	• Do you have tattoos? (Ask for details) In which country were they done, and were they done professionally?
	• Have you had ever had a piercing or other body modification done? In which country was this done, and was it done professionally?
	• Have you ever had a sexual partner or household member who had hepatitis B or C?
	• Have you ever had a sexual partner or household member who was at risk of hepatitis B or C?
	• Have you ever been in prison?

activities. Other non-penetrative sexual practices, such as sadomasochism and piercing during sex (which may involve mucosal trauma or blood-to-blood contact), may have a moderate-to-high risk of transmission for HIV. Examples of questions to be asked during sexual risk assessment are listed in Table 3.6.

While engaging in sex work may not be common for the clientele of most primary care practitioners, it is considerably more common than most clinicians imagine. Both women and men may engage in sex work for varying periods of time for a variety of different reasons. Experienced sex workers will probably know more about safe sex practices than most clinicians, but the young, those 'working' opportunistically, those working on the street (perhaps to support a drug habit) and some sex workers newly arrived in Australia or those with a poor grasp of English may be putting themselves at risk through unprotected sex. Clinicians should keep the possibility of sex work in the back of their minds and also, with male patients, whether they are clients of sex workers. Questions about these matters need to be asked sensitively and only when very good rapport has been established with the patient—probably not on the first visit.

When discussing sexual practices it is important that the clinician and patient understand each other. The clinician may seek to maximise understanding through specific questioning, explanation and clarification. 'Have you been sexually active?' may be taken to mean only vaginal or anal penetrative sex, so it may be appropriate to indicate that the question also relates to oral or other sexual activity. Specific questions such as 'Do you ever have oral sex, where you suck on his penis? Does he ejaculate (or come) when his penis is in your mouth?' or 'Does your partner ever bleed following vaginal penetration?' may be useful in establishing the level of risk. Table 3.7 provides a checklist of information to gather when taking a sexual history.

Where appropriate, condom use, including use of the female condom, should be explored in detail. Female condoms are more expensive, less readily available, noisy during use, and for some people have an unacceptable appearance and feel, but they are effective and suit some patients (especially those allergic to latex). They should not be forgotten. Questions relating to condom usage, as outlined in Table 3.6, form part of risk assessment and provide an opportunity to discuss effective safer sex practices. In addition, discussion may address other safe sex measures.

For example, cervical diaphragms may offer some protection and latex dams can be used for oral-anal and oral-vaginal sex by men and women. Latex gloves or condoms can be used for digital and sex toy penetration. Lubricants may reduce the risk of vaginal trauma and subsequent infection.

TABLE 3.7 Sexual history checklist

• Number of sexual partners and their gender
• Any same-sex sexual activity ever, even if uncommon or intermittent
• Specific sexual practices
• Presence of a sexual partner with an STI or with risk factors for infection
• Awareness of risk reduction techniques and extent of compliance with these
• Sexual health check-ups in the past
• Past STIs and their treatment
• Sex work or being a client of sex workers
• If MSM, use of 'beats' or visits to sex on premises venues (SOPVs)

Every primary care clinician will have in their practice some men who have sex with men (MSM) and some women who have sex with women (WSW) even if those patients do not always, or even often, engage in same-sex sexual activity. These patients have particular sexual health needs and clinicians should gain some basic knowledge about homosexually active men and women—it is counter-productive to reveal ignorance about lifestyle and sexual practices when trying to take a sexual history.

Some MSM (including those who have a regular female partner or wife) seek male sexual partners in risky situations like public toilets ('beats') or sex-on-premises venues (SOPVs) which include male saunas and sex clubs. If, as is often the case, the behaviour is impulsive or unplanned, condoms may be unavailable and unprotected sex may take place.

In SOPVs, sex with more than one partner may occur and even if condoms are used for penetrative anal sex, other STIs may be acquired through oral sex (including syphilis, herpes, urethral gonorrhoea or chlamydia). Believing lesbian women to be at low risk for STIs generally, clinicians sometimes provide WSW with a false sense of security and even recommend that routine Papanicolaou smears are unnecessary. A significant percentage of WSW do have sex with men throughout their lives and are therefore exposed to transmission of STIs (including high risk human papillomavirus (HPV) types like 16 and 18) from male partners.

Oral sexual practices and sharing sex toys will lead to STI transmission risk and this includes WSW. Even exclusively lesbian women are at increased risk of bacterial vaginosis.

Prevention and harm reduction messages

Opportunities for educating about harm reduction and safe sex often arise during an assessment of risk. The primary care clinician may take these opportunities to ensure the patient understands the risks of sexual activity and drug use, as well as safe practices. Many people will be well informed about safer practices but may not adhere to these all the time. Occasions of risk-taking can be identified and explored. It is important that the patient feels he or she can discuss episodes of unsafe behaviour without being judged or lectured. Gaining an understanding of the patient's perspective and responding to his or her emotions will help in facilitating behavioural change. Common themes in a discussion of risk-taking may include negotiating safer sex with partners, drug and alcohol consumption, or apathy and depression.

The clinician may engage the patient in generating his or her own solutions to unsafe practices. Questions such as 'Has this happened before?', 'What did you think or do on that occasion?', 'What were the outcomes?' and 'How did you feel?' may assist the patient to identify and avoid particular situations and reinforce safe practices. Acknowledgement of the difficulties a person may face in trying to adopt or negotiate safe sex or safe injecting may facilitate a more productive discussion. Consideration should be given to the difficulty in challenging entrenched cultural norms such as 'men are in charge of condoms' or 'he looked young and healthy, so he couldn't have HIV'.

Encouraging patients to have sexual health check-ups can be a harm reduction strategy in itself. This may seem paradoxical and defeatist at first, implying that lapses in safe sex practices are to be expected. However, safe sex practices which allow unprotected oral sex do not always protect patients from common STIs like chlamydia, gonorrhoea, genital herpes and HPV. For MSM, those who change partners frequently or those with multiple partners, it is sensible to recommend regular check-ups. For others, the recommendation should be that a sexual health check-up should follow the break up of a relationship, a casual encounter or the commencement of a new sexual partnership.

Clinicians need to think about members of special groups in their practice, learn about such groups and tailor their preventive and harm reduction messages so they are appropriate and relevant for their special needs. Such groups include MSM, WSW, adolescents and young adults, Indigenous Australians, physically and intellectually handicapped people and people from culturally and linguistically diverse communities.

TABLE 3.8 Tips on safe sex and harm reduction messages

• Check the patient's base line knowledge about HIV, STIs, HBV, HCV. Correct misconceptions and, if necessary, provide basic information
• Check the patient's understanding about sexual and drug-use behaviours that carry risk of transmission
• Explore safe sex and safe using options (such as non-injecting techniques) specific to the patient's needs
• Discuss correct use of condoms (including the female condom and non-latex condoms) and where they can be obtained
• Discuss where new fits can be obtained and the correct method of cleaning fits (Appendix 4)
• Discuss circumstances in which unsafe practice has taken place or is likely to occur
• Discuss the link between alcohol and other drug use and unsafe sex
• Encourage regular sexual health check-ups except for those in stable monogamous relationships

Being able to show empathy and to convey an understanding of the patient's situation is an essential component of the clinician's repertoire. As an example, when dealing with young patients, although it is hard for many of us to project ourselves back into our teens, it is helpful to even catch a distant memory of how emotionally overwhelming early sexual encounters can be and how difficult it is for young people caught up in the passion of the moment to think rationally about risk reduction and harm minimisation. In the long run, empathy and understanding achieve the best outcomes when talking with patients about sex and drug use. If a clinician chooses not to explore safe sex and harm-reduction strategies with a patient during a consultation, the topics may be noted and raised during a subsequent appointment.

Alternatively, the clinician may decide to refer the patient to another service or clinician, a community group or a specialist counsellor or educator (Chapter 15). Having written information can be useful in ensuring that a patient can have information to take away with them. This information is available through Hepatitis Councils, peer based injecting drug-user groups and State and Territory AIDS Councils. Table 3.8 provides a check-list of general tips on safe sex and harm reduction education.

Cross-cultural issues

There is great potential for misunderstanding and communication breakdown when talking to patients about sexual practice and drug use in a culturally and linguistically diverse country such as Australia. Use of interpreters may help communication. For clinicians who work with a significant number of patients from a particular ethnic or cultural group, it can be useful to learn about relevant attitudes and practices prevalent in that cultural group.

Alternatively, the clinician can ask the patient whether the line of questioning is appropriate. In situations where it is difficult to consult with a patient of the opposite sex, arrangements should be made for the patient to see another clinician if possible.

Patients with disabilities or psychiatric problems

People of all ages and abilities may be sexually active. Some individuals, such as people with intellectual or physical disabilities, may have particular problems accessing information and harm reduction and safe sex measures, such as condoms. They may also have particular difficulty negotiating safer sex. Ensuring adequate knowledge and support for people with disabilities or psychiatric problems may require involvement with family and carers, and consideration of issues specific to the patient's particular situation.

Summary

Detailed drug-use and sexual history-taking may be conducted over several consultations and provides the basis for an accurate assessment of risk for HIV, STIs, HBV and HCV infection, as well as other infections. Clear and non-judgemental communication facilitates accurate history-taking and appropriate management. Impediments to history-taking may be overcome by application of good communication techniques, consideration of the patient's particular needs, consultation with colleagues and a willingness to learn about alternative lifestyles. However, if impediments persist, referral to another clinician or service is recommended.

References

1 Curtis JR, Patrick DL, Caldwell E, Greenlee H, Collier AC. The quality of patient-doctor communication about end-of-life care: a study of patients with advanced AIDS and their primary care clinicians. AIDS 1999;13:1123–31.

2 Roberts KJ, Volberding P. Adherence communication: a qualitative analysis of physician-patient dialogue. AIDS 1999;13:1771–8.

3 Epstein RM, Morse DS, Frankel RM, Frarey L, Anderson K, Beckman HB. Awkward moments in patient-physician communication about HIV risk. Ann Intern Med 1998;128:435–42.

4 Epstein RN, Frafey BA, Beckman HB. Talking about AIDS. AIDS Patient Care, STDs 1999;13:545–53.

5 National Health and Research Medical Council. Australian alcohol guidelines. Health risks and benefits. Canberra, Department of Health and Ageing, 2003. Available at www.alcoholguidelines.gov.au

6 Australian Government. Department of Health and Ageing. Lifestyle Prescriptions: Alcohol Use Assessment. Available at http://www.health.gov.au/internet/wcms/publishing.nsf/content/phd-pub-lifescripts-practitioner-cnt.htm/$FILE/tools-alcohol.rtf .

7 Australian Injecting and Illicit Drug Users League. Cleaning Fits. Canberra: National Hepatitis C Education and Prevention Program, Australian National Council on HIV/AIDS and Related Diseases; 2001. Australian Intravenous Injecting League. Safer Injecting. Canberra: National Hepatitis C Education and Prevention Program, Australian National Council on HIV/AIDS and Related Diseases; 2001.

Exposure and acute HIV infection

4

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Introduction

Early diagnosis, monitoring and treatment of patients with recently acquired human immunodeficiency virus (HIV) infection may alter the long-term course of HIV disease. Knowledge of the clinical signs and symptoms of primary HIV infection, as well as the serological and virological markers, enables early HIV diagnosis by clinicians and provides patients with timely options for intervention choices, as well as opportunities for receiving appropriate referral, support and education on prevention of transmission.

Pathogenesis of acute HIV infection

Knowledge of the pathogenesis of primary HIV infection in adults helps the clinician to understand HIV-related pathology testing. Within 12–24 hours of exposure, cells at the site of a mucosal infection are infected with HIV. Forty-eight hours after exposure, HIV has spread to regional lymph nodes where rapid replication occurs within immune cells, primarily CD4 cells. Cells in the gut become infected as well as those of the central nervous system and the skin.[1,2] Over the next 5–40 days, the host immune response to massive HIV viraemia results in the production of neutralising antibodies and a cytotoxic T-cell response mounted by CD8 T-cell lymphocytes. The T-helper CD4 cells control the cytotoxic response but also are infected by HIV. Many, but not all, of these infected CD4 cells are killed by the cytotoxic CD8 responses, causing a fall in the CD4 cell numbers. These changes can be observed clinically by monitoring CD4 and CD8 cell counts in the peripheral blood.

The flu-like symptoms of primary HIV infection are caused by the release of cytokines during the process of infection and immune response. As a result of the immune response, the blood concentration of the virus (the viral load) falls and new CD4 cells are produced by the bone marrow via the thymus. For reasons that are unclear, the cytotoxic CD8 cell response is not able to clear or completely control HIV, as occurs with some, but not all viral infections.

Key points

- Early diagnosis of HIV disease has significant potential benefits and the likelihood of ongoing transmission may be reduced through implementation of safe sex and risk reduction strategies.
- Acute HIV infection may be difficult to distinguish from other acute viral illnesses. Clinical features that should alert the clinician to the possibility of acute HIV infection in the presence of a mild-to-severe flu-like illness include a 'glandular fever-like' illness, meningeal involvement, a recent sexually transmissible infection and transient neurological symptoms.
- Post-exposure prophylaxis (PEP) may reduce the risk of HIV infection if offered within 72 hours of HIV exposure.
- When a patient presents reporting a high-risk exposure to HIV, immediate referral to an antiretroviral prescriber, sexual health centre or hospital emergency department is necessary to access non-occupational post-exposure prophylaxis.
- Symptoms of primary HIV infection can usually be managed in the primary care setting by the general practitioner. Decisions about antiretroviral therapy need to be made in conjunction with an HIV-experienced clinician.
- While newly diagnosed patients may require ongoing specialist services from a range of providers, the general practitioner remains an important source of initial and continued information and support.

Detecting primary HIV infection

Primary HIV infection: acute retroviral syndrome

Familiarity with the range of presentations associated with primary HIV infection (also called acute retroviral infection or seroconversion illness) enables the early diagnosis and management of HIV infection. Clinical suspicion of acute HIV infection should be followed by a thorough risk assessment (Chapters 2 and 3). As the symptoms and signs of acute HIV infection are similar to

Table 4.1 Symptoms and signs of primary HIV infection[9,10]

Symptoms of HIV seroconversion illness

	Symptom	Frequency
Generalised	Fever	>80%
	Lethargy and general malaise	>70%
	Myalgia and arthralgia	50-70%
	Lymphadenopathy	40-70%
	Night sweats	50%
Gastrointestinal	Pharyngitis	50-70%
	Diarrhoea	30%
	Oral ulcers	10-30%
Neurological	Headache	40-70%
	Aseptic meningitis	
	Transient reversible neurological signs (neuropathies, Guillain-Barré)	Rare
Skin	Rash	40-80%
	Genital ulcers	5-15%
Initial laboratory finding	Thrombocytopenia	45%
	Leukopenia	40%
	Raised liver enzymes	20%
Diseases caused by transient immunosuppression	Oral/oesophageal candidiasis Gut infections Pneumocystis jiroveci pneumonia (PCP)	Rare

those of many common infections, the presence of HIV infection is more likely when a recent high-risk exposure has been reported.

Signs and symptoms

Signs and symptoms of acute HIV infection can present as early as three days or as late as 10 weeks following transmission. Most commonly they occur at 10–14 days. The onset of symptoms often coincides with the appearance of HIV antibodies although the patient may be HIV antibody negative (ELISA) for up to three weeks after onset of symptoms. The duration of the illness is most commonly four to 14 days but may be longer.[3,4] Approximately 50–90% of patients report signs or symptoms suggestive of primary HIV infection at the time of seroconversion.[4-7] Patients who experience symptomatic primary HIV infection appear to have more rapidly progressive HIV disease than those who do not.

The frequency of symptoms varies and severity ranges from very mild to very severe (Table 4.1). No single symptom distinguishes acute HIV infection from other acute viral illnesses. However, there are some factors that should alert the clinician to the possibility of acute HIV infection in the presence of a flu-like illness such as:

- Epstein-Barr seronegative 'glandular fever-like' illness
- 'Flu-like' symptoms outside usual influenza season (e.g. myalgia, arthralgia, headache, malaise)
- Fever for more than three days
- Maculo-papular rash
- Meningeal involvement
- Transient neurological syndromes (e.g. Guillain-Barré syndrome, neuropathies)
- Recent evidence of sexually transmissible infections or genital ulcers
- Recent high-risk exposure

TABLE 4.2 Pathology tests for diagnosis of primary HIV infection

HIV antigen tests	
P24 antigen	P24 antigen may become positive within a few days of symptoms and be absent after two weeks.
Quantitative HIV RNA viral load by reverse transcriptase polymerase chain reaction (RT PCR)	HIV RNA viral load may become positive within a few days. However, the quantitative viral load assay is generally not recommended to diagnose acute HIV infection due to a reported low false-positive rate in the acute setting (usually indicated by low viral levels).
HIV antibody tests	
HIV antibodies (EIA)	EIA may take up to three weeks to become positive after onset of clinical signs and symptoms.
HIV Ag/Ab Combo Test	75% of labs use this test as the standard HIV antibody screening test. This is a combined p24 antigen plus HIV antibody test and so it will become positive before a test using HIV antibody alone in acute infection.
HIV antibodies (Western Blot)	Western Blot may take up to three weeks to become positive after onset of clinical signs and symptoms.

Note: Other tests may be indicated and should be performed in conjunction with specialist centres and laboratories.

Recent risk exposure

Patients reporting recent risk exposure should be thoroughly assessed and monitored for HIV infection. The possibility of HIV infection can be an emotionally difficult time for the patient. Providing the full pre-test discussion and sharing information are required to prepare the patient for the possibility of a positive diagnosis and to provide him or her with the required information about HIV infection (Chapter 9).

For high-risk HIV exposures that have occurred within the last 72 hours, non-occupational post-exposure prophylaxis (NPEP) should be considered.[8] Case study 2 and the Box entitled 'Non-occupational post-exposure prophylaxis (NPEP): is prevention of HIV infection possible after exposure?' in this chapter address assessment and referral for NPEP.

Potential exposure to HIV often indicates a risk of hepatitis B virus (HBV) and hepatitis C virus (HCV) infection as well as a risk of other sexually transmitted infections (STIs). Consequently, investigations for STIs prevalent in the community, HBV and HCV should be considered in the context of acute HIV infection.

Investigations

When risk assessment or clinical presentation indicate the possibility of acute HIV infection, laboratory testing ensures correct diagnosis. HIV antibody tests (HIV ELISA and Western Blot) may be negative or equivocal up to three weeks after the start of primary HIV illness (Table 4.2). However, HIV viraemia appears in the blood in the early days of the illness and may allow detection of virus particles or proteins (antigens) in the absence of antibodies. If available, tests for viral antigens included in later generations of HIV antibody and antigen assays may facilitate early diagnosis of HIV infection during the window period.

It should be noted that the molecular tests currently available in Australia (listed in Table 4.2) do not have approval from the Therapeutic Goods Authority (TGA) needed for their use in the primary diagnosis of HIV infection. Molecular tests should therefore be considered confirmatory (of an indeterminate serology result) when used in this setting.

Interpreting test results with regard to acute HIV infection can be confusing and, if necessary, clinicians are advised to seek guidance from their pathology laboratory or the National Serology Reference Laboratory (Chapter 15).

Management of acute HIV infection and recent exposure

Acute HIV infection

People with primary HIV infection can usually be managed in the community by their own general practitioner (GP), with the support of either an HIV-experienced GP and a hospital-based specialist. Most of the physical symptoms of the infection are treatable with simple analgesics and antiemetics. Occasionally hospital admission may be required for rehydration or management of rare manifestations such as encephalitis or Guillain-Barré syndrome (Table 4.3).

TABLE 4.3 Management of primary HIV infection checklist
• Referral to an HIV-experienced GP and/or a hospital-based clinician
• Support for the primary care clinician from an HIV-experienced GP and/or a hospital-based clinician
• Physical symptom relief such as analgesia for headache, myalgia and arthralgia, and antiemetics for nausea
• Appropriate treatment for opportunistic infections
• Psychosocial support of the patient by the clinician and referral to an experienced mental health professional as appropriate
• Early and frequent follow-up

Very early treatment with antiretroviral therapy – a controversy

Treatment of HIV infection during the early stages of chronic infection remains a controversial and changing area of HIV medicine. Some HIV clinicians treat primary HIV infection with combination antiretroviral medications after one or more of the confirmatory tests have returned positive. The rationale for treatment during this phase of HIV disease is to minimise immune system damage, to lower the viral replication 'set point' (Chapter 1) and to minimise viral dissemination throughout the body.

Others have argued that the early immune response to HIV may require the ongoing presence of HIV antigens and that disturbing this response may be harmful. In addition, short-term and long-term side effects of therapy can be considerable (Chapter 10).

While there are theoretical benefits associated with early treatment, there have been no randomised, controlled trials examining the efficacy of very early treatment in terms of time to progression to AIDS or death. Ongoing randomised studies such as the SPARTAC study (an international trial comparing three different strategies of intervention in patients recently infected with HIV to determine whether early treatment for a limited duration delays damage to the immune system and consequently prolongs time to initiation of long-term antiretroviral therapy) may help provide answers. Clinicians inexperienced in the management of HIV infection need to contact an HIV-experienced GP or a hospital centre to discuss further management.

If the patient proceeds with treatment during primary infection, preferably within a clinical trial, HIV-inexperienced clinicians are encouraged to maintain contact with their patients as part of the treatment team, especially as newly diagnosed and infected people require considerable information and support from a trusted and accessible source.

Contact tracing

Contact tracing of people who may have been exposed to HIV prior to identification of primary infection should be undertaken. Discussion with the patient regarding how to proceed with contact tracing may be appropriate.

The clinician may ask the patient to consider recent blood-to-blood or sexual contacts as well as recent blood donations. Review of appropriate State or Territory guidelines and discussion with public health authorities may be considered.

Public health notification

Public health authorities must be notified when HIV infection has been diagnosed. In most States and Territories notification can be undertaken by clinicians or pathology laboratories, although there are differences in legislative and regulatory requirements (Chapter 14).

Supporting newly diagnosed patients

The ongoing psychological adjustment of patients to HIV infection can be affected by the nature of early consultations with their doctor after diagnosis. In particular, having a long consultation when the HIV diagnosis is given has been positively correlated with better long-term adjustment, as have the quality of information given and the attitude of the person giving the diagnosis.[11,12]

Newly diagnosed patients have major issues to face and adjustments to make during early consultations. For example, patients may suddenly confront their mortality or have concerns about future income and relationships with partners, family and friends.[13-15]

Patients with children often have concerns about how their children will deal with the diagnosis and whether they will be able to continue to provide for the children materially and emotionally.[16] For women of childbearing age, there may be fears and concerns about how HIV affects their future reproductive life.[17] Simple acceptance, in the face of perceptions of social stigma and discrimination, may be the most valuable support

CASE STUDY 1

Diagnosing and managing HIV seroconversion illness

Severe flu or HIV seroconversion illness?

John is a 39-year-old engineer who presents to his general practitioner, Dr Lewis, with a flu-like illness in April. He has been unwell for a week with muscle aches and pains, fever, headache and retro-orbital pain, particularly upon lateral gaze. He has spent the last four days on the couch at home and has noticed that his urine is very dark.

Dr Lewis considers a differential diagnosis of HIV seroconversion illness and conducts a risk assessment. 'I need to ask some sensitive questions. Nowadays we need to ask people about risk behaviours for HIV when they present with an unusual flu-like illness. Have you done anything in the past few weeks that might worry you or might put you at risk for HIV? What I mean is, any unprotected sex or sharing needles?'

John relates that he recently started a relationship with Sam and that they have been having sex without condoms for four months. They intended to have HIV tests but 'hadn't got around to it'. While John was HIV-negative when tested last November, he is unsure when Sam was last tested. John has been vaccinated against hepatitis A and B and reports never using needles.

Given his high-risk activity for HIV transmission, Dr Lewis suggests HIV testing to John: 'While lots of other common viruses cause symptoms like this, we should consider testing for HIV infection. The first illness that some people get when they are infected with HIV can look like flu.' Following pre-test counselling, John consents to testing for HIV and HCV. Three days later, the laboratory rings Dr Lewis about John's test results.

Results

Standard (EIA) test for HIV antibodies – negative
P24 antigen test – positive
Western Blot test result – pending
Liver enzymes – slightly elevated
Hepatitis C antibodies – negative

John's tests confirm a clinical diagnosis of HIV primary infection. He is referred to a GP experienced in the management of HIV infection after indicating that he would prefer to see a community-based HIV clinician. After lengthy discussion about treatment options, the HIV-experienced clinician and John decide to go ahead with antiretroviral treatment.

Dr Lewis continues regular follow-up with John to address his ongoing medical and psychosocial needs following the HIV diagnosis. In addition to assistance in taking medications, John raises relationship and sexuality issues. Dr Lewis refers him to the local AIDS Council for support and offers written resources for HIV-positive people.

CASE STUDY 2

Non-occupational post-exposure prophylaxis (NPEP) presentation and issues of safe sex and disclosure

NPEP, safe sex and disclosure

David is a middle-aged, married man who presents to his general practitioner, Dr Betheras, for non-occupational HIV post-exposure prophylaxis (NPEP) the morning after a condom break during receptive anal sex in a sex-on-premises venue.

Dr Betheras immediately organises referral to a general practitioner who can prescribe antiretroviral therapy (antiretroviral therapy prescribing practitioners' contact details are listed in the *ASHM Directory* at http://www.ashm.org.au/ashm-directory/). Before David leaves for his next appointment, Dr Betheras advises him that he will need to institute condom use when having sex with his wife and any other sexual partners until he has his final, week-24 test results. 'How will I explain this to my wife?' David asks. Dr Betheras explores his concerns about the risk episode and the fear, guilt and shame he is experiencing. She also discusses with him the issues involved in talking about the episode with his wife, if and when he decides to do so.

David returns to see Dr Betheras several days later to discuss the issue of safe sex.

He decides that he must tell his wife but is reluctant to do so immediately. In the meantime, he decides to say that he has a urinary infection and needs to use condoms for a while. Dr Betheras suggests that it might be a good idea to see a counsellor about these issues. David agrees and referral details are provided.

Dr Betheras also discusses the case with her medical insurer and gets advice about the legal issues of duty of care and confidentiality regarding both David and his wife (Chapter 14). She continues to monitor the situation in conjunction with the general practitioner providing NPEP.

a clinician can offer in early consultations. Patients may also need help in deciding whether to disclose their HIV status and, if so, to whom.[18]

Emotional support and acceptance can also assist the person to make beneficial alterations to his or her lifestyle, such as changes to diet and exercise, reduced drug and alcohol use and practising safe sex.[14]

Support services and the role of the clinician

In addition to the support that clinicians can offer, patients should be referred to other agencies for information, counselling and support as appropriate (Chapter 15). Research has identified the importance of contact with HIV-positive communities in helping newly diagnosed patients come to terms with their status and continue with their lives.[15]

However, while acknowledging that specialist counselling may best meet the psychosocial needs of patients, clinicians must recognise that they may be the first and most important source of this support and information in their patients' lives. This is especially true during the early stages of HIV infection. Maintaining contact with the patient after the initial diagnosis, as either the key HIV-treating clinician or as a partner in care, helps to support the patient through the many difficulties that may lie ahead.

Non-occupational post-exposure prophylaxis (NPEP): Is prevention of HIV infection possible after exposure?

There is some evidence that a four-week course of antiretroviral therapy, commenced as soon as possible within 72 hours of exposure to HIV (whether it be an occupational or non-occupational exposure [NPEP]), can reduce the risk of HIV infection.[20] Such therapy is called post-exposure prophylaxis (PEP). Antiretroviral therapy for HIV infection is listed under Section 100 of the Pharmaceutical Benefits Scheme and can only be prescribed by approved clinicians. In addition, none of the individual antiretroviral drugs are licensed for use in post-exposure prophylaxis and must be covered under state-based services. Each state determines how PEP is made available and this is usually through hospital emergency departments and public sexual health clinics. Community s100 prescribers can assess cases and write scripts for PEP, but the drugs are dispensed from hospital pharmacies.

Risk assessment

To respond appropriately to a possible HIV exposure requires an assessment of the likelihood of HIV infection in the source, the risk associated with the exposure and the effectiveness of treatment options. Highest risk is defined as sexual exposure with an HIV-infected person via receptive intercourse (without intact condom) or exposure to HIV-infected blood via injecting equipment where percutaneous exposure has occurred with a used hollow needle (Chapters 2 and 3).

For percutaneous, occupational exposures, the National Needlestick Injury Hotline (1800 804 823) can provide advice to health care workers regarding the level of risk (Chapter 15).

Assessment should address whether the source is known to have HIV infection or viral hepatitis or risk factors for blood-borne viruses, including a history of unprotected sex with homosexual or bisexual men, a history of injecting drug use, or haemophilia (Chapters 2 and 3). If the source is available and willing, testing for HIV and viral hepatitis should be conducted with full pre-test and post-test discussion and information sharing.

NPEP

Following assessment, all individuals with high-risk exposures should be immediately referred to an approved antiretroviral prescriber, a sexual health centre, or the emergency department of a major hospital for provision of NPEP.[8] The sooner the post-exposure antiretroviral treatment is commenced the greater the theoretical chance of success. Details of how to contact antiretroviral prescribers are given in the ASHM Directory. NPEP involves a one-month course of dual or triple drug therapy. It must be taken strictly as prescribed to reduce the risk of drug resistance. Antiretroviral drugs cause common side-effects such as nausea and diarrhoea as well as rare, severe side-effects, so monitoring by an HIV clinician is required.

The possibility of exposure to HIV causes anxiety and concern. Patients need considerable support at this time, due not only to the possibility of new HIV infection, but also to help manage the adverse effects of the antiretroviral medications. Enabling a patient to examine and modify his or her sexual and injecting drug use risk behaviours is a vital component of the NPEP process. Patients may require referral to an experienced counsellor.

Testing for HIV and other sexually transmitted infections and blood-borne viruses is required at baseline, at three months (HIV and syphilis) and at six months (HCV) after exposure, to exclude the possibility of late seroconversion. During this time, patients should adopt safe sexual practices with all partners and should not donate blood, body tissues or semen, and female patients should not breast-feed infants.

National guidelines on the use of PEP for non-occupational HIV exposures have been produced by ASHM.[19]

Other sexually transmitted infections

Assessment for acute HIV and potential recent exposure typically reveals risks for, or symptoms of, other STIs. So, just as the choice of investigations for symptoms must take account of the many possible causes of those symptoms, screening for relevant STIs must be considered standard of care at this time. The detection and treatment of STIs is very important in its own right, but their treatment can also reduce the risk of HIV transmission. Australian non-occupational post-exposure prophylaxis guidelines[19] recommend baseline testing for chlamydia, gonorrhoea (see Chapter 8), hepatitis B and syphilis with repeat syphilis testing at three months. The same STI tests are appropriate after any sexual risk exposure including sexual assault[20] (also refer to National/State guidelines regarding management of sexual assault). The use of post-exposure prophylactic antibiotics against STIs like chlamydia is not recommended after risk exposure, although they may be indicated after some types of sexual assault.[19]

Summary

The primary care clinician has a key role in identifying cases of primary HIV infection and facilitating the clinical monitoring and management of infected individuals. Following diagnosis of primary HIV infection, referral to an HIV-experienced clinician is recommended for consideration of antiretroviral therapy, preferably in the context of clinical trials. To reduce the risk of infection after a high-risk exposure to HIV, post-exposure prophylaxis may be taken within 72 hours of the exposure. Reported exposure provides an opportunity to review risk behaviours, safe sex practices, harm minimisation strategies and assessment for other STIs. Provision of information and psychosocial support are key elements of management following a possible HIV exposure or diagnosis with primary HIV infection.

References

1. Brenchley JM, Schacker TW, Ruff LE, Price DA, Taylor JH, Beilman GJ, et al. CD4+ T cell depletion during all stages of HIV disease occurs predominantly in the gastrointestinal tract. J Exp Med 2004; 200(6): 749–59.
2. Kelleher AD, Zaunders JJ. Decimated or missing in action: CD4+ T cells as targets and effectors in the pathogenesis of primary HIV infection. Curr HIV/AIDS Rep 2006; 3(1): 5–12.
3 Cooper DA, Maclean P, Finlayson R, Barnes TG, Michelmore HM, Brooke P, Penny R. Acute AIDS retrovirus infection: Definition of a clinical illness associated with seroconversion. Lancet 1985;1:537–40.
4 Schacker T, Collier AC, Hughes J, Shea T, Corey L. Clinical and epidemiologic features of primary HIV infection. Ann Intern Med 1996;125:257–64.
5 Tindall B, Barker S, Donovan B, Barnes T, Roberts J, Kronenberg C, et al. Characterization of the acute clinical illness associated with human immunodeficiency virus infection. Arch Intern Med 1988;148:945–9.
6 Keet IPM, Krijnen P, Koot M, Lange JMA, Miedema F. Goudsmit J, Coutinho RA Predictors of rapid progression to AIDS in HIV-1 seroconverters. AIDS 1993;7:51–7.
7 Schacker T, Collier AC, Hughes J, et al. Clinical and epidemiologic features of primary HIV infection. Ann Intern Med 1996;125:257–64.
8 Lange JMA, Parry JV, de Wolf F, Mortimer PP, Goudsmit J. Diagnostic value of specific IgM antibodies in primary HIV infection. AIDS 1988;2:31–5.
9 Adapted from Kahn JO, Walker BD. Acute HIV type 1 infection. New Engl J Med 1998:339;33–9.
10 Vanhems P, Hughes J, Collier AC, Vizzard J, Perrin L, Cooper DA, et al. Comparison of clinical features, CD4 and CD8 responses among patients with acute HIV-1 infection from Geneva, Seattle and Sydney. AIDS 2000:14;375–81.
10 Jackson LD and Selby MJ. Communicating an HIV-positive diagnosis. In Roth NL and Fuller LK, (eds). Women and AIDS: Negotiating safer practices, care, and representation. New York: The Haworth Press, 1998:131–53.
11 Pergami A, Catalan J, Hulme N, Burgess A, Gazzard B. How should an AIDS diagnosis be given? The view of patients. Int J STD AIDS 1994;5(1):21–4.
12 Rinken S. The event of diagnosis: Diagnosis of HIV/AIDS as a crisis of self-description. Social Systeme 1997;3(1):101–21.
13 Roth N, Nelson M. HIV diagnosis rituals and identity narratives. AIDS Care 1997;9(2):161–79.
14 Kleine-Kraft AE. How HIV positive gay men perceive seropositivity and what significance they give this diagnosis as evidenced by sexual behaviour changes and care needs. Dissertation Abstracts International: Section B: The Sciences and Engineering 1995;55(9-B):3817.
15 Thorne C, Newell ML, Peckham CS. Disclosure of diagnosis and planning for the future in HIV-affected families in Europe. Child Care Health Dev 2000;26(1):29–40.
16 McDonald K, Grierson J, de Visser R, Bartos M. A complex uncertainty: Women on health, hope and living with HIV in Australia. Monograph Series Number 19. Melbourne: Australian Research Centre in Sex, Health and Society, 2000.

17 Mansergh G, Marks G, Simoni JM. Self-disclosure of HIV infection among men who vary in time since seropositive diagnosis and symptomatic status. AIDS 1995;9(6):639–44.

18 Lurie P, Miller S, Hecht F, Chesney M, Lo B. Postexposure prophylaxis after nonoccupational HIV exposure: clinical, ethical, and policy considerations. J Am Med Assoc 1998;280:1769–73.

19 Australasian Society for HIV Medicine. Australian guidelines for non-occupational post exposure prophylaxis. Approved 2007. [Online] [access April 2007] Available from http://www.ashm.org.au/pep-guidelines/

20 Mein JK, Palmer CM, Shand MC, Templeton DJ, Parekh V, Mobbs M, et al. Management of acute adult sexual assault. Med J Aust 2003;178:226-30. Available from http://www.mja.com.au/public/issues/178_05_030303/mei10448_fm.html

Exposure and acute viral hepatitis

5

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Acute hepatitis

Epidemiology

In Australia, 300–500 cases of hepatitis A virus (HAV) infection and around 250 cases of newly acquired hepatitis B virus (HBV) infection are reported annually.[1] An estimated 9,700 new cases of hepatitis C virus (HCV) infection occurred in 2005, but only 354 cases of newly acquired HCV were reported because most cases are subclinical and go unnoticed.[1,2] Acute hepatitis secondary to excessive alcohol consumption is also common. Various forms of chronic liver disease may present clinically as an acute hepatitis. These include autoimmune hepatitis and Wilson's disease, as well as chronic HBV, which may present as a hepatitis flare. Drug-induced hepatitis also should be considered in all cases of sudden liver enzyme elevation.

Outcomes of acute hepatitis

Less than 1% of all cases of viral hepatitis with jaundice develop acute liver failure. Infection with HAV causes acute hepatitis but is not associated with the development of chronic infection. In contrast, infection with HCV and HBV can result in acute and chronic infection (Table 5.1). Infants and children with HBV infection are more likely to develop chronic HBV infection than adults. Early studies of HCV infection suggested that a significant proportion (85%) of people acutely infected develop chronic viraemia, but later studies suggested that rates of chronic infection may be as low as 55%.[3] A recent meta-analysis of the natural history of acute hepatitis C suggested that spontaneous clearance rates were around 25%.[4] Chronic hepatitis secondary to HCV and HBV infection may progress to cirrhosis, liver failure and hepatocellular carcinoma (HCC). Some patients with chronic HCV infection may develop glomerulonephritis, mixed cryoglobulinaemia, or a syndrome of non-deforming arthritis similar in distribution to rheumatoid arthritis. Chronic HBV may also be associated with extrahepatic manifestations.

Key points

- The hepatotropic viruses (HAV, HBV, HCV) cause most cases of acute hepatitis, although other infectious agents and drugs need to be considered. Acute HCV infection is probably under-recognised.
- Primary care clinicians should make a definitive diagnosis where possible, and refer patients with unclear diagnoses or rare, treatable conditions. Patients should be monitored for acute liver failure and hospitalised if signs are detected.
- Primary care clinicians play a critical role in the prevention of viral hepatitis. Interventions such as education, vaccination, contact tracing, post-exposure prophylaxis and public health notification are critical to the control of epidemics and prevention of disease in individuals at high risk.
- Preventive interventions should be offered to persons with clinical acute hepatitis, those recognised to be in at risk populations and those who have been exposed to hepatotropic viruses.

Symptoms and signs of acute hepatitis

The symptoms and signs of acute viral hepatitis are not specific for a particular aetiological agent and are the same for acute hepatitis and chronic viral hepatitis (Chapter 7). They include nausea, vomiting, anorexia, lethargy, jaundice and tender hepatomegaly. Patients who present with a prolonged prodromal illness, including arthralgia and rash, may have immune complex disease associated with HBV infection. Rarely, acute liver failure supervenes. Signs and symptoms of acute liver failure include intractable vomiting, encephalopathy, asterixis (liver flap) and fetor hepaticus.

Incubation periods

The average time from exposure to the development of symptoms varies for the three major hepatotropic viruses:

- HAV – 3 weeks (range 2–7 weeks);
- HBV – 10 weeks (range 4–26 weeks);
- HCV – 7 weeks (range 2–21 weeks).

TABLE 5.1 Outcomes of acute viral hepatitis
Hepatitis A virus
• Approximately 0.1% of patients with HAV develop acute liver failure. Less than 40% of patients with acute liver failure die or receive a liver transplant.
• Chronic hepatitis does not occur following HAV infection.
• Lifelong immunity occurs after infection.
Hepatitis B virus
• Less than 1% of clinical cases develop acute liver failure. 80–90% of patients with acute liver failure die or receive a liver transplant.
• Less than 5% of adults with acute HBV infection develop chronic hepatitis.
• 90% of infants infected at birth develop chronic hepatitis.
• Those who go on to develop chronic infection are at risk of cirrhosis, hepatocellular carcinoma and liver failure.
• Those with chronic infection have persistent HBsAg and are infectious to others.
• Those who clear infection have lifelong immunity, maintain anti-HBc, and may or may not preserve anti-HBs.
Hepatitis C virus
• Acute liver failure is rare, but may occur in persons with HBV co-infection.
• Approximately 75% of adults with acute HCV infection develop chronic HCV.
• Those who go on to develop chronic infection are at risk of cirrhosis, hepatocellular carcinoma and liver failure.
• 5% of infants born to HCV-infected women develop HCV infection.
• If infection resolves and the virus is cleared, the person is NOT immune and can be re-infected. After resolution of infection, antibodies persist for a variable amount of time (20 years in some cases).

Diagnostic approach

The diagnosis of acute hepatitis relies predominantly on serological testing, although other features are important to consider.

History should include consideration of:

- Symptoms consistent with acute hepatitis
- A review of any symptoms that may suggest an alternative diagnosis (e.g. infectious mononucleosis)
- Epidemiological clues (Table 5.1 and Chapter 2)
- A history of alcohol and drug use (including illicit drugs, over-the-counter medications and complementary therapies)
- Travel history
- Vaccination history
- Family history of liver disease

An awareness of current epidemiological information is useful (such as a current outbreak of HAV).

Examination should specifically include evaluation for fever, icterus, rash, arthritis, tender hepatomegaly, splenomegaly, injection sites, tattoos, piercings and signs of hepatic encephalopathy (asterixis, fetor hepaticus and altered mental state). A general examination should be performed.

Non-serological investigations

Basic investigations should include liver enzymes, full blood count and coagulation profile. Specific results can assist in establishing the cause of acute hepatitis. For example:

- In viral hepatitis, the alanine aminotransferase (ALT) is usually 10–100 times the upper limit of normal with the aspirate aminotransferase (AST)/ALT ratio less than one.
- In alcoholic hepatitis, the ALT is generally 2–10 times the upper limit of normal with the AST/ALT ratio greater than 1.5; bilirubin is usually elevated.
- In drug-induced hepatitis, a mixed profile may be seen with raised hepatic (AST and ALT) and cholestatic (alkaline phosphatase and GGT) markers.

- Atypical lymphocytosis may suggest a viral aetiology and thrombocytopenia may indicate acute alcohol exposure or the presence of chronic liver disease with portal hypertension.
- The coagulation profile may reveal a prolonged prothrombin time or international normalised ratio (INR) suggestive of liver failure.

Serological investigations

All serological investigations should be undertaken after appropriate pre-test counselling and the results given in conjunction with post-test discussion (see Case Study 1 and Chapter 9). Specific serological investigations are indicated in Figure 5.1 and Tables 5.2–5.4.

If the diagnosis is unclear, the initial serological investigations may be repeated after 1–2 weeks. Serological investigation of Epstein-Barr virus infection and investigation of less common causes of hepatitis can be undertaken at this time. If the diagnosis is still unclear, specialist referral is indicated.

Key considerations when testing for acute viral hepatitis

In the context of acute HAV infection, anti-HAV IgM is invariably present. False negative results are rare.

Acute HBV infection is best detected by testing for HBsAg and anti-HBc IgM. Anti-HBc IgG and anti-HBs appear later in the course of the illness. HBV DNA is not routinely used as a diagnostic tool in acute HBV infection. In patients with HBV infection, hepatitis D virus (delta or HDV) should also be considered, particularly in a patient with chronic HBV who develops a new episode of acute hepatitis or if the disease is severe. Anti-HDV IgG and IgM testing is available at a limited number of laboratories (there have been virtually no cases of HDV in Australia for 10–20 years).

In acute HCV infection, HCV antibody may be present at the onset of hepatitis or may develop in the following weeks. If it is not present, and HCV is suspected on epidemiological grounds, HCV RNA polymerase chain reaction (PCR) should be performed to detect viraemia directly. HCV antibodies are usually present within three months of exposure.

Supportive therapy

Most cases of acute viral hepatitis do not require hospitalisation.

Hospital assessment is recommended for patients who are unable to maintain an adequate fluid intake and all patients with an ALT greater than1000 IU/L, or progressive rise in bilirubin (greater than 60 mmol/L) and INR greater than 1.3. The most ominous signs are falling ALT and rising bilirubin and INR as this indicates severe liver injury with significant loss of hepatocytes. These patients may exhibit signs of encephalopathy.

Most drugs should be avoided during acute hepatitis. Analgesics are generally not required and aspirin, narcotics and sedatives should be avoided. Small amounts of paracetamol may be used for the management of constitutional symptoms. Patients should be advised to avoid alcohol. If the cause of hepatitis is unclear, a careful medical review should be undertaken and potential hepatotoxins should be ceased. Small meals may be easier for the patient to tolerate.

TABLE 5.2 Clues to diagnosis – epidemiological and exposure risks

• Knowledge of current epidemiology, e.g. HAV cluster
• Contact with a case of acute or chronic hepatitis
• Travel to endemic area without vaccination or passive prophylaxis – HAV, HBV, yellow fever
• Travel to endemic areas – HAV, HBV, HEV, dengue fever, leptospirosis etc.
• Unprotected penetrative sex – HBV
• Unprotected oro-anal sex – HAV
• Occupation, e.g. sewerage workers, childcare workers – HAV
• Occupation, e.g. health care workers – HAV, HBV, HCV
• Injecting drug use – HAV, HBV, HCV
• Alcohol consumption
• Family history – HBV, Wilson's disease, alpha1-antitrypsin deficiency
• Country of birth – HAV, HBV
• Tattoos and/or body piercings – HBV, HCV
• Blood transfusion and medical/dental procedures – HBV, HCV
• Needle-stick injury or other significant occupational exposure – HBV, HCV
• History of imprisonment – HCV

Specific therapy

There is little role for specific agents in the management of acute viral hepatitis A and B. However, in prolonged cholestasis after HAV infection, corticosteroids may reduce serum bilirubin and relieve itch. In the case of acute HBV, infection will resolve spontaneously in the majority of adults and antiviral therapy is not usually indicated. The role of nucleoside analogues in the treatment of acute HBV is not established. However, recent guidelines do suggest consideration of the use of a nucleoside analogue (lamivudine, telbivudine or entecavir) for cases of fulminant or protracted severe

TABLE 5.3 Serodiagnosis of HAV and HCVs

Interpretation	anti-HAV IgM	anti-HAV total	HBsAg	anti-HBs	anti-HBc		HBeAg	anti-HBe	HBV DNA	anti-HCV	HCV PCR
					IgM	total					
Acute hepatitis A	+	–	–	–	–	–	–	–	–	–	–
Past hepatitis A	–	+	–	–	–	–	–	–	–	–	–
Acute hepatitis C	–	–	–	–	–	–	–	–	–	+ or –	+
Chronic hepatitis C (symptomatic or asymptomatic)	–	–	–	–	–	–	–	–	–	+	+
Resolved hepatitis C	–	–	–	–	–	–	–	–	–	+ or –	–

Note: co-infection or superinfection may make interpretation more complicated.

TABLE 5.4 Serological, virological and biochemical profiles of HBV[*5]

	HBsAg	Anti-HBs	Anti-HBc (total)	Anti-HBc IgM	HBeAg	Anti-HBe	HBV DNA (IU/ml)	ALT
Acute HBV	+	-	+	+	+	+/-	High	↑
Chronic HBeAg positive								
Immunotolerant Phase	+	-	+	-	+	-	High	N
Immunoclearance Phase	+	-	+	-	+	+/-	High	↑
Chronic HBeAg Negative								
'Inactive Carrier state'	+	-	+	-	-	+	<20 000	N
'Precore mutant'	+	-	+	-	-	+	>20 000	↑
'Occult'	-	-	+	-	-	+/-	Very low	N
Reactivation HBV	+	-	+	+/-			High	↑
Vaccinated	-	+	-	-	-	-	-	N
Resolved HBV	-	+	+	-	-	+/-	-	N

* By kind permission of Dr Mark Danta
+ = positive, - = negative, N= normal, ↑ = elevated.

acute hepatitis B.[6] Patients with undiagnosed chronic HBV may develop severe spontaneous flares of hepatitis which appear clinically as an acute hepatitis. In this situation, resolution may be enhanced with nucleoside analogue therapy (Chapters 1 and 11).

In the case of acute hepatitis C there is evidence that treatment with pegylated (PEG)-interferon-based therapy alone in the acute phase of infection results in greater rates of viral clearance than treatment in the chronic stage of hepatitis C infection.[7,8] However, since some people will spontaneously clear HCV without treatment, the ideal time to commence PEG-interferon therapy remains to be determined. A strategy of waiting 12 weeks to establish whether spontaneous clearance will occur and commencing PEG-interferon therapy if not has been proposed.[9] This subject is still the focus of ongoing clinical trials and referral to a specialist for further advice should be considered for all patients diagnosed with acute hepatitis C. Section 100 of the PBS does not fund PEG-interferon treatment for acute HCV infection.

Clinical monitoring

Liver function tests should be performed once or twice per week in addition to an assessment of coagulation profile and clinical status.

Acute liver failure is the most serious complication of viral hepatitis, occurring in less than 1% of HAV and HBV cases. It remains unclear whether acute HCV can result in acute liver failure. In viral hepatitis, acute liver failure results from massive, immune-mediated hepatocyte necrosis. Risk factors for the development of acute liver failure in viral hepatitis are not fully understood, but older age and concomitant liver disease have been implicated. Death may occur even when the liver has begun to regenerate.

Altered mental status (hepatic encephalopathy) and coagulopathy in the setting of acute hepatitis defines acute liver failure. Typically, non-specific symptoms such as malaise, nausea, intractable vomiting and sleep disturbance develop in the previously healthy person, followed by jaundice, the rapid onset of altered mental

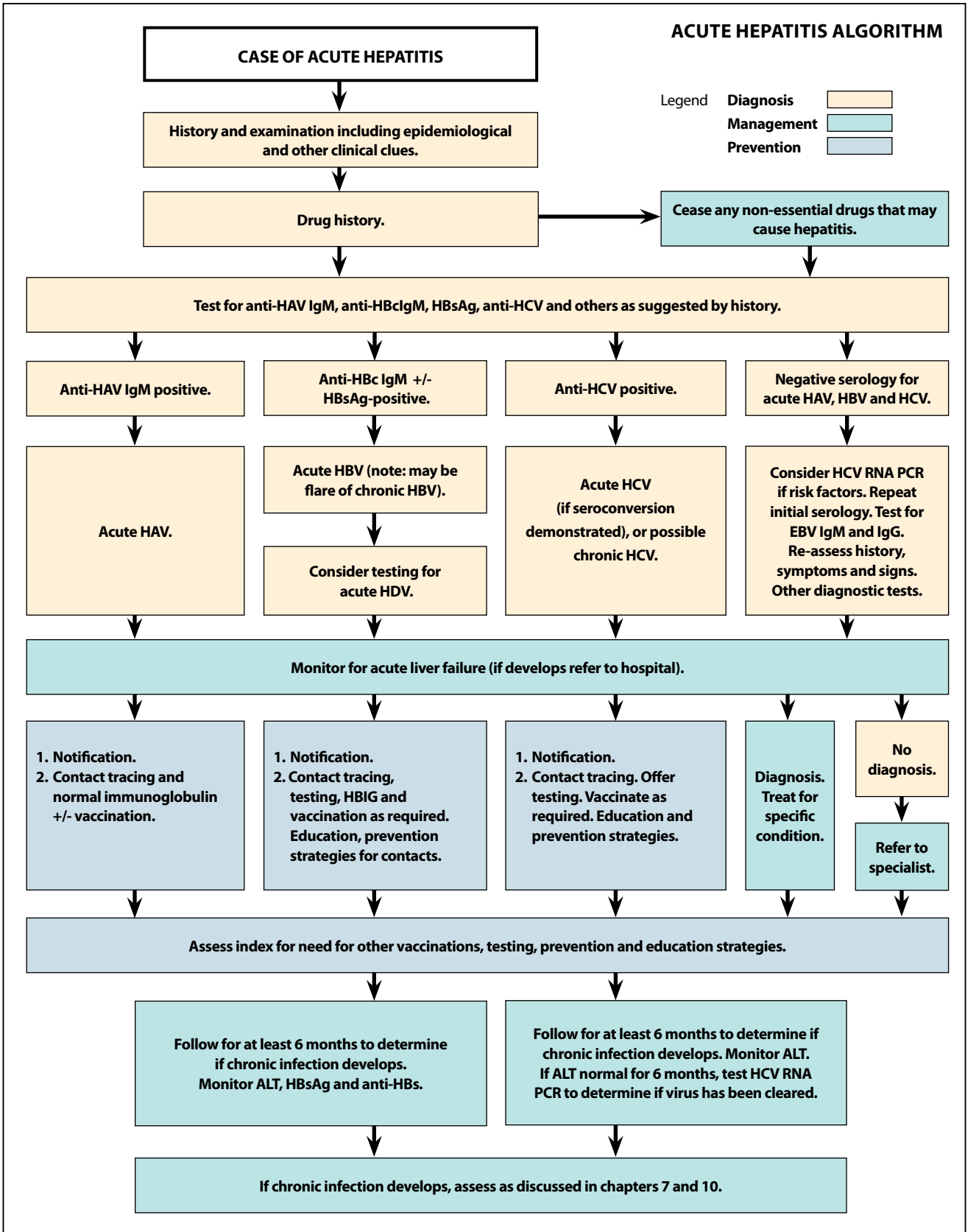

FIGURE 5.1 Diagnostic and management algorithm for cases of acute hepatitis.

status and coma. Thus, the patient goes from being healthy to moribund within 2–10 days. Supportive laboratory findings include high serum ALT, low blood glucose levels and worsening coagulopathy.

The management of acute liver failure begins with the recognition that patients with coagulopathy or encephalopathy may die. Due to the potential for rapid deterioration in their clinical status and the need for close monitoring, patients with acute liver failure are best cared for in hospital. Liver transplantation may be required in a small proportion of cases.

Referral to a liver transplant unit is indicated where:
- The patient is in a remote hospital
- There is any evidence of encephalopathy
- There is worsening coagulopathy

To determine whether chronic infection has been established, the recommended follow-up time for acute hepatitis is at least six months. Repeatedly normal ALT results and a negative HCV RNA PCR at six months indicate viral clearance. Table 5.4 and Figure 5.1 provide details of HBV follow-up.

Contact tracing

Contact tracing of individuals who may have been exposed during the infectious period of acute hepatitis should be undertaken to enable preventative measures to be implemented. Discussion with the patient regarding how to proceed with contact tracing may be appropriate. The clinician may ask the patient to consider recent blood-to-blood or sexual contacts as well as recent blood donations. With regard to HAV, household and occupational contact tracing may be relevant. It is recommended that primary care practitioners keep up to date with the relevant State or Territory guidelines.

Public health notification

Cases of hepatitis are notifiable by doctors and diagnostic laboratories. Public health units coordinate the response to outbreaks of acute hepatitis and can provide advice on the appropriateness of post-exposure prophylaxis for suspected contacts.

Opportunistic diagnosis and prevention strategies

An episode of acute hepatitis should lead to risk assessment and testing for other transmissible infections with similar routes of transmission (Chapters 1–3). The opportunity for implementing harm reduction and preventive measures, such as vaccination, should also be taken.

Specialist and hospital referral

Referral to hospital is appropriate in cases where the primary care clinician assesses an individual to have severe hepatitis or possible acute liver failure. Specialist referral is recommended:
- Where the primary care clinician is unable to make a definitive diagnosis
- Where multiple diagnoses appear to co-exist
- For consideration of antiviral therapy in acute hepatitis
- Where other, treatable conditions have been diagnosed

CASE STUDY 1

Hepatitis B diagnosis: managing the anxious patient

Anxious patient with acute viral hepatitis

Peter is a 19-year-old man of European background who presents to a general practice clinic. He has recently been told by another service that he has hepatitis B after an episode of jaundice. Peter has no idea whether he has acute or chronic infection and believes that it is 'for life'. He is distressed and expresses fear about sharing food with his family, kissing and hugging. Peter believes that he will never be able to have sex again because he is contagious.

Peter is confused about the differences between acute and chronic infection, and he has an exaggerated sense of how easily HBV can be transmitted. People with the infection are often extremely fearful of infecting loved ones and need accurate information from health professionals to enable them to continue in their usual activities and maintain closeness with family and friends.

The clinician contacts the other service, establishes how the diagnosis was made and uses the serology and other investigations to determine that Peter has acute hepatitis B infection. Peter is queried regarding symptoms such as intractable vomiting, disturbed sleep and altered mental state, and examined for physical signs including asterixis (hepatic flap) and fetor hepaticus, to ensure that there is no evidence of liver failure. Peter agrees to have further liver function tests and INR as recommended by the clinician.

Although serology shows Peter is negative for HCV and HIV antibodies as well as HAV IgM, the clinician assesses Peter for risk factors for viral hepatitis and discusses the ways in which other blood-borne viruses and sexually transmitted infections can be prevented.

The clinician explains how HBV is transmitted and, importantly, also discusses ways in which it is not transmitted (Chapters 1 and 2). The clinician states that over 90% of adults clear acute HBV infection (Table 5.1) but even if Peter does develop ongoing or chronic infection, he can still kiss, hug, share food and even have sex without transmitting HBV. The clinician explains that an effective vaccine is available for his loved ones ('Post-exposure prophylaxis' and 'Immunisation' in this chapter), although Peter will need to use condoms for sexual intercourse until any sexual partners are effectively vaccinated.

The clinician tells Peter that he requires follow-up for at least six months to ascertain clearance or persistence of HBV infection. Peter is invited to return the following week to discuss his test results and review other issues discussed during the consultation.

Because of the fear and uncertainty associated with viral hepatitis, it is especially important that health professionals give accurate information about transmission and prognosis at the time of diagnosis, and explore the availability of treatment options if chronic infection with HBV develops.

Work
Persons with HAV infection are infectious for up to a week after the onset of jaundice and should not work. Workers in high-risk areas, for example food handlers and childcare workers, may require extended leave. Given that cases in high-risk workers will usually be followed-up by the local public health unit, advice should be sought from the relevant State or Territory health authority (Chapter 15). Persons with acute HBV or HCV infection do not need to be excluded from work if they are clinically well, unless they are health care workers who perform exposure-prone procedures (Chapter 13). Further information may be obtained from relevant State and Territory health departments or medical registration boards (Chapter 15).

Post-exposure management
The management of a person potentially exposed to viral hepatitis will vary according to the nature of the exposure, the available information about the source of the exposure, knowledge of the exposed person's immunity to viral hepatitis and the time that has elapsed since the exposure. Exposed individuals may self-present for assessment or may be detected after contact tracing. As well as an assessment of the current exposure, an assessment of future or ongoing risk should be made and preventive strategies put into place. In cases of workplace exposure to hepatitis or potentially infected bodily fluids, appropriate documentation should be completed for worker's compensation purposes.

Exposure to HIV as well as viral hepatitis should be considered following exposure to blood or bodily fluids. See Chapter 4 for a discussion of HIV post-exposure prophylaxis.

Source status
Details of the source's clinical status should be obtained where possible. Cases of clinically apparent, acute hepatitis represent the most straightforward category but cases of exposure to bodily fluids from people without acute hepatitis may be encountered. An assessment should be made of risk factors for blood-borne viral infections in the source. If the source is available and willing, screening for viral hepatitis and HIV should be conducted with full pre-test and post-test discussion.

In cases where the source has a history of HBV infection, an urgent assessment of HBsAg status will guide decisions regarding infectivity and hence recommendations regarding post-exposure prophylaxis.

Knowledge of the source's HCV status does not change the immediate management, as post-exposure prophylaxis is not currently available. However, the infectivity of a source who is repeatedly negative for HCV RNA in serum is probably negligible.[10]

Exposed person's immunity
After exposure to HAV, no specific tests of immunity are undertaken. Prophylaxis is given to all close contacts.

After exposure to HBV, an urgent assessment of the exposed person's immunity is required. This entails a history of previous HBV infection or immunisation and response to vaccination. If the history is unclear, or response to previous immunisation is unknown, then tests to ascertain immunity to HBV may be undertaken if the results can be obtained rapidly. Administration of hepatitis B immunoglobulin (HBIG) should not be delayed beyond 72 hours. Check anti-HBc (as a marker of previous infection) and anti-HBs (if assessing response to immunisation). If such tests are not available within this time frame, the person should be assumed to be non-immune.

Post-exposure prophylaxis
HAV
Post-exposure prophylaxis is recommended for the close contacts of people with HAV. This includes household and sexual contacts who have had contact with the index case two weeks before, or up to one week after, the onset of jaundice. Normal human immunoglobulin (NHIG) is recommended and should be given within 14 days of the exposure. The standard dose is 2.0 mL (1.0 mL for persons 25–50 kg; 0.5 mL for persons under 25 kg in weight). It is given as a single intra-muscular injection. If the patient is a food handler, all other food handlers at his or her place of work should receive normal human immunoglobulin. Where the patient is associated with a day-care or preschool facility (attendee child, staff member or household contact of either) and there is any concern about the possibility of further transmission, NHIG should be offered to children and susceptible staff in the relevant age groups or classes at the facility. HAV vaccine can be commenced simultaneously with normal human immunoglobulin and should be considered for those at ongoing risk of HAV infection.[11]

HBV
Individuals who are HBsAg-positive (HBsAg+) should be considered infectious. Non-immune individuals with a definite HBV exposure through heterosexual or homosexual sex, sharing of injecting equipment, mother-to-child exposure or occupational exposure (percutaneous, ocular, mucous membrane exposure) should be given HBIG as soon as possible within 12 hours of birth; within 72 hours of percutaneous/ocular/mm exposures and 14 days of sexual contact.[11] (The dose of HBIG is 400 IU for adults and 100 IU for children.) Concomitantly, HBV vaccination should be injected at a separate site and a full course completed.

HCV
No post-exposure prophylaxis against HCV infection is currently available.

Post-exposure follow-up

After exposure to HAV, no specific serological testing is required. Clinical follow-up is sufficient.

For HBV and HCV, the aim of initial follow-up is to detect the development of acute or chronic infection. Serological follow-up after exposure to HBV and HCV should occur at one, three and six months as both infections can have prolonged incubation periods.

The HCV RNA PCR assay is currently funded such that a single test can be undertaken for the diagnosis of acute HCV infection. Additional testing may be performed at the expense of the patient. Most cases are viraemic at four weeks, although some may have transient viraemia that clears before this time. A single negative HCV RNA result does not exclude infection with HCV and full serological follow-up represents the current gold standard of diagnosis.

Psychosocial issues

In managing patients who report potential exposure to viral hepatitis or patients who present with symptoms of acute viral hepatitis, a range of psychosocial issues may be addressed in a timely and sensitive manner. For example, risk behaviours may be explored and appropriate referral to community support or counselling services offered (Chapter 15).

The anxieties and concerns of the patients regarding transmission to sexual partners and family can be addressed by a discussion of modes of transmission and preventive strategies (Case study 1; Chapters 2 and 3). Describing potential health outcomes, as well as the process of determining infection status, may also assist the patient.

Prevention

Prevention of perinatal transmission

Newborn babies of HBV-infected mothers should receive HBIG and be started on a course of HBV vaccination at birth. This strategy effectively prevents transmission of HBV infection. There are no effective strategies to prevent perinatal transmission of HCV, although avoidance of invasive foetal monitoring may be important. Potential benefits of caesarean section have not been proven and there is no place for routine caesarean sections in HCV-infected mothers. Breastfeeding is regarded as safe unless blood is present in the milk.

Immunisation[11]

HAV vaccination is recommended for some populations at high risk (Table 5.5). Screening for immunity prior to immunisation is recommended for persons born before 1950, for those who spent their childhood in endemic countries (China, South East Asia and Pacific countries) and for those who report previous hepatitis. The recommended schedule is an initial dose with a booster dose 6–12 months later.

HBV vaccine is provided free through the National Immunisation Program to all infants (at birth, two months, four months and six or 12 months) and, in school-based programs, to adolescents between 10 and

TABLE 5.5 Persons for whom hepatitis A vaccine is recommended[11]

(This vaccine is provided free under the National Immunisation Program for Aboriginal and Torres Strait Islander infants living in areas of higher risk [Queensland, Northern Territory, Western Australia and South Australia])

• Travellers to endemic areas
• Visitors to rural and remote Aboriginal communities
• Childcare and pre-school personnel
• The intellectually disabled and their carers
• Health care workers who provide care for substantial populations of Indigenous children
• Sewage and waste disposal workers
• Men who have sex with men
• Injecting drug users
• Persons with chronic liver disease
• Persons with chronic HCV infection
• Sex workers
• People with HBV

TABLE 5.6 Persons for whom hepatitis B vaccination is recommended[11]

• Infants and young children	• Persons with HCV infection
• Young people aged 10 to 13 who have never received a primary course of HBV vaccine	• Persons with clotting disorders who require multiple blood product administration
• Liver transplant recipients	• Health care workers with direct patient or human tissue contact
• Household contacts of people with acute HBV or HBV carriers	• Prisoners and staff of long-term correctional facilities
• Sexual contacts of people with acute HBV or HBV carriers (these people should also be offered hepatitis B immunoglobulin)	• Residents and staff of facilities for persons with intellectual disabilities
• Men who have sex with men	• Embalmers
• Injecting drug users	• Haemodialysis patients
• Individuals adopting HBsAg+ children	• At-risk emergency services personnel, police and waste disposal workers
• People with HIV infection or impaired immunity	• People with chronic liver disease
• Tattoists and body piercers	• Sex workers

13 years of age who have not previously been vaccinated. HBV vaccination is also recommended for populations at high risk (Table 5.6). Vaccination is safe for people with HIV, although protection is likely to be weak or transient compared with the highly effective, protective immunity produced among immunocompetent individuals. Serological confirmation of post-vaccination immunity is not required after routine child and adolescent vaccination but is recommended for some high risk individuals (see current edition of the Australian Immunisation Handbook).[11] Booster doses are not recommended in immunocompetent people but may be required for those with impaired immunity, who should have regular monitoring of their anti-HBs levels at six to 12 month intervals.

The recombinant HBV vaccine entails an initial dose followed by two further doses at one and six months. The vaccination schedule may vary according to likelihood of compliance. The rapid schedule (0, 7 and 21 days) may be more appropriate in highly mobile populations.[11] Access to free HBV vaccination is available through sexual health clinics, some councils and other selected clinics.

A combined vaccine for HAV and HBV is available and should be considered for individuals at risk of both infections and for people with chronic HCV. Such persons may include health care workers and students, long-term visitors to endemic countries, men who have sex with men, injecting drug users, prisoners and prison workers. There is no vaccine for HCV.

Education and harm minimisation

Education about risk reduction and harm minimisation methods may lower the incidence of hepatitis in at-risk individuals. Chapter 3 discusses prevention and harm reduction messages.

Concurrent assessment for drug treatment programs may be considered for those who inject drugs. Referral to injecting drug user groups (such as the Australian IV League or local equivalent) for education and support may also be considered (Chapter 15).

Travellers require accurate advice and appropriate vaccination or passive immunisation prior to travelling to endemic areas.

Hand-washing is important to prevent transmission of HAV.

Summary

The primary care clinician has a key role in identifying cases of acute hepatitis and facilitating the clinical monitoring and management of infected individuals. Specialist referral is advised if signs of acute liver failure develop or if the diagnosis is unclear. Following a possible exposure to viral hepatitis or a diagnosis of acute viral hepatitis, prevention measures and harm minimisation strategies should be fully explored to reduce ongoing transmission.

References

1 National Centre for HIV Epidemiology and Clinical Research (NCHECR). HIV/AIDS, viral hepatitis and sexually transmitted infections in Australia. Annual Surveillance Report 2006. Sydney: NCHECR, 2006.

2 Ministerial Advisory Committee on AIDS, Sexual Health and Hepatitis: Hepatitis C Sub-Committee. Hepatitis C virus projections working group: estimates and projections of the hepatitis C virus epidemic in Australia 2006. Sydney: University of New South Wales, 2006.

3 Alter HJ, Seef LB. Recovery, persistence and sequelae in hepatitis C infection: a perspective on long-term outcome. Sem Liver Disease 2000;20:17–35.

4 Micallef JM, Kaldor JM, Dore GJ. Spontaneous viral clearance following acute hepatitis C infection: a systematic review of longitudinal studies. J Viral Hepatitis 2006;13(1):34–41.

5 Matthews G, Robotin M (eds). B Positive: all you wanted to know about hepatitis B - a guide for primary care providers. Sydney: Australasian Society for HIV Medicine and Cancer Council of NSW, (at press).

6 Lok AS, McMahon BJ. Chronic hepatitis B. Hepatol 2007;45(2):507–39.

7 Wiegand J, Buggisch P, Boecher W, Zeuzem S, Gelbmann CM, Berg T, et al. for the German HEP-NET Acute HCV Study Group. Early monotherapy with pegylated interferon alpha-2b for acute hepatitis C infection: the HEP-NET acute-HCV-II study. Hepatol 2006;43(2):250–6,

8 Zekry A, Patel K, McHutchison JG. Treatment of acute hepatitis C infection: more pieces of the puzzle? J Hepatol 2005;42(3):293–6,.

9 Kamal SM, Fouly AE, Kamel RR, Hockenjos B, Al Tawil A, Khalifa KE.et al. Peginterferon alfa-2b therapy in acute hepatitis C: impact of onset of therapy on sustained virologic response. Gastroenterol 2006;131(3):979. Published erratum on Gastroenterol 2006;130(3):632–8.

10 Dore GJ, Kaldor JM, McCaughan GW. Systematic review of the role of the polymerase chain reaction in defining infectiousness among people infected with hepatitis C virus. Br Med J 1997;315:333–7.

11 National Health and Medical Research Council. The Australian Immunisation Handbook. 9th edn. Canberra: Department of Health and Aged Care; 2008.

Signs and symptoms of chronic HIV disease

6

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Introduction

Since the mid-1990s, the clinical manifestations of chronic human immunodeficiency virus (HIV) infection have changed dramatically amongst people with access to combination antiretroviral therapy.[1,2] This chapter covers the 'classical' signs and symptoms of unmodified HIV disease that can provide a basis for an initial clinical diagnosis. It also discusses the clinical issues seen in the large proportion of people with HIV infection who are now taking combination antiretroviral therapy.

Acquired Immunodeficiency Syndrome (AIDS) was characterised in the early 1980s before HIV had been identified. The Centers for Disease Control (CDC) in the USA listed a group of secondary conditions that suggested immunodeficiency which had been identified in clusters. The original case definition of AIDS has been modified somewhat over the years but it remains a list of conditions, now rare in the Australian setting, that are seen predominantly in people who present late with untreated HIV infection and severe immunodeficiency (Table 6.1). AIDS remains notifiable in Australia, but the prognostic significance is less important in treated populations than other markers of HIV, such as CD4 cell count and viral load (Chapter 10).

Many HIV specialist clinicians and people with HIV infection now favour terms such as 'early' and 'late' HIV disease rather than 'AIDS'. Alternatively, clinicians may describe patients in terms of their surrogate markers and clinical status.

When should HIV be considered in the differential diagnosis?

The focus of this chapter is on specific clinical illnesses, laboratory abnormalities and aberrant responses to therapeutic interventions which may indicate HIV infection as a differential diagnosis to the astute clinician (see Table 6.2). Whenever HIV antibody testing is recommended, there should be an awareness of the psychosocial impact of testing and full pre-test discussion should be undertaken (Chapter 9).

Key points

- Clinical diagnosis of HIV infection requires consideration of HIV aetiology in relation to a range of sub-acute, chronic and acute clinical presentations.
- Chronic symptoms of immune activation (e.g. lymphadenopathy, night sweats, fever) may indicate HIV infection.
- Mild, HIV-related immune deficiency may be indicated by persistent oral or skin conditions.
- Laboratory markers such as thrombocytopenia, neutropenia and lymphopenia may suggest HIV infection.
- The incidence of 'classical' AIDS-defining illnesses has fallen dramatically in Australia since the introduction of combination antiretroviral therapy. These conditions are now most common among patients with advanced HIV disease whose HIV status has been undiagnosed.
- Combination antiretroviral therapy has dramatically altered the course of clinical HIV disease. Immune reconstitution illness and treatment-related side-effects are now common causes of clinical symptoms.

A differential diagnosis of HIV may be considered in individuals who report exposure risks for HIV infection during general health assessments. Testing for HIV is commonly part of the management of pregnant women and as part of screening for sexually transmissible infections (STIs). HIV antibody screening is performed as part of blood, tissue and organ donation, prior to military service and may be requested for some visas and work permits. Consideration should be given to HIV infection amongst other risks for immunosuppression prior to live viral vaccinations, at consideration of transplantation and when prescribing immunosuppressant medications. The assessment of HIV risk and subsequent counselling and management of the patient are detailed in Chapters 2, 3 and 9.

Immune activation symptoms – primary infection

The acute retroviral syndrome characteristic of primary HIV infection includes prominent features of immune activation, such as fever, night sweats, myalgia, arthralgia and lymphadenopathy (Chapter 4).

For a proportion of people with HIV, these symptoms may become chronic, indicating persistent activation of the immune system.

Clinical latency

The long phase of clinical latency that follows primary HIV infection conceals substantial virological and immunological activity.[3] Some HIV-infected people are able to control HIV replication and to maintain CD4 cell levels for an extended period; they are known as 'slow progressors' or 'long-term non-progressors'. A small but significant proportion of people with HIV have been infected for close to 20 years but still have low viral loads and near normal immune function. For most untreated people with HIV infection, however, there is a gradual decrease in CD4 cell numbers over a period of 5–10 years, when clinical HIV disease becomes apparent.

Mild immunodeficiency

A variety of infectious agents can become more troublesome relatively early in the course of untreated HIV infection when the CD4 cell count falls below 500 cells/μl (Tables 6.1–6.3). Most of these are other chronic viral infections and the appearance of clinical disease in people with HIV infection is usually due to re-activation of latent virus rather than new infection.

Shingles

An episode of classical herpes zoster can often occur quite early in the course of chronic HIV infection, particularly after another illness such as a respiratory infection. It can be managed effectively using aciclovir, valaciclovir or famciclovir. Admission to hospital for intravenous aciclovir may be warranted for those with severe pain or multi-dermatomal or disseminated herpes zoster.

Herpes simplex

Orofacial and anogenital herpes simplex outbreaks occur more frequently in people with HIV infection. These may be extensive and persistent. In people with more advanced disease, the ulcers often coalesce, especially around the anus, to form large, extremely painful ulcers. Herpes lesions continuously present for more than a month were part of the original case definition for AIDS. However, the advent of effective treatment for the herpes simplex virus (HSV) means that symptomatic chronic herpes is now rare. Recurrent or persistent herpes may be a sign of HIV infection in undiagnosed patients and may be a trigger for risk assessment and further physical examination.

Kaposi's sarcoma

This malignancy, which in the days before the HIV epidemic was seen only in elderly men, is now known to be caused by human herpesvirus type 8 (HHV-8). HHV-8 appears to be sexually transmitted. Additionally, high levels of virus have been demonstrated in saliva. In Africa, horizontal transmission among children may be important. In Australia, Kaposi's sarcoma is a sign of HIV infection, especially in healthy men.

Kaposi's sarcoma is most commonly manifested as purple, nodular lesions on the skin or oral mucosa (Figure 6.1) but can occur in visceral organs such as the lungs and the gastrointestinal system. Unpleasant or unsightly local tumours are amenable to local therapy, intralesional chemotherapy or palliative

TABLE 6.1 AIDS indicator diseases

• Candidiasis (oesophagus)
• Cryptococcosis (invasive)
• Cervical carcinoma (invasive)*
• Cryptosporidiosis with diarrhoea > 1 month
• Cytomegalovirus of retina, brain, spinal cord, gastrointestinal tract
• Herpes simplex mucocutaneous ulcer > 1 month
• HIV-associated dementia, disabling cognitive ± motor dysfunction
• HIV-associated wasting loss >10% body weight plus diarrhoea, weakness and fever > 30 days*
• Isosporiasis with diarrhoea > 1 month*
• Kaposi's sarcoma
• Lymphoma, brain or non-Hodgkin's (B-cell or immunoblastic)
• Mycobacterium avium complex or kansasii (disseminated)
• Mycobacterium tuberculosis disseminated or pulmonary*
• *Pneumocystis jiroveci* pneumonia
• Pneumonia (recurrent bacterial)*
• Progressive multifocal leukoencephalopathy
• Salmonella septicaemia (non-typhoidal, recurrent)*
• Toxoplasmosis (brain)

* Requires HIV diagnosis.

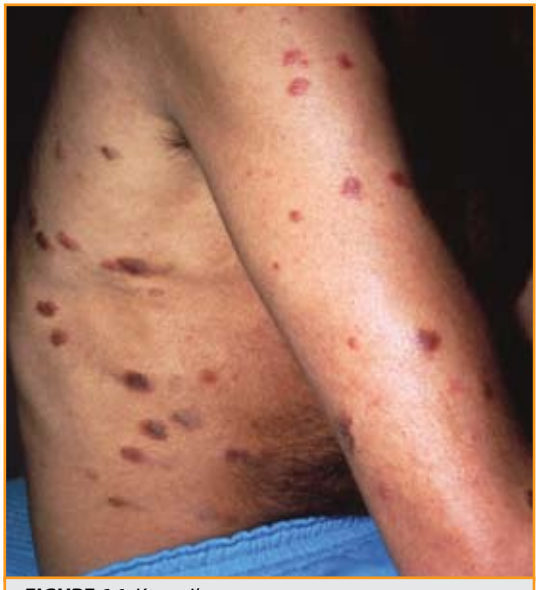

FIGURE 6.1 Kaposi's sarcoma

radiotherapy. For progressive disseminated disease, systemic chemotherapy is often beneficial but the mainstay of management involves restoration of immune function by controlling HIV replication through antiretroviral therapy.

Anogenital warts and squamous dysplasia

Anogenital warts are common in people with HIV infection and usually represent re-activation of a previous viral infection of the skin with the human papillomavirus (HPV). In patients without an HIV diagnosis, anogenital warts, especially recurrent warts, indicate the need for HIV risk assessment and further examination.

Anal or genital warts in the presence of HIV infection may be conservatively managed, particularly if the person is considering the institution of antiretroviral therapy for HIV. Warts often regress spontaneously.

Standard methods of treatment may be employed. In the case of surgically removed anal warts, biopsy tissue should be sent for histopathology. Squamous dysplasia is often seen and indicates that close follow-up is required. There is some evidence to suggest that squamous carcinoma of the anal canal is more common in people with HIV and is probably related to HPV infection.

Cervical carcinoma is significantly more prevalent in women with HIV and is also probably related to HPV infection. It is generally recommended that Papanicolaou smear cytology be performed every 6–12 months in this group, with management of abnormalities undertaken according to the usual approach.

Molluscum contagiosum

These nodular lesions with a central punctum commonly occur on the face, neck or anogenital area. Although it does occur in people without HIV infection, persistent appearance of molluscum contagiosum in adults should lead to consideration of HIV infection. Molluscum contagiosum is caused by a poxvirus and, in people with HIV infection, its incidence and severity relate to the degree of immunosuppression. The condition is diagnosed clinically. Differential diagnosis in the patient with HIV infection would include cutaneous cryptococcosis infection and, in people from South East Asia, infection with Penicillium marneffei. Lesions commonly regress with immune recovery due to antiretroviral therapy or may be controlled with local therapy.

Dermatoses

Rashes are common in people with HIV infection at any level of immune function. Persistent, new or unusual skin conditions may be the first symptom of HIV infection. The clinician should be alert to the possibility of HIV infection and undertake a full risk assessment and physical examination if extensive, atypical or persistent rash is encountered.

TABLE 6.2 Alarm bells suggestive of HIV infection

Clinical conditions where HIV should be considered
• Oral candidiasis (especially in the absence of antibiotic use)
• Atypical mononucleosis syndrome (not EBV- or CMV-related)
• Aseptic meningitis with severe systemic symptoms
• Difficult to manage psoriasis, dermatoses
• Tuberculosis
• Non-Hodgkin's lymphoma
• Cerebral space-occupying lesions
• Persistent lymphadenopathy and symptoms of immune activation
• Chronic vaginal thrush
Laboratory abnormalities where HIV should be considered
• Thrombocytopenia, neutropenia, lymphopenia without cause
• Anergy unexplained
• Hypergammaglobulinemia new or unexplained
Therapeutic responses where HIV should be considered
• Pneumonia unresponsive to standard therapy
• Recurrent antibiotic-associated rash

TABLE 6.3 Febrile syndromes in people with HIV infection

Differential diagnosis of undifferentiated fever in the patient with HIV infection

Current or nadir CD4 cell count < 200 cells/μL	Current or nadir CD4 cell count ≥ 200 cells/μL
• Disseminated Mycobacterium avium complex	• Bacterial infections, e.g. pneumonia, septicaemia
• Pneumocystis jiroveci pneumonia	• Drug fever
• Cryptococcal infection	• Tuberculosis
• CMV infection	• Disseminated Salmonella, Campylobacter infection
• Toxoplasmosis	• Fever associated with malignancy, e.g. lymphoma
• Less common infections, e.g. Histoplasma, Bartonella	

The most common form of rash associated with HIV infection is seborrhoeic dermatitis (Figure 6.2) which is seen in most people at some stage in the disease. It occurs at the classical sites of scalp, ears, eyebrows, chest, axillae, groin and feet. Standard treatment with steroid creams or topical ketoconazole is often effective in controlling the problem but recurrence is usual. This condition generally improves dramatically when effective antiretroviral treatment is instituted. Dermatophyte infections are also very common and can sometimes be difficult to differentiate from seborrhoea. These infections can be very extensive, particularly on the feet, and secondary bacterial infection is common. Misdiagnosis of a dermatophyte infection leads to ineffective treatment with steroid creams that may in turn modify the clinical appearance of the condition.

Other puzzling rashes are often seen in people with HIV infection. Early skin biopsy may be a useful guide when response to therapy is inadequate. Eosinophilic pustular folliculitis is one such pruritic papular condition that commonly occurs on the upper arm and chest for which phototherapy has induced response in many patients. Antiretroviral therapy often leads to resolution of dermatoses.

Psoriasis occurs in people with HIV infection with the typical erythematous scaly lesions occurring over elbows, hands and feet. The guttate form is also common. Pre-existing psoriasis can be exacerbated by HIV infection and newly diagnosed psoriasis has also been described. Immune recovery has been shown to improve these psoriatic lesions in people with HIV infection.

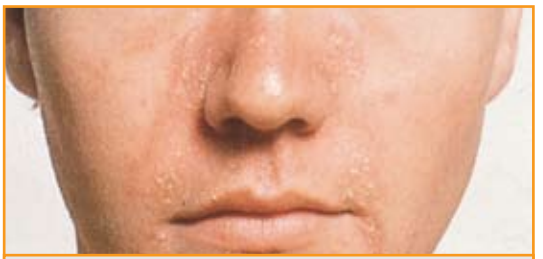

FIGURE 6.2 Seborrhoea

Oral conditions

A condition called oral hairy leukoplakia is commonly seen prior to serious HIV-related opportunistic infections. It is manifest as distinctive white areas on the lateral margins of the tongue that cannot be rubbed off with gauze (unlike candidiasis). Its aetiology remains unclear, although one theory is that oral hairy leukoplakia is a manifestation of mucosal Epstein-Barr virus (EBV) infection. The condition is almost pathognomonic of HIV infection and will sometimes prompt the consideration of HIV testing when noticed by an astute dentist or medical clinician at routine examination.

Oropharyngeal candidiasis becomes more common in HIV disease when immunosuppression occurs. Often it has the classical appearance of cheesy plaques that can be rubbed off; occasionally, it is subtler with an area of slightly furry reddening, particularly on the palate. Candidiasis is much less common in HIV-infected individuals who are taking effective antiretroviral therapy. Mycological examination of a wet swab will confirm the diagnosis. Treatment is only required when the condition is symptomatic, and topical amphotericin lozenges will often be effective for mild disease. If the disease is more severe and persistent, a course of oral fluconazole will usually control it for a period.

Aphthous mouth ulcers appear to be more common and more persistent in people with HIV than among the HIV-negative population. These ulcers may be quite large and are painful. When simple measures are ineffective, topical steroids appear to be beneficial in a proportion of patients and, in very severe cases, thalidomide may be useful with appropriate precautions.

A particularly aggressive form of gum disease, known as acute necrotizing ulcerative gingivitis is commonly seen in the months before clinical progression of HIV. Skilled care from a dentist who is sensitive to

the needs of people with HIV infection is required to prevent the loss of otherwise healthy teeth. Once again, the condition is likely to abate significantly with the commencement of effective antiretroviral therapy for HIV infection. Severe gingivitis may be suggestive of possible HIV infection and may prompt further enquiry in the undiagnosed patient.

Hepatitis co-infection

As other HIV-related opportunistic infections are prevented or controlled, liver disease secondary to co-infection with HBV or HCV and liver toxicity from antiretroviral agents have become more prominent. Co-infection may cause difficulty tolerating HIV antiretroviral therapy, especially in the initial immune reconstitution phase when hepatic transaminase levels may rise. Close monitoring of liver function is required at this time.[4]

The presence of HIV leads to more aggressive HCV disease and higher HCV viral load, and the use of interferon and ribavirin in people with co-infection requires consideration of treatment for the hepatitis prior to initiation of antiretroviral therapy if possible, or modification of the antiretroviral regimen to enable concomitant treatment with pegylated interferon and ribavirin. Careful monitoring of liver function tests and markers of HCV infection (polymerase chain reaction and genotype), and avoidance of other hepatotoxins, such as alcohol, is recommended (Chapters 10 and 11).

In the person with HIV infection, infection with HBV may be associated with flares of hepatitis during immune deficiency, especially if lamivudine (which is active against both HIV and HBV) is withdrawn. Optimal management of HIV-HBV co-infection has not yet been defined.

Immune reconstitution disease

In untreated people with advanced HIV infection (CD4 cell count below 100 cells/μL), marked immunodeficiency inhibits the inflammatory response that would normally occur to a variety of infectious agents such as cytomegalovirus (CMV), HCV and Mycobacterium avium complex. When treatment reduces HIV viral load, there is rapid restoration of the ability to mount inflammatory reactions. Consequently, infectious agents that have 'peacefully co-existed' with the host during extreme immunodeficiency are met with a marked inflammatory response, and clinical disease becomes apparent where few signs or symptoms were evident previously (Figure 6.3). This phenomenon has been named 'immune reconstitution disease' and was first described in Australia.[5] An immune reconstitution illness is usually transient because the inflammatory effect is ultimately successful at combating the infectious agent. However, immune reconstitution illnesses can be clinically significant while present. In the case of CMV retinitis, vision can be permanently impaired by an episode of intense inflammation during immune reconstitution.

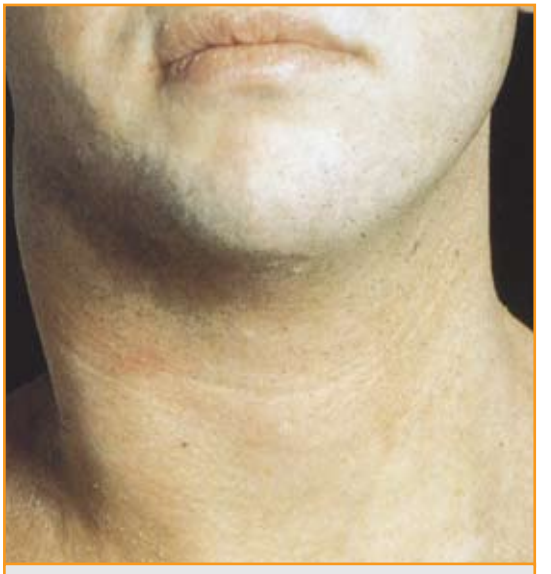

FIGURE 6.3 Immune reconstitution and *Mycobacterium avium* complex (MAC)

When a patient presents with new symptoms soon after starting antiretroviral therapy, immune reconstitution should be considered as a possible cause and appropriate referral and investigation is advised.

Severe immunodeficiency

More serious, life-threatening opportunistic infections generally appear when the CD4 count falls below 200–250 cells/μL (Tables 6.1–3).

Pneumocystis jiroveci pneumonia

In the untreated person with HIV, Pneumocystis jiroveci pneumonia (previously known as Pneumocystis carinii pneumonia, PCP) is often the first serious opportunistic infection. In the early days of HIV management, PCP was often fatal. Risk of PCP increases when the CD4 cell count falls below about 200 cells/μL.

It is often insidious in onset and typically presents as a persistent, dry cough and exertional dyspnoea, sometimes accompanied by mild-to-moderate constitutional upset with fevers, sweats, lethargy and fatigue. If left untreated, respiratory function can decline dramatically, leading to the need for ventilation and intensive care management. The diagnosis can often be made from a chest X-ray and is confirmed by microbiological examination of sputum induced by inhalation of nebulised hypertonic saline. The condition is now uncommon in people with an HIV diagnosis because simple and effective prophylaxis is available. Double-strength co-trimoxazole taken once daily by people with CD4 cell counts below 250 cells/μL has dramatically reduced the incidence of this condition.

In Australia and other countries where antiretroviral therapy and PCP prophylaxis are widely available, PCP is now most often seen in people with longstanding, but undiagnosed, HIV infection.

Mycobacterium avium complex (MAC)

Systemic infection with atypical mycobacteria is commonly seen in people with CD4 cell counts below 50–100 cells/μL. It produces a syndrome of non-specific malaise, often accompanied by night sweats, weight loss, anaemia and sometimes respiratory or abdominal symptoms. Its symptoms merge with those of advanced HIV itself and a high index of suspicion is required. MAC is an important differential diagnosis of non-specific fever in people with HIV infection (Table 6.3). The diagnosis of MAC is confirmed by culture of blood collected in special media. However, the organism is slow to grow, so treatment with a combination of anti-mycobacterial drugs is often commenced presumptively. In those with epidemiological risk factors, tuberculosis should be considered as a differential diagnosis and isoniazid added to presumptive therapy until tuberculosis is excluded.

Upon treatment, significant clinical improvement is usually seen and maintenance therapy is continued indefinitely, unless marked and sustained immune recovery is achieved with antiretroviral treatment. Effective prophylactic regimens for MAC are now available. Azithromycin given as a single dose of 1200 mg weekly is most widely used and is usually commenced when the CD4 cell count is consistently below 100 cells/μL.

Diarrhoeal diseases

Diarrhoea is an extremely common condition in people with HIV infection.

Among patients with known HIV infection, diarrhoea is often related to the adverse effects of antiretroviral medication, particularly some protease inhibitors. When advanced immunodeficiency is present (CD4 cell count below 100 cells/μL), opportunistic infections due to Cryptosporidium and Microsporidium should be considered. Stool examination is recommended if no obvious cause for persistent diarrhoea is found in a person with HIV infection. It is also important to ask the laboratory to look specifically for parasites, such as Microsporidium species, as this requires special processing of the specimen. Colonoscopy and mucosal biopsy may reveal CMV colitis in people with very severe immunosuppression.

Advanced HIV disease is associated with diarrhoea and, if no specific cause is found after a full diagnostic assessment, anti-diarrhoeal agents such as loperamide may be effective. The prolonged use of quite high doses is not uncommon. Bulking agents such as psyllium husk may also be useful.

Non-Hodgkin's lymphoma

People with HIV infection have a 250- to 650-fold increased risk of AIDS-related lymphoma over the background population, with lymphoma occurring most frequently in people with CD4 cell counts below 100 cells/μL. Eighty-five percent of all AIDS-related lymphomas are systemic non-Hodgkin's lymphoma (SNHL), 15% are primary central nervous system lymphoma (PCNSL), while primary effusion lymphomas occur uncommonly. Almost all AIDS-related lymphomas are high-grade diffuse large B-cell (immunoblastic variant) or Burkitt's-like lymphomas. EBV has a clear pathogenetic role in PCNSL, a probable role in SNHL, and also may be involved in primary effusion lymphoma where HHV-8 is implicated in disease pathogenesis. Isolated enlarged lymph nodes, systemic febrile illnesses and focal neurological abnormalities are among the common presentations. Referral to specialists in oncology and HIV-related malignancies is recommended. Chemotherapy, radiotherapy and combination antiretroviral treatment provide the usual basis of therapy.

Neurological conditions

The direct effects of HIV on the brain can be evident at any level of immune function but may become more prominent as the disease progresses. Minor cognitive deficits are quite common and, in the absence of treatment, a significant minority of people with HIV infection will develop a clinical brain disorder. In the early phase, this may manifest as a syndrome that is almost indistinguishable from mania, but a progressive, subcortical dementia commonly evolves. The condition is characterised particularly by extreme slowness of movement and mentation which are severely disabling. HIV-associated dementia often responds dramatically to antiretroviral treatment; however, the regimen must be carefully chosen as only some of the available agents penetrate the blood-brain barrier.

Space-occupying lesions of the brain also are relatively common in people with advanced HIV infection. The most likely diagnoses are primary lymphoma of the brain and abscess resulting from reactivation of toxoplasmosis. Toxoplasma abscesses respond to appropriate antibiotic therapy, so early diagnosis is important.

Other neurological conditions that were common in the days before combination antiretroviral therapy are cryptococcal meningitis and progressive multifocal leukoencephalopathy.

Referral to an infectious diseases physician is recommended when a neurological condition is suspected in a patient with HIV infection.

Body composition changes

Weight loss and preferential loss of lean body tissue is characteristic of progressive HIV infection and was common in people with AIDS in the 1980s and early 1990s. Although this condition is still seen in people who are unable to tolerate antiretroviral medication, or where viral resistance limits its effectiveness, most bodily changes in people with HIV infection now appear to be related to treatment.

Loss of facial and peripheral fat can be striking in people taking antiretroviral therapy, creating a distinctive and easily identifiable appearance (Figure 6.4). Patients may sometimes complain first of 'varicose veins' when their healthy leg veins become more obvious as the surrounding subcutaneous tissue is lost. The latest research suggests that this syndrome may be related in part to prolonged exposure to nucleoside analogue reverse transcriptase inhibitor (NRTI) drugs.[6]

A proportion of people with HIV infection on therapy also develop accumulation of fat in the abdomen and sometimes the 'buffalo hump' over the lower neck posteriorly. Protease inhibitors are associated with marked dyslipidaemia in a high proportion of patients and also may be involved in this fat accumulation.

Psychosocial issues

In cases where clinical signs and symptoms lead to a HIV diagnosis, consideration should be given to the management of psychosocial concerns as well as the clinical manifestations of the infection. Post-test discussion and psychosocial follow-up are fundamental following a positive HIV result and issues for assessment and discussion may include relationships, family, sex, work and disclosure (Chapter 9).

People with HIV infection now face a variety of serious challenges, including new manifestations of HIV-related illnesses and medication-related toxicities. While improved prognosis has led some patients with HIV infection to reassess issues such as education, work and relationships, difficulty with adherence to therapies and chronic toxicities have in some cases led to a re-evaluation of lifestyle, self-image or sense of wellbeing. In addition, the challenges of living with a chronic or life-threatening condition, HIV infection itself and some medications' side effects may induce symptoms of depression or anxiety which require acknowledgment and management (Chapter 10).

FIGURE 6.4 Body composition changes

Conclusion

Although the rate of HIV infection in Australia is relatively low, the primary care clinician may give consideration to HIV infection in relation to a range of conditions, particularly when present in young and otherwise healthy individuals. In the age of combination antiretroviral therapy, clinical diagnosis of HIV infection is likely to lead to improved health and extended lifespan in the patient.

While prescribing antiretroviral therapy requires special training, many people with HIV infection also visit general practitioners, who are ideally placed to detect adverse developments at an early stage and to facilitate optimal therapy. Chapter 10 addresses management of the patient with HIV infection, particularly in regard to antiretroviral therapy, psychosocial management, and support and referral.

References

1 Li Y, McDonald A, Dore G, Kaldor J. Improving survival following AIDS in Australia, 1991-1996. AIDS 2000;14(15):2349–54.

2 Grulich A. Update: cancer risk in persons with HIV/AIDS in the era of combination antiretroviral therapy. AIDS Read 2000;10(6):341–6.

3 Ho DD, Neumann AU, Perelson AS, Chen W, Leonard JM, Markowitz M. Rapid turnover of plasma virions and CD4 lymphocytes in HIV-1 infection. Nature 1997;387:188.

4 Greub G, Ledergerber B, Battegay M, Grob P, Perrin L, Furrer H, et al. Clinical progression, survival and immune recovery during antiretroviral therapy in patients with HIV-1 and hepatitis C virus coinfection: the Swiss HIV Cohort study. Lancet 2000;356:1800–5.

5 John M, Flexman J, French MA. Hepatitis C virus-associated hepatitis following treatment of HIV-infected patients with HIV protease inhibitors: an immune restoration disease? AIDS (US) 1998;12(17): 2289–93.

6 Carr A, Miller J, Law M, Cooper D. A syndrome of lipoatrophy, lactic acidaemia and liver dysfunction associated with HIV nucleoside analogue therapy: contribution to protease inhibitor-related lipodystrophy syndrome. AIDS 2000;14(3):F25–32.

Signs and symptoms of chronic viral hepatitis

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Introduction

Acute infection with hepatitis B virus (HBV) or hepatitis C virus (HCV) can result in chronic hepatitis if the infection persists for more than six months. The rate of spontaneous clearance varies according to the virus, the age at onset of infection and other factors.

Spontaneous clearance of HCV generally occurs during the first six months of infection in approximately a quarter of people with the infection, with the remainder developing chronic hepatitis. Although gradual histological progression occurs in most people, the condition is often asymptomatic for an extended period of time. Symptoms arise with the development of complications of advanced liver disease, but non-specific symptoms and impaired quality of life are common among those with earlier stages of liver disease. Cirrhosis occurs in an estimated 15–20% of people who develop chronic HCV infection, 15–40 years after the original infection. Among those who develop cirrhosis, liver failure occurs in 20–30% and hepatocellular carcinoma (HCC) develops in 10–15% over 10 years.[1] Estimates of disease progression in hepatitis C are outlined in Figure 7.1.

The natural history of HBV infection is primarily determined by the age of the person at the onset of infection. When acquired at birth or during early childhood, the risk of developing chronic infection is high, with only 2% of infants spontaneously clearing the virus within three years of infection and 15% clearing the virus within 20 years. Among people with perinatally-acquired HBV, 40–50% of males and 15% of females die from the liver-related causes.[2]

In the case of adult-acquired HBV infection, however, the situation is reversed, with spontaneous clearance being the rule. Acute liver failure occurs rarely, and only 3–5% of adults with acute infection go on to develop chronic HBV infection. In many cases, chronic HBV infection does not result in symptoms or long-term problems, although 20–30% of people will progress to cirrhosis.

Key points

- The presence of significant liver disease in patients may not be apparent from symptoms or clinical examination. Conversely, multiple symptoms in chronic hepatitis infection do not necessarily mean the existence of significant liver disease.
- Progressive liver disease in chronic hepatitis B often involves hepatic 'flares', whereas progressive disease is often asymptomatic in chronic hepatitis C.
- There is a poor correlation between biochemical and virological markers of chronic viral hepatitis and symptoms and signs, particularly in chronic hepatitis C.

These differences in outcome between perinatal and adult-acquired infection are outlined in Figure 7.2. Of those with compensated cirrhosis, 20–30% will develop liver failure (decompensated cirrhosis) and 10–20% will develop HCC over the next ten years. Survival rates are high among those with compensated cirrhosis but much lower among those with liver failure (85% versus 25% at five years).

Symptoms and signs of chronic viral hepatitis

Chronic viral hepatitis is frequently hidden due to the asymptomatic nature of liver disease in a large proportion of people and the slowness or absence of progression to advanced liver disease. The absence of symptoms and abnormal clinical signs, therefore, does not exclude significant liver disease. However, early diagnosis and treatment may improve prognosis and, where appropriate, patients should be offered treatment options.

Although there is a great deal of overlap, symptoms and signs of chronic viral hepatitis can be divided into those associated with:

- Early or slowly progressive liver disease
- Progressive liver disease
- Advanced liver disease complications
- Extrahepatic manifestations

In this classification, 'early or slowly progressive liver disease' includes people with chronic hepatitis C who progress slowly and may have early fibrosis.

'Progressive liver disease' covers people who progress to cirrhosis or, in the case of chronic HBV infection, have clinical evidence of progressive disease such as hepatitis 'flares' but retain adequate liver function (e.g. compensated cirrhosis).

'Advanced liver disease complications' includes people who have developed clinical liver failure (decompensated cirrhosis, e.g. hepatic encephalopathy and failure of synthetic function with increases in International Normalised Ratio [INR]), portal hypertension (e.g. ascites, oesophageal varices) and hepatocellular carcinoma (HCC). 'Extrahepatic manifestations' refers to a broad range of clinical conditions associated with either chronic hepatitis B or chronic hepatitis C.

Clearly these groups are not mutually exclusive. For example, it is possible to have progressive liver disease and extrahepatic manifestations of chronic hepatitis. In addition, there may be little clinical distinction between 'early or slowly progressive disease' and 'progressive disease'. A long asymptomatic phase followed by signs associated with cirrhosis or decompensation is not uncommon.

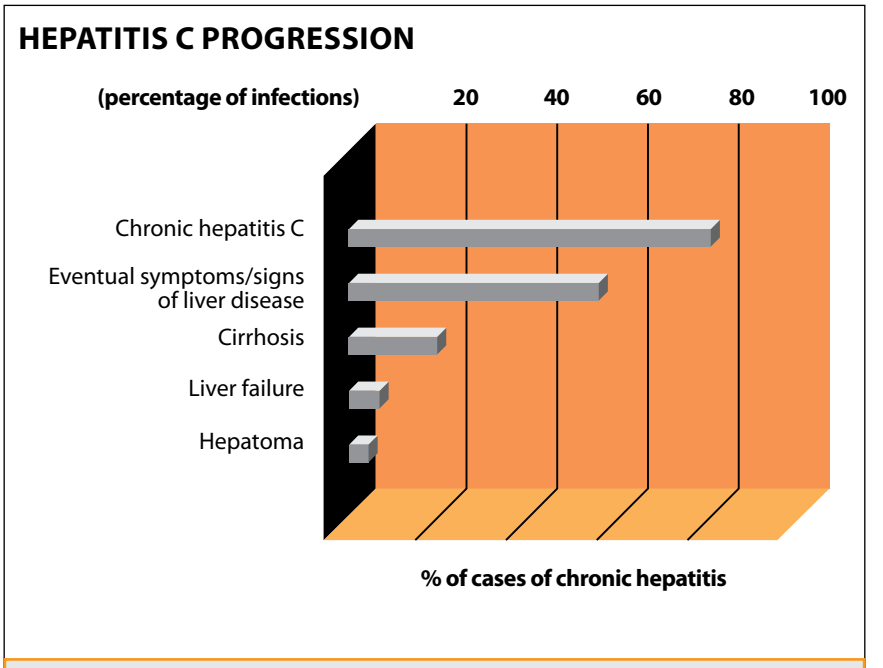

FIGURE 7.1 The proportion of HCV-infected persons who develop complications.

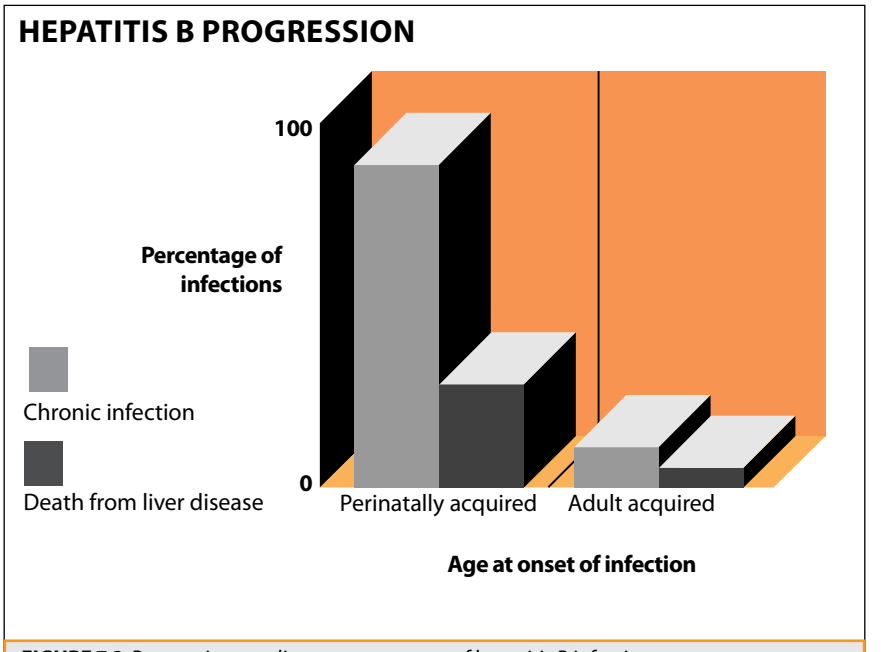

FIGURE 7.2 Prognosis according to age at onset of hepatitis B infection.

Early or slowly progressive liver disease

Symptoms of chronic viral hepatitis associated with early and/or slowly progressive liver disease are generally non-specific. Individuals frequently complain of tiredness, anorexia, nausea, intolerance to fatty foods, and abdominal discomfort, particularly in the right upper quadrant region. Others report general feelings of being unwell but are unable to elaborate further. Fevers and night sweats can also occur.

A number of recent studies have shown that people with chronic HCV infection score poorly on many quality-of-life parameters, including a range of physical and psychological measures of wellbeing. Again, these impairments are relatively non-specific, and include reductions in general health perception, mental health, physical function, social function and vitality. These measures may also be impaired in many people with chronic hepatitis B. Successful clearance of HCV through antiviral therapy has been shown to improve quality-of-life scores.

The major feature of the symptomatology of early or slowly progressive liver disease in chronic viral hepatitis is its highly variable nature. For many people, this stage of liver disease, which may be the only stage they experience, is completely asymptomatic. On the other hand, many people have considerable symptoms despite the presence of mild liver disease or the absence of biochemical evidence of liver inflammation (normal alanine aminotransferase [ALT] and asparate aminotransferase [AST] levels). In fact, in chronic hepatitis C there is little correlation between the ALT level and presence of symptoms. Furthermore, the stage of liver disease (prior to liver failure) and the viral load in chronic hepatitis C have a poor association with the extent of symptoms.

People with early or slowly progressive liver disease generally have few clinical signs associated with their chronic viral hepatitis. The most common clinical examination reveals either no abnormal findings or mild hepatomegaly. Presence of peripheral stigmata of chronic liver disease, such as multiple spider naevi and palmar erythema, would generally indicate cirrhosis.

Progressive liver disease

Although the vast majority of people with chronic viral hepatitis will not develop advanced liver disease complications, many will eventually have progressive liver disease. The symptoms covered above may also be present in progressive liver disease.

In chronic hepatitis B, particularly in the case of perinatal or early childhood infection, a prolonged asymptomatic period (immune tolerance phase) is followed by a more symptomatic period (reactivation-clearance phase) in which flares of clinical hepatitis may occur as the body's immune system attempts to clear infection.[2] These flares are generally milder than an acute hepatitis B clinical presentation, however, they often consist of similar symptoms and signs. These include lethargy, nausea, anorexia, food intolerance, abdominal discomfort and jaundice. These clinical flares in chronic hepatitis B are closely associated with biochemical evidence of increased hepatic inflammation. Marked elevations of ALT and AST together with increased serum bilirubin levels are often seen. A small proportion of people each year in this reactivation/clearance phase will 'seroconvert', initially from hepatitis B 'e' antigen positive (HBeAg+) to HBeAg-negative (generally with development of anti-HBe). In some cases there is subsequent loss of hepatitis B surface antigen (HBsAg). People with frequent flares who have not seroconverted may experience faster disease progression and are at high risk of cirrhosis and HCC. In addition, people who have entered the clearance phase and seroconverted to anti-HBe can have reactivation of disease at a later date with the emergence of 'pre-core mutant' disease. This stage of hepatitis B is characterised by negative HBeAg but abnormal liver function tests (LFTs) and elevated HBV DNA. This form of chronic hepatitis B is also associated with more aggressive disease. All patients with chronic hepatitis B (HBsAg positive), particularly with abnormal LFTs or elevated HBV DNA (> 103 IU/mL) should be referred for specialist review and consideration of therapeutic intervention.

In chronic hepatitis C, clinical hepatitis flares are rare and people often progress to cirrhosis without development of significant symptoms. Prior to development of liver failure, there may be little to distinguish a person with early or slowly progressive liver disease from a person with progressive liver disease. If present, symptoms are generally non-specific, as with early and slowly progressive liver disease. Factors associated with progressive liver disease in chronic hepatitis C are listed in Table 7.1.[1,3] Peripheral stigmata of chronic liver disease, such as spider naevi, liver nails and palmar erythema, may develop if there is progression to cirrhosis. However, a completely normal clinical examination may also be found in the presence of cirrhosis related to both chronic hepatitis B and hepatitis C.

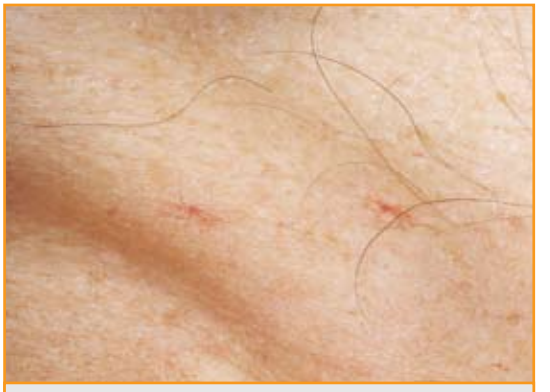

FIGURE 7.3 Spider naevi in chronic hepatitis

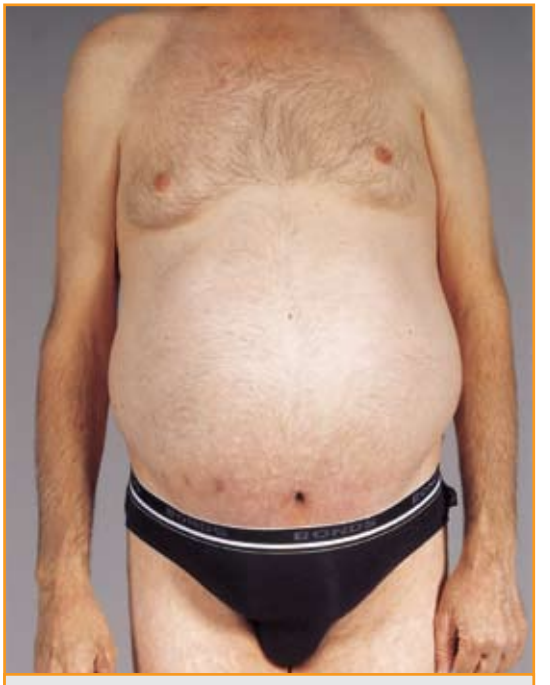

FIGURE 7.4 Decompensated cirrhosis secondary to hepatitis C

Advanced liver disease complications

Advanced liver disease complications of both chronic HBV and HCV infection consist of liver failure (decompensated cirrhosis), often in association with signs of portal hypertension such as refractory ascites and variceal bleeding, and HCC. In chronic hepatitis C, HCC only develops if there is underlying severe fibrosis or cirrhosis. In contrast, as HBV itself is oncogenic, HCC can develop in people with chronic hepatitis B without significant liver fibrosis.

Symptoms and signs of liver failure are the same for chronic HBV and HCV, and are similar to symptoms and signs associated with other causes of decompensated cirrhosis. Consistent with the underlying lack of synthetic function (hypoalbuminaemia and coagulopathy), early symptoms of liver failure may include ankle and mild abdominal swelling, and easy bruising. Increasing lethargy is generally also a feature. Clinical examination should reveal some peripheral stigmata of chronic liver disease, as well as some evidence of either peripheral oedema or ascites. Later signs may include jaundice, which indicates a poor prognosis in the presence of liver failure, loss of hair and gynaecomastia. Clinical evidence of portal hypertension may include abdominal venous distension, splenomegaly and ascites. Patients who have ascites may develop spontaneous bacterial peritonitis (SBP). Patients with unexplained fever or encephalopathy should raise the suspicion of SBP and they should be referred for diagnostic paracentesis. In addition, the presence of peripheral neuropathy and cerebellar ataxia may suggest alcohol as a contributing cause of liver disease.[4]

A history of haematemesis in a person with other evidence of advanced liver disease suggests the presence of oesophageal varices related to underlying portal hypertension. Hepatic encephalopathy also may be present in advanced liver disease and may be subclinical in early stages. A history of reversal of diurnal sleep patterns, forgetfulness or inappropriate behaviour may signal the onset of early hepatic encephalopathy. Presence of either hepatic encephalopathy or oesophageal varices indicates a poor prognosis.

Table 7.2 summarises the different signs and symptoms related to stages of liver disease in chronic hepatitis B and C.

Extrahepatic manifestations

Extrahepatic manifestations, although uncommon, represent clinically important aspects of hepatitis B and C (Table 7.3). Specific treatment can be directed towards these conditions.

Dermatological presentations include porphyria cutanea tarda (PCT), lichen planus and vasculitic rashes associated with cryoglobulinaemia. These presentations should alert the clinician to the possibility of chronic viral hepatitis. In patients with PCT, which is typically associated with chronic hepatitis C, blistered lesions, which are exacerbated by exposure to the sun, occur on the dorsum of the hands and forearms, and ferritin levels are often mildly elevated. These patients respond very well to venesection.

Rheumatological manifestations include arthropathy, Sjogren's syndrome and polyarteritis nodosa. A high serum globulin level, often associated with positive antinuclear antibody (ANA) and rheumatoid factor, may indicate the presence of cryoglobulinemia, which may be associated with systemic complications such as glomerulonephritis and vasculitis.

Other haematological abnormalities include thrombocytopenia and leucopenia. Thrombocytopenia may be the result of hypersplenism or drug therapy, or it may be immune-mediated. Neurological complications may be related to cryoglobulinemia and present with mononeuritis of cranial or peripheral nerves. Thyroid disease may be subclinical. A variety of thyroid diseases have been described in association with chronic viral hepatitis. Patients who test positive for ANA are more prone to developing thyroid disorders, particularly when treated with interferon. These thyroid disorders, however, are generally reversible.

TABLE 7.1 Factors associated with progression to advanced liver disease in chronic hepatitis C

- Age at acquisition of infection (>40 years)
- Heavy alcohol intake (>40 grams/day)
- Male gender
- Longer duration of infection
- Moderate to severe hepatic fibrosis on baseline liver biopsy
- Coinfection with HIV and/or chronic hepatitis B
- Obesity

Note: There is no evidence for an association between HCV viral load and risk of disease progression.

Assessment of the presence and stage of disease

An assessment of the presence and stage of disease often requires a step-wise investigation of serological, virological, biochemical, ultrasonographic and histological markers of viral hepatitis and liver disease. In addition, clinical examination may provide some indication of the stage of disease, particularly when advanced liver disease is present. The results of these investigations may determine access to antiviral treatment, which is funded under Section 100 of the Pharmaceutical Benefits Scheme (Chapter 11).

Serological markers

In hepatitis C, a positive HCV antibody result indicates prior or current infection but does not distinguish between these two conditions.

In hepatitis B, serological testing provides useful information on the presence of active infection. HBsAg is a marker of current infection. It may disappear

TABLE 7.2 Symptoms and signs of chronic viral hepatitis by stage of disease

	Chronic hepatitis B		Chronic hepatitis C	
	Symptoms	**Signs**	**Symptoms**	**Signs**
Early and/or slowly progressive liver disease	Generally none	Often none Hepatomegaly	Often none Lethargy Anorexia Nausea Abdominal discomfort Intolerance to alcohol and fatty foods	Often none Hepatomegaly
Progressive liver disease	Often episodic Hepatic flares	Hepatomegaly Mild jaundice Peripheral stigmata of CLD* (palmar erythema, spider naevi, leuoconychia) if cirrhosis	Often none Lethargy Anorexia Nausea Abdominal discomfort Intolerance to alcohol and fatty foods	Sometimes none Hepatomegaly Peripheral stigmata of CLD* (palmar erythema, spider naevi, leuchonychia) if cirrhosis
Advanced liver disease *CLD – chronic liver disease	Increasing lethargy Fluid retention Bruising Prolonged bleeding	Peripheral stigmata of CLD* Gynaecomastia Ascites/oedema Splenomegaly Distended abdominal veins Bruising Hepatic encephalopathy Jaundice (poor prognostic sign)	Increasing lethargy Fluid retention Bruising Prolonged bleeding	Peripheral stigmata of CLD*. Gynaecomastia Ascites/oedema Splenomegaly Distended abdominal veins Bruising Hepatic encephalopathy Jaundice (poor prognostic sign)

following acute infection or persist in a person who has HBV infection. Anti-HBs appears following the disappearance of HBsAg, and is a marker of both naturally acquired and vaccine-induced immunity. The presence of anti-hepatitis B core (HBc) IgM generally indicates recent infection since it usually appears following acute infection and disappears within a year. Occasionally, anti-HBc IgM may be positive during hepatic flares in people with chronic hepatitis B. Anti-HBc IgG can persist indefinitely following an infection, and signifies exposure to HBV.

Most people exposed to HBV as adolescents or adults clear the infection and will test anti-HBc positive (anti-HBc+) and HBsAg negative. HBeAg is a marker of viral replication and hence infectivity. Anti-HBe generally develops as HBeAg disappears, signalling resolution of acute infection or cessation of replication. More complete clearance of HBV infection is indicated by development of anti-HBs.[2] Refer to Table 7.2 for a summary of serological and virological markers of acute and chronic hepatitis.

Virological tests

HCV RNA testing by polymerase chain reaction (PCR) can indicate the presence of HCV, as well as viral load. A qualitative HCV RNA test generally distinguishes between a person who has chronic hepatitis C and a person who has cleared HCV either spontaneously or during treatment. People who have cleared HCV will continue to test positive for the anti-HCV but will be negative for HCV RNA. Thus, if symptoms and signs of active infection are present in a person with normal serum ALT levels who is HCV antibody positive and HCV RNA negative, a cause other than hepatitis C should be sought.

On the other hand, the vast majority of people with elevated serum ALT levels who test positive for HCV antibody, particularly in the presence of a risk factor

for infection, have active infection (viraemia). In these people, HCV RNA will be positive and of no use in assessing the severity of the disease. A quantitative HCV RNA or viral load test does not provide information on the stage of disease because there is little or no correlation between the HCV viral load and the extent of hepatic fibrosis or risk of disease progression (in distinct contrast to the situation with HIV).[5] However, HCV viral load has prognostic value with regard to response to antiviral therapy, and the HCV genotype is even more predictive of response. HCV viral genotyping is essential in determining the likely response and optimal duration of antiviral treatment (Chapter 11).

HBV DNA is also a marker of active replication and can be assessed quantitatively to predict likely response to antiviral treatment, with low levels being associated with better outcome. The vast majority of people who are HBeAg+ will be positive on HBV DNA testing.

Liver function profile

The serum ALT level may give an indication of hepatic inflammation although levels may be normal despite progressive liver disease. Nevertheless, people with either chronic HBV or HCV who have consistently normal ALT levels are at low risk of progression to cirrhosis.[6] Although people with abnormal ALT levels are at increased risk of progressive liver disease, the level of ALT in chronic hepatitis C is a relatively poor predictor of disease stage or disease progression. In contrast, in chronic hepatitis B recurrently high ALT levels generally indicate more active underlying disease and risk of disease progression. An 'inverted' AST/ALT ratio (higher AST than ALT) may indicate underlying cirrhosis in either chronic HBV or HCV infection.

Albumin level (along with the prothrombin time) gives an indication of the synthetic function of the liver. Hypoalbuminaemia and prolonged prothrombin time indicate decompensated cirrhosis. Evidence from a cohort of people with chronic hepatitis C demonstrated that one of the strongest prognostic measures was albumin level, with higher rates of progression to liver disease complications among people with levels below 35 g/L, particularly if less than 30 g/L7.

Liver imaging

Abdominal ultrasound is used to assess the liver and biliary tree, as other causes of right upper quadrant pain, such as gallstones, often need to be excluded. In addition, abdominal ultrasound helps to screen for HCC and to assess for small amounts of ascites where doubt exists. However, a normal ultrasound does not exclude cirrhosis and this investigation is probably unnecessary in a person with no clinical evidence of chronic liver disease. Alpha-fetoprotein (AFP) level should also be measured at baseline, and monitored every six months, especially in people with chronic hepatitis B and those with cirrhosis, since this is a useful marker of HCC.

TABLE 7.3 Extrahepatic manifestations of chronic hepatitis

Haematological	Cryoglobulinaemia
	Thrombocytopenia
	Granulocytopenia
Renal	Glomerulonephritis
Rheumatological	Sjogren's syndrome
	Polyarteritis nodosa
	Arthropathy
Dermatological	Lichen planus
	Porphyria cutanea tarda
Endocrine	Thyroid disorders
Neurological	Mononeuritis
	Peripheral neuropathy

Other investigations

Other tests are used to identify complications or co-existing problems that may impact on prognosis and treatment decisions. For example, a low platelet count may signal the development of portal hypertension and hypersplenism. The presence of co-existing HBV, HCV or HIV may alter prognosis and treatment options. In treating hepatitis C, hepatitis A virus (HAV) and HBV status should be determined in order to offer vaccinations against superinfection by these organisms, which might worsen prognosis. Similarly, in treating hepatitis B, vaccination against HAV should be considered.

Thyroid function tests are useful to exclude associated thyroid disorders. They also should be conducted prior to antiviral therapy, which has been known to cause toxicity to the thyroid gland. Ferritin levels, alpha-1-antitrypsin, caeruloplasmin and copper levels are measured to exclude the other hepatic pathologies: haemochromatosis, alpha-1-antitrypsin deficiency and Wilson's disease. ANA, anti-smooth muscle (SMA) antibody (SMA) and liver kidney microsomal antibody (LKM) are markers for auto-immune liver disease. Low titres of ANA and SMA may be present in liver disease and may not indicate auto-immune liver disease.

Liver biopsy

Liver biopsy for HCV was previously performed in the majority of patients undergoing assessment for antiviral therapy and was required under Section 100 guidelines. However, the requirement for liver biopsy has now been dropped and it is anticipated that the number of HCV patients undergoing treatment will increase. Liver biopsy is now not necessary in many patients prior to treatment with pegylated interferon and ribavirin. Biopsy remains, however, the definitive test for staging of liver disease and can still be an important tool in determining prognosis and guiding therapeutic decisions in selected patients.

In patients with chronic hepatitis B, liver biopsy remains a valuable investigation as fibrosis progression is far less predictable. Patients are frequently frightened of the invasive nature of this test. In addition, some patients mistakenly believe that they will not receive pain relief if they disclose a history of drug use. This should be addressed by explaining that liver biopsy is the most accurate way to assess the level of liver damage and by offering information about the procedure itself and the expertise of the people performing the biopsy. The role of other non-invasive methods of assessing liver fibrosis remains to be established.

Patients are often puzzled because of the lack of correlation between their symptoms, their blood tests and the serious consequences that can be associated with viral hepatitis. It is important to stress that the absence of symptoms, signs and abnormal ALT levels does not exclude significant liver damage.

A summary of the investigations used in chronic viral hepatitis is provided in Table 7.4.

Clinical examination

Physical examination of patients with suspected or confirmed viral hepatitis consists of general inspection as well as attention to specific signs of chronic liver disease and associated systemic disorders. Examination should include:

- General appearance and mental state of the patient
- Peripheral examination of the hands (for palmar erythema, Dupuytren's contracture, leuchonychia, blistered lesions)
- Examination of the arms or trunk (for abnormal bruising, spider naevi, loss of hair and gynaecomastia)
- Inspection for jaundice, anaemia and parotid enlargement
- Inspection of the abdomen (for evidence of collateral circulation, herniae, hepatomegaly, splenomegaly and ascites)
- Signs of fever or encephalopathy
- Peripheral neuropathy and cerebellar ataxia (which suggest alcohol as a cause of liver disease)
- A history of reversal of diurnal sleep patterns, forgetfulness or inappropriate behaviour, which may signal the onset of early hepatic encephalopathy.

Summary

Chronic hepatitis C and chronic hepatitis B are generally asymptomatic and therefore frequently hidden to both the patient and the clinician. Since a history of risk behaviour is often not disclosed to doctors, a reason to offer testing and diagnosis may not present itself. When symptoms do occur, they are largely non-specific and common symptoms that may be the result of a myriad of diseases. Consequently, the diagnosis of HCV or HBV infection can be easily missed. Being alert to the possibility of chronic viral hepatitis as a cause of many clinical presentations will allow early diagnosis and the offer of treatment.

Blood tests and ultrasound imaging help to assess hepatic function and the presence of complications and other associated disease that may be critical to decisions about prognosis and treatment. However, a lack of symptoms and signs and normal ALT levels does not exclude progressive damage in chronic hepatitis. Liver biopsy may be required in some patients, particularly in the context of chronic hepatitis B, and remains the definitive test to identify the stage of liver disease.

Many patients who are aware that they may have put themselves at risk of contracting HBV or HCV are reluctant to seek a diagnosis, not only because of fear of prejudice and hesitancy in facing a potential serious illness, but also because they are pessimistic about treatment outcomes. It is essential that clinicians present optimism, since in recent years there have been substantial gains in outcomes following treatment. Support groups such as State and Territory Hepatitis C Councils (Chapter 15) can be helpful in providing additional resources to help present a more optimistic view and give patients a better sense of control over this chronic condition.

TABLE 7.4 Investigations in chronic hepatitis	
Investigation	Reason
HCV antibody (anti-HCV)	Exposure to HCV.
Qualitative HCV RNA PCR	Detects presence of HCV.
Quantitative HCV PCR RNA viral load	Provides quantitative HCV viral load measurement.
HCV genotype	Predicts response and optimal duration of treatment.
HBsAg	Indication of natural hepatitis B infection. Occurs with acute infection and may disappear or persist indefinitely. Marker of ongoing infection.
Anti-HBs	Indication of immunity to hepatitis B (from natural infection or vaccination).
HBcAg	Found in the liver only and not usually measured.
Anti-HBc IgM	Marker of recent exposure to hepatitis B virus. Does not persist more than a year following acute infection.
HBeAg	Indication of hepatitis B viral replication and high infectivity. Useful serological marker in the investigation of a person who is found to be HBsAg+.
Anti-HBe	Indication of hepatitis B viral clearance and occurs following loss of HBeAg. May also occur in the presence of 'pre-core mutant' disease in association with abnormal ALT and elevated HBV DNA.
HBV DNA	Indication of viral replication. Quantitative level may help to predict response to antiviral treatment (higher levels associated with poorer outcome) and monitor response to treatment. Useful serological marker in the investigation of a person who is found to be HBsAg+.
ALT	Detection of abnormal ALT suggests antiviral treatment should be considered.
Albumin	Indication of synthetic liver function, i.e. low albumin indicates liver failure.
FBC	Platelet counts may be low due to the progression of fibrosis or portal hypertension.
INR	Indication of synthetic function.
HAV, HBV and HIV serology	To determine need for vaccination to prevent superinfection with HAV and HBV. Presence of HIV alters prognosis.
Thyroid function tests	To exclude associated thyroid disorder and as a baseline investigation prior to interferon treatment (which can cause toxicity).
Ferritin	To exclude haemochromatosis (may reflect severity of liver disease).
U&E and creatinine	Baseline prior to treatment. To exclude possible renal involvement, i.e. glomerulonephritis.
Alpha-feto-protein	Baseline investigation for hepatocellular carcinoma.
Caeruloplasmin and copper	To exclude Wilson's disease.
Alpha-1-antitrypsin	To exclude alpha-1-antitrypsin deficiency.
ANA, SMA, LKM	To exclude autoimmune disease.
Abdominal ultrasound	To assess liver and biliary tree and to screen for hepatoma. Can also be useful to detect small amounts of ascites.
Liver biopsy	May be required to assess severity of disease.

References

1 Seeff LB. Natural history of hepatitis C. Hepatology 1997;26(Suppl 1): 21S–28S.

2 Lee WM. Hepatitis B virus infection. N Engl J Med 1997;337:1733–45.

3 Poynard T, Bedossa P, Opolon P. Natural history of liver fibrosis progression in patients with chronic hepatitis C. Lancet 1997;349:825–32.

4 Bacon BB, Di Bisceglie AM. Viral Hepatitis: Clinical features in liver disease: Diagnosis and management. Churchill Livingstone,2000:79–97.

5 Thomas DL, Astemborski J, Rai RM, Anania FA, Schaeffer M, Galai N et al. The natural history of hepatitis C virus infection: host, viral, and environmental factors. J Am Med Assoc 2000;284:450–6.

6 Marthurin P, Moussalli J, Candranel JF. Slow progression rate of fibrosis in hepatitis C virus patients with persistently normal alanine transaminase activity. Hepatology 1998;27:868–72.

7 Khan MH, Farrell GC, Byth K, Lin R, Weltman MD, George J, et al. Which patients with hepatitis C develop liver complications? Hepatology 2000;31:513–20.

Testing for STIs and STI signs, symptoms and syndromes

8

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Introduction

It is always easier to talk about something rather than nothing. This fact accounts for the emphasis that is always placed on the symptoms and signs of sexually transmitted infections (STIs) rather than on the much more common situation—infectiousness without symptoms or signs. Sexual health physicians of the old school always possessed their mandatory box of battered old slides (scanned more recently into much smarter power point presentations) depicting the ravages wrought by venereal infection. It was believed that the shock and horror value of photographs of the more alarming manifestations of STIs must surely have a salutary effect—to modify risky sexual behaviour and, in our general practice population, to jolt our professional audiences out of complacency. Our faith was misplaced for, in our endeavours, we failed dismally. In fact, we were more than likely counter-productive. We might just as well have filed our depressing old slides in the waste paper basket for all the practical good they did. Our clientele decided the lecture didn't apply to them as they had never observed any of those awful discharges or ulcers on themselves or their sexual partners; our professional audiences at drug company dinners felt cheated that their appetites were temporarily disturbed by the pictures, but breathed a sigh of relief that none of their patients were the sort of people who developed such gross pathology. Meanwhile our patients continued to acquire and transmit asymptomatic STIs and health professionals continued to fail to diagnose them.

This chapter will place due emphasis on testing for asymptomatic STIs and its importance both for good patient management and good public health. It will also briefly mention the common presenting symptoms and signs of STIs and the specific infections likely to cause such clinical presentations.

Testing

STIs are usually asymptomatic for a variable period of time before they declare themselves clinically and during that time people with infection are infectious to their sexual partners. These people with infection, with ongoing sexual exposures, are unwittingly promoting transmission. At the time they are least aware of their own infection, they are most infectious to their partners. Thus, testing for infection in those at risk, and rapid treatment of those found to have an infection are the only practical ways to have any significant impact on preventing significant morbidity developing in the patient with the infection and interrupting ongoing transmission to others.

For these general statements of principle to be achievable in practice two key things are necessary: suitable tests for use with asymptomatic people; and effective treatments. There are well accepted criteria determining the suitability of testing for diseases. They require knowledge of: the disease (or infection); the performance of the test; and the patient population (Table 8.1).

Key points

- Testing for STIs in those at risk and rapid treatment of those found with infection are practical ways to have a significant impact on the prevalence of both STIs and HIV in communities.
- In practice two key elements are necessary: suitable screening tests and effective treatments (or clear management plans) for the individual STI.
- Opportunistic screening means a clinician takes any opportunity which presents itself to screen patients for STIs.
- No laboratory test is perfect: in low-prevalence populations for any infection, false positives can occur with any test no matter how good its overall performance.
- Appropriate information sharing about STIs must always precede screening tests and patients must be helped to understand the associated risks they have run, why testing for a particular STI is relevant for their situation and how the clinician proposes to manage a positive result in their case.
- The presence of HSV infection can increase the transmission and acquisition of HIV, so it may be useful to test for HSV type specific antibodies in MSM and especially HIV-positive MSM.
- Testing patients for the presence of common STIs and perhaps less common but significant STIs like syphilis and HIV is now best practice.

It is known that no test is perfect, and that clinicians often accept pathology results uncritically. But even a cursory glance at Table 8.1 will indicate that these are ideal criteria: very few of the tests currently available, the STIs of interest, and the affected populations meet the standards. Genital chlamydia infections perhaps come closest to the ideal situation but even here there are difficulties. Chlamydia poses a threat to public health and causes significant and expensive morbidity in women (pelvic inflammatory disease [PID], infertility, enhanced risk of ectopic pregnancy, chronic pelvic pain). If the target population is those 15 to 25 years old, the prevalence of infection in most countries (including Australia and New Zealand) is sufficiently high to justify testing and the risk of false positives (always a concern when screening very low prevalence populations) is minimised. Both males and females are often asymptomatic for reasonably extended periods of time before complications develop, and uncomplicated chlamydia is readily amenable to treatment.

A highly effective single dose treatment with very few side effects is available, and in Australia and New Zealand there are ample facilities to deliver treatment. The drawback is that azithromycin is a relatively expensive drug which the public health systems of some countries can't afford. Nucleic acid amplification tests (NAATs) are highly sensitive and specific for *Chlamydia trachomatis* and can be performed with reliable and reproducible results on a range of specimens such as first catch urine (FCU), self-collected urethral or vaginal swab and clinician-collected endocervical swab. The ability to perform non-invasive tests, the simplicity of the test for the clinician and the easy interpretation of results all make it an outstanding test. However, it is an expensive test and although shown to be cost effective for genital chlamydia infection in resource-rich countries, its cost means it is out of reach for most resource-poor countries where the burden of disease due to chlamydia is greatest.

Despite the cost, genital chlamydia infection does approach the ideal criteria for testing. Similarly, in populations with a known moderate to high prevalence for gonorrhoea and trichomonal infection (e.g. some Indigenous Australian and New Zealand communities), testing individuals for these infections is clinically justified. NAATs for *N. gonorrhoeae* and *T. vaginalis* on FCU specimens in males or females, or self collected vaginal swabs in women are non-invasive tests, acceptable to most individuals.[1,2]

TABLE 8.1 Criteria for suitable testing for STIs (adapted from WHO Guidelines[1])

The infection
• Poses a threat to public health
• Has significant sequelae (morbidity or mortality) for the individual
• Is present in the population screened with reasonable probability
• Can be detected while patient is still asymptomatic with a reasonable chance that significant damage has not occurred
• Is amenable to treatment
The test
• Good sensitivity allowing detection of asymptomatic disease
• Good specificity reducing false positives to a minimum
• Well accepted by the patient population
• Simple to perform and simple to interpret result
• Cost effective
The patient population
• Infection sufficiently prevalent to reduce false positive rate
• Effective treatment available and appropriate facilities and personnel to administer it
• Patients willing to accept treatment, follow-up and further assessment if necessary

Unfortunately a NAAT for *T. vaginalis* is not yet commercially available, although some laboratories have their own in-house polymerase chain reaction (PCR) test. Of course, microscopy and culture for *T. vaginalis* can be used instead, but FCU is not an appropriate test for this purpose and sensitivity and specificity on vaginal swabs subjected to microscopy and culture is inferior to NAA testing.

HIV testing and testing for syphilis fulfil many of the criteria for testing in asymptomatic individuals; excellent serological tests are available for both infections. The HIV antibody test, now accompanied in Australia by a test for HIV p24 antigen, is perhaps the most ideal test ever available to clinicians with its extremely high sensitivity and specificity. False positives can still occur in very low-prevalence populations but these can soon be detected by further Western blot testing. The sensitivity of the rapid plasma regain (RPR) test is poor in very early and late syphilis; however, the sensitivity can be improved by using both the RPR and a specific test (enzyme immunoassay [EIA] or *Treponema pallidum* particle agglutination [TPPA]) for testing asymptomatic people.

TABLE 8.2 Suggested sexual health check in asymptomatic patients
(This check list presupposes adequate information sharing and patient consent before testing)
Heterosexual women (in all major cities in Australia and New Zealand i.e. low prevalence areas for gonorrhoea and syphilis)
• First catch urine (FCU) or self-collected high vaginal swab (HVS) for NAAT (usually PCR or LCR) for chlamydia
• Serology for hepatitis B (HBcAb) if not previously vaccinated; on first visit
• Papanicolaou smear if not done in the previous two years
• Optional extras (determined by sexual history): FCU or self-collected HVS for NAAT for gonorrhoea; throat swab for gonorrhoea (culture and sensitivity); rectal swab for gonorrhoea (culture and sensitivity); rectal swab for chlamydia (NAAT); HVS for trichomoniasis (NAAT, if available, or swab in transport medium); Serology for HIV and syphilis (EIA or RPR and TPPA); serology for HCV if any risk; serology for rubella in nulliparous women
Heterosexual men (in all major cities in Australia and New Zealand i.e. low prevalence areas for gonorrhoea and syphilis)
• FCU for NAAT (usually PCR or LCR) for chlamydia
• Serology for hepatitis B (HBcAb) if not previously vaccinated; on first visit
• Optional extras (determined by sexual history, local prevalence and especially overseas travel): FCU for NAAT for gonorrhoea; FCU for trichomoniasis (only possible with NAAT, if available); serology for HIV and syphilis (EIA or RPR and TPPA); serology for HCV if any risk
Heterosexual women (in areas where prevalence for gonorrhoea and syphilis is higher, i.e. in Indigenous communities and in some regional cities, rural and remote communities in Australia and New Zealand)
• FCU or self-collected HVS for NAAT (usually PCR or LCR) for gonorrhoea and chlamydia
• Serology for syphilis (EIA or RPR and TPPA)
• Serology for hepatitis B (HBcAb) if not previously vaccinated; on first visit
• Papanicolaou smear if not done in the previous two years
• Optional extras (determined by sexual history): throat swab for gonorrhoea (culture and sensitivity); rectal swab for gonorrhoea (culture and sensitivity); rectal swab for chlamydia (NAAT); HVS for trichomoniasis (PCR, if available, or swab in transport medium); serology for HIV; serology for HCV if any risk; serology for rubella in nulliparous women
Heterosexual men (in areas where prevalence for gonorrhoea and syphilis is higher, i.e. in Indigenous communities and in some regional cities, rural and remote communities in Australia and New Zealand)
• FCU for NAAT test (usually PCR or LCR) for gonorrhoea and chlamydia
• Serology for syphilis (EIA or RPR and TPPA)
• Serology for hepatitis B (HBcAb) if not previously vaccinated; on first visit
• Optional extras (determined by sexual history): throat swab for gonorrhoea (culture and sensitivity); FCU for trichomoniasis (only possible with NAAT, if available); serology for HIV; serology for HCV if any risk

continued >

TABLE 8.2 Suggested sexual health check in asymptomatic patients *(continued)*

Women who have sex with women (WSW)
• FCU test or self-collected HVS for NAAT (usually PCR or LCR) for gonorrhoea and chlamydia
• Serology for syphilis (EIA or RPR and TPPA)
• Serology for hepatitis B (HBcAb) if not previously vaccinated; on first visit
• Papanicolaou smear if not done in the previous two years
• HVS for bacterial vaginosis (microscopy)
• Optional extras (determined by sexual history and local prevalence): throat swab for gonorrhoea (culture and sensitivity); rectal swab for gonorrhoea (culture and sensitivity); rectal swab for chlamydia (NAAT); HVS for trichomoniasis (NAAT, if available, or swab in transport medium); serology for HIV; serology for HCV if any risk; serology for rubella in nulliparous women
Men who have sex with men (MSM)
• FCU for NAAT for gonorrhoea and chlamydia
• Serology for HIV and syphilis (RPR and TPPA or EIA)
• Serology for hepatitis B (HBcAb) and hepatitis A (IgG), if not previously vaccinated; on first visit
• Serology for HSV type specific antibody test*
• Throat swab for gonorrhoea (culture and sensitivity)
• Rectal swab for gonorrhoea (culture and sensitivity)
• Rectal swab for chlamydia (NAAT)
• Optional extras (determined by sexual history and availability): ano-rectal Papanicolaou smear if available (usually only in specialist centres); serology for HCV if any risk

* see text for rationale
NAAT = nucleic acid amplification test, PCR = polymerase chain reaction, LCR = ligase chain reaction, HBcAb = hepatitis B core antibody, EIA = enzyme immunoassay, RPR = rapid plasma reagin, TPPA = treponema pallidum particle agglutination, HVS = high vaginal swab, FCU = first catch specimen of urine

In general terms, testing asymptomatic people for the viral infections human papillomavirus (HPV) and herpes simplex virus (HSV) is impractical at the present time, because so few of the ideal criteria are met, although, of course, the Papanicolaou smear cytology program is actually an indirect screening method for high-risk types of HPV.

Testing for STIs in primary care

STI testing in asymptomatic individuals happens in two situations. One is termed population testing and occurs where testing takes place in a given population with a known high STI prevalence (e.g. an Indigenous community or a specific community of men who have sex with men [MSM]) as part of a public health strategy. Population testing is not our concern in this monograph. The other type of testing is relevant to primary care practice. It is termed opportunistic testing, which implies the clinician takes any opportunity which presents itself to test asymptomatic high risk patients for STIs.[3,4]

It is relatively easy to set out the tests that should constitute a standard sexual health check in an asymptomatic person. Table 8.2 details a suitable check list as a guideline. It is not so easy in the primary care clinic to decide who should be screened; people commonly front up to sexual health clinics asking for a sexual health check, but they do this much less commonly in other branches of primary care.

So who to test?

Who not to test is probably the better question. In the present context perhaps a handy aphorism for a clinician could be: get into the habit of asking yourself in any consultation, for any reason with any pubertal or post-pubertal patient, 'why should I not suggest an STI check-up for this patient?' Obviously there will be clinical situations where STI testing is inadvisable and particular people whom you will immediately deem inappropriate for testing, but beware of making assumptions. The real hurdle is broaching the subject. STI testing should be so normalised in primary care

practice that no one will think it strange if their doctor suggests an STI check. Normalising STI testing in our own everyday practice is an essential start. Practical tips on who to consider for testing are listed in Table 8.3.

It goes without saying that good information sharing about HIV infection must precede testing for HIV and must include the implications, for that individual patient, of a positive or negative result. The same is true of testing for hepatitis C infection. It is less widely accepted, but none the less essential in good primary care practice, that appropriate information sharing about STIs always precedes testing and that patients are helped to understand risks they may have run, why testing for a particular STI is relevant for their situation and how the clinician proposes to manage a positive result in their case.

Tests to use and the rationale for using them

The tests suggested for asymptomatic testing are set out in Table 8.2 in six broad categories based on sexual behaviour and local prevalence. They are only guidelines and clinicians must decide on specific tests needed for their individual patients given their sexual histories and the local known prevalence of specific STIs. Testing for chlamydia is a must in almost everybody with any STI risk at all. In general terms, all the NAATs are equally good whether LCR, PCR, strand displacement amplification (SDA) or transcription mediated assay (TMA). It depends on what your local laboratory uses. NAAT tests are validated for chlamydia and gonorrhoea on FCUs, urethral swabs, cervical swabs and self-collected vaginal swabs.

In low-prevalence populations for any infection, false positives can occur with any test no matter how good its overall performance. To avoid false positives entirely, test specificity must be 100% which is seldom, if ever, attainable.[5] NAATs have good specificity for chlamydia but slightly lower specificity for gonorrhoea; however, their specificity is not 100% for either infection. This fact is of great practical importance, especially when testing for gonorrhoea in most big cities in Australia and New Zealand where the prevalence of gonorrhoea is extremely low at the time of writing. When the prevalence of gonorrhoea is low in the local population and a NAAT for gonorrhoea shows an unexpected positive in a patient at low risk for STIs, the clinician should regard the result with some suspicion; it may prove to be a false positive. Many laboratories automatically run a further confirmatory test (e.g. a different NAAT) when the initial test gives a positive result, but it is good practice for clinicians to adopt a policy of sending off a further gonorrhoea culture themselves on unexpected positive NAAT results.

TABLE 8.3 Patients to consider for STI testing in primary care

• 15–25 year old men and women
• Individuals who have more than one partner, have recently changed partners, ended a long-term relationship or started a new relationship
• People living with HIV, injecting drug users (IDUs) and those with a previous history of STIs
• Women and men who are concerned about their partner's behaviour and fidelity
• Indigenous patients
• Antenatal women
• Older patients who have lost a partner through death or divorce and have resumed sexual activity
• Male and female sex workers; whether working in the sex industry or opportunistically, and their regular partners
• Men who travel a lot on business and their regular partners
• Men who are clients of sex workers and their regular partners
• Men who have sex with men (MSM) and their female partners (if any)
• Women who have sex with women (WSW) and their male partners (if any)
• Overseas travellers who have had sex overseas

NAATs for gonorrhoea are unvalidated for throat and rectal swabs and at this time shouldn't be used; at these sites, swabs for gonococcal culture are the appropriate tests. Although NAATs for chlamydia still remain unvalidated for rectal swabs, their widespread and increasing use in this situation indicates general acceptance.[5] In clinical practice their performance is good in rectal swabs. Take rectal swabs blind in asymptomatic patients (i.e. without use of an anoscope or proctoscope) or allow the patient to take their own swab—the swab can be moistened with tap water first then gently inserted past the anal sphincter and angled laterally so that the cotton tip touches the side wall of the rectum, then withdrawn. Routine testing for pharyngeal chlamydia infections is not thought to be cost effective at this time because even in high-risk populations (highly sexually active MSM) the yield is very low.

In low-prevalence populations, the EIA test is a good test for syphilis as it is highly sensitive; however, in moderate-to-high prevalence populations, many EIA positives will indicate old, previously treated disease. It is more useful to use the RPR test combined with a specific test (EIA TPHA TPPA) in those populations as the titre will give some indication of recent infection (RPR 1/16 or greater). When a genital lesion(s) is present,

PCR testing is now replacing darkfield microscopy examination and may have a place in the diagnosis of extremely early infections, especially when clinical suspicion is high and initial serology is negative (see Chapter 12: Primary Care Management of STIs). The treponemal PCR test is not useful, however, in testing completely asymptomatic people.

There's debate about the best screening test for hepatitis B. The purpose of testing for hepatitis B virus (HBV) is twofold; to diagnose chronic HBV infection, and to offer vaccination for those not previously exposed to HBV. A positive HBcAb is sensitive and specific and will indicate any exposure for HBV. To differentiate chronic HBV infection in those who are HBcAb positive, a further HBsAg test can then be requested. Most laboratories will automatically do surface antigen and antibody testing anyway if the core antibody is positive. Presence of HBsAb will indicate successful vaccination in those unsure of their vaccination history (as is often the case). In general terms, people who are HBcAb positive do not require HBV vaccination. Testing for hepatitis A virus (HAV) antibodies in MSM is a sensible measure so that those who are not immune can be offered vaccination. HAV is transmitted by the faecal-oral route and there have been a couple of mini-epidemics of hepatitis A in communities of urban gay men over the past two decades.

HIV testing is listed in the Table as an optional extra for all except MSM. Although the prevalence of HIV is low in Australasia in all groups except MSM, it is the STI with the most serious consequences for the person with HIV infection. Most patients who are being tested for other STIs will accept HIV testing, but clinicans should concentrate on ensuring that all patients who are actually diagnosed with an STI are offered HIV testing in line with national HIV testing guidelines (see Case study 1).

HIV testing in pregnant women (see Table 8.3) is obviously an important issue because if the clinician is aware that an antenatal patient is HIV infected, appropriate management and antiretroviral therapy can substantially reduce the risk of the baby becoming infected. On a global level, a small but significant number of HIV positive diagnoses have been missed during the antenatal period because HIV testing has been offered only to those with a clear history of HIV risk behaviour. Even in Australasia, the potential for missing HIV infections in the antenatal period does exist, so pregnant women should always be offered HIV testing, irrespective of their risk, provided good pre-test information sharing and discussion takes place.

CASE STUDY 1

A patient decides on HIV testing along with other STI testing

Bronnie was an 18 year old young woman living in a regional city in Northern Australia when she presented to her general practitioner with mild tonsillitis. In general discussion the clinician established that Bronnie was sexually active—in fact she had had sex with three different young men over the past four months and had only used condoms with one of them ('because he was a one night stand'). Until four months ago, she had been in a regular relationship for three years with her first sexual partner (a school boy sweetheart) before he had to leave for study in Sydney. She had never had a Pap smear, nor been vaccinated for hepatitis B. On examination, she had mildly inflamed tonsils which the clinician thought was probably viral; however, she arranged for a throat swab for culture and sensitivity and a first catch urine specimen (FCU) for NAAT for chlamydia as Bronnie agreed an STI screen was a good idea. She gave Bronnie some literature about STIs and the HIV test and arranged for her to return in a week for a Pap smear. Bronnie promised she would think about a blood test for further STI screening before that time.

Bronnie returned next week to discover that she had a positive chlamydia test on her FCU and, surprisingly, her throat swab had grown *Neisseria gonorrhoeae* which was sensitive to ciprofloxacin. The clinician prescribed azithromycin and ciprofloxacin for Bronnie and the two had quite a long chat about HIV and STIs while vaginal examination and the Pap smear was proceeding. In view of the presence of two other STIs, the clinician sent an HVS for microscopy and a NAAT for trichomoniasis. Bronnie had decided to have a blood test, so the two agreed together that serology for syphilis, hepatitis B and HIV was appropriate.

All tests were negative except for Bronnie's HIV test which proved positive both on EIA and Western blot testing. Subsequently, through contact tracing in collaboration with the local Sexual Health Clinic, one of Bronnie's recent partners also proved to be HIV positive, probably because he had lived for a year in Thailand and had unprotected sex with several Thai women during his time there. The other recent partner with whom she had unprotected sex had been treated for gonorrhoea by his GP two months before but was HIV negative.

Suggesting testing for bacterial vaginosis in asymptomatic WSW is perhaps unjustified but as symptomatic bacterial vaginosis is a significant concern in this patient group, most WSW will want to know the state of their vaginal ecosystem and if abnormal, will want to discuss possible ways of returning it to normal acidic levels.

The place of the ano-rectal Papanicolaou smear ('CHAP' smear) is unclear at present. Some centres in Melbourne and Sydney are offering this test for MSM and especially MSM with HIV infection. To take a smear from the ano-rectal junction is simple and well within the capacity of any primary care clinician;

the difficulty lies in finding a cytologist with the necessary expertise, the interpretation of the result and most importantly, knowing what are the most appropriate interventions for high grade-squamous intraepithelial lesions (HSIL).

Serological testing for genital HSV infection

Type specific HSV antibody tests are now available to differentiate between HSV-1 and HSV-2 antibodies. They are highly sensitive EIA tests but are not quite so highly specific; false positives can only be excluded by doing further, much more expensive, Western blot testing. They give no indication of the anatomical site of infection; while one can make a reasonably accurate assumption that most HSV-2 antibody-positive people will have genital infection, the same does not apply to HSV-1 antibody-positive people—they may have either genital or oral infection. There are some clinical situations where HSV serology might guide management (e.g. in a pregnant woman whose partner has a known history of herpes), but in a testing situation it has little place at the present time, except in MSM[6] (see Table 8.2). There is good evidence that the presence of HSV infection can increase the transmission and acquisition of HIV so it may be useful to test for HSV type specific antibodies in MSM, with a view to informing those with positive HSV-2 antibodies (who are also HIV negative) of their possible HSV diagnosis combined with advice on how best to reduce risks of acquiring HIV in the presence of genital HSV infection. This will obviously involve reinforcing the importance of condom use with anal sex. Clinicians should inform those men living with HIV, who have HSV-2 infection as well (as demonstrated by a positive type specific antibody test) that their risk of transmitting HIV is much greater when they are shedding HSV from genital sites.[7] Condom use will reduce the risk but it is also likely that taking suppressive antiviral therapy (e.g. with valaciclovir or famciclovir) for HSV will further reduce their risk of transmitting HIV (as well as HSV); in patients with symptomatic recurrences of HSV, clinicians have a clear indication already for prescription of suppressive antiviral therapy; in patients who never suffer symptomatic attacks, the public health value of suppressive antiviral therapy has not yet been proven, so use of suppressive antiviral therapy is problematic. Ongoing clinical trials in MSM should give an answer to this question fairly soon.

How often to test?

Patients who have had their first sexual health screening often ask when they should have their next check-up and how often should they have them. The answer is that it all depends. Certainly there is no clear evidence base to guide clinicians on this question. The patient's pattern of sexual behaviour and the incidence of any unprotected sexual exposures are important factors to take into account. Where people have regular casual contacts, or fairly regular partner change (e.g. some MSM), establishing a regular three-monthly or six-monthly attendance for a sexual health check-up seems sensible and justified. In the more common situation where people tend to stay with one partner for variable periods of time, a sexual health check when a relationship ends, or just before a new one starts is a safe option. Some people attend as a couple soon after commencing a new relationship so they are both tested for STIs at the same time before deciding to abandon condom use. If couples do attend together the clinician should try to clarify what their expectations are regarding access to each other's test results and to document this in the clinical file for future reference. For medico-legal purposes it is preferable to suggest written (signed) permission if a patient is happy for their sexual partner to have access to their test results. Unfortunately, most people find that contemplating this pragmatic approach seems too calculated and unromantic. Clinicians just have to tailor their advice about frequency of testing to accommodate the patient's needs.

Symptoms and signs of STIs

Although mostly asymptomatic, STIs can eventually cause symptoms and signs. There are several classical syndromes which group together the main symptoms and signs of STIs. When considering diagnosis and management of STIs in primary care it is more helpful to think in terms of these syndromes rather than about each individual STI because patients tend to present with a syndrome rather than with one STI—this is called syndromic management. In resource-poor settings there are various algorithms developed for the management of each syndrome which have proved extremely useful in the provision of rapid, mostly effective treatment even when exact diagnosis of the individual STI (or STIs) responsible for the syndrome is impossible. The major drawback of the syndromic approach is that over-treatment for infections that are not in fact present often occurs. In resource-rich nations like Australia and New Zealand, a syndromic approach combined with appropriate judicious testing will combine the best of both worlds—rapid effective treatment of the presenting syndrome accompanied by exact diagnosis of the precise STI (see Chapter 12 for the management of syndromes). Refer to Table 8.4 for a brief description of STI syndromes.

Urethral discharge

A discharge from the urethra is almost always abnormal even if clear, mucoid or intermittent. The only exceptions are the scant discharge resulting from frequent 'milking' or squeezing the urethra to check if a discharge is present in the overanxious patient, and the typical mucoid discharge which can occur while on the toilet as a result of straining to open the bowels in a constipated patient. Urethral discharge can occur in females but is hardly ever going to be noticeable.

Vaginal discharge

There are two main problems in trying to interpret vaginal discharge. Is the discharge of which the patient complains physiological or pathological? If the discharge is deemed to be abnormal, it is important to know where it is coming from—the urethra, the vagina, the cervical canal or the endometrial lining of the uterus. Even with excellent history-taking and scrupulously careful examination, the answers to these questions is often not readily apparent. This fact explains why the algorithm for syndromic management of vaginal discharge in resource-poor settings is the least helpful of all the algorithms for genital syndromes. In Australia and New Zealand we have easily accessible and reliable tests to help us sort out vaginal discharge, but sometimes the true cause of the patient's complaint still proves elusive.

Ano-genital ulcer disease (GUD)

Traumatic abrasions and erosions are the most common cause of ano-genital ulcers, but these generally heal very quickly without treatment—in fact, attempts to self-treat by patients using antiseptics, insecticides, detergents and over soaping often result in more persistent ulceration which may perplex the unwary clinician. STIs associated with genital ulceration are HSV, syphilis (the primary chancre and the mucous membrane lesions seen in secondary disease), chancroid, lymphogranuloma venereum (LGV) and donovanosis. Chancroid, LGV and donovanosis are virtually never seen in primary care in Australia and New Zealand so these possible diagnoses can be disregarded, with the following provisos: chancroid has been diagnosed in Australia and New Zealand in recently returned (i.e. in the past week) travellers from endemic areas (South East Asia); there is a current outbreak of LGV in some highly sexually active groups of MSM, but it has been as proctitis rather than as genital ulceration that LGV has revealed itself in this highly specific situation; donovanosis still occurs (but extremely rarely now) in remote Indigenous communities in northern and central Australia and in Papua New Guinea. Where patients have scratched their scabetic genital lesions excessively, traumatic ulceration sometimes results but the complaint of overwhelming local itching makes the diagnosis easy. In primary care practice in Australia and New Zealand genital herpes is far and away the major cause of genital ulceration, with syphilis being a rare cause except in populations with a higher than average prevalence for syphilis (Indigenous communities and MSM).

Ano-genital warts

The warty lumps and bumps characteristic of HPV infection (usually associated with types 6 and 11) and molluscum contagiosum are the major infectious causes of lumps and bumps in the ano-genital region. Lumps and nodules due to sexually transmitted scabies also occur and are traps for the unwary clinician; the characteristic itching gives the clue. Other lumps and bumps are almost invariably non-infectious and are not due to an STI. Many are normal variants (such as pearly penile papules, Fordyce spots and sebaceous glands); some represent minor skin pathology (such as sebaceous cysts and seborrhoeic keratoses). Rarely, neoplastic lesions may present initially as nodules or papules. Clinicians should consult larger sexual health or dermatology texts to familiarise themselves with these genital lesions which can cause enormous concern, especially in young patients.

TABLE 8.4 STI syndromes

- Urethral discharge
- Vaginal discharge
- Ano-genital ulcer disease
- Ano-genital lumps and bumps
- Ano-rectal syndromes
- Pelvic pain syndrome in women
- Scrotal swelling
- Skin rash – genital or generalised

Ano-rectal syndromes

Ano-rectal syndromes are a rather heterogeneous and somewhat artificial group of symptoms and signs of STIs which predominantly affect the peri-anal area, the anus, the ano-rectal junction, the rectal mucosa and more rarely the gastro-intestinal tract. It's an anatomical syndrome more than anything else. As such, virtually all the STIs and some enteric infections not usually regarded as sexually transmitted (such as shigellosis, salmonellosis, hepatitis A and amoebiasis etc.) can be included. Most ano-rectal syndromes result from infections transmitted during various anal sexual activities (peno-anal, oro-anal, fingers, toys, fists in the anus etc.) and are therefore seen most often in MSM, but any patients, men or women, engaging in receptive anal sexual practices can of course have an infection, and oro-anal insertive patients may acquire gastro-intestinal (GIT) infections from the anal area of a sexual partner. Predominant symptoms of ano-rectal syndromes are perianal itch, anal or more deep-seated rectal pain, anal discharge (often noted as mucopurulent material on the surface of bowel motions), diarrhoea and, rarely, rectal bleeding. The key to diagnosing ano-rectal STI syndromes is to recognise their sexual connection and to appreciate that all ano-rectal pathology is not surgical. In acute primary herpes infections the anal canal and rectal mucosa may be grossly inflamed, ulcerated and may even bleed. A relevant sexual history will allow the clinician to determine the correct diagnosis and to review the person in 2–4 weeks before deciding to refer for colonoscopy.

Pelvic pain syndromes

Pelvic pain in women can be acute or chronic. Acute (i.e. recent onset) pelvic pain has a variety of different causes such as PID, ectopic pregnancy, endometriosis, ovarian cyst, urinary tract infection, appendicitis and lower bowel disorders. Both PID and ectopic pregnancy require early diagnosis and appropriate intervention, vital for prevention of further morbidity and even mortality. A high index of suspicion for PID in any sexually active woman, and the ability to eliminate ectopic pregnancy as a cause of symptoms before anything else in any woman of child bearing age are prerequisite skills for primary care clinicians. It's important to appreciate how subtle chlamydia PID can be in its early stages—almost asymptomatic infection may be the rule rather than the exception, yet irreversible damage to fallopian tubes may result.

Scrotal swelling

Scrotal swelling may be painless or painful. Any scrotal swelling in young men (under 35 years of age) must be taken seriously because of the greater risk of testicular neoplasms in this age group. Acute onset painful swelling in young men may be due to torsion or epididymo-orchitis or, much more rarely, a tumour. Differentiation between torsion and epididymo-orchitis is sometimes extremely difficult. The key point is not to miss a torsion. Missing a diagnosis of epididymo-orchitis with resultant delay in treatment is not the disaster that missing the diagnosis of testicular torsion becomes. Taking a good history (including a sexual history), being familiar with the rudiments of scrotal anatomy, performing a careful examination and arranging a quick ultrasound scan will save most potential disasters from happening.

Rash: genital and more generalised

Genital rashes are mostly not the result of a genital STI. The exceptions are:

- The rash due to scratching because of pubic lice (crabs) or scabies
- The rash due to local candidal infection (balanitis or vulvo-vaginitis)
- The more severe vulval and intertriginous rash sometimes associated with profuse discharge in severe vaginal trichomonal infection
- The episodic non-specific rash that occurs with atypical recurrent genital herpes

Other genital rashes and skin conditions are associated with dermatological conditions like lichen sclerosus, lichen planus and genital psoriasis and are beyond the scope of this monograph.

There are only three generalised skin rashes associated with STIs which a clinician should be aware of:

- The rash of secondary syphilis
- The rash of primary HIV infection
- The rash of disseminated gonococcal infection

The first two rashes share some characteristics: they both tend to be non-itchy; both may involve the palms and soles; both may be accompanied by systemic symptoms (fever and malaise); and both tend to be erythematous maculo-papular rashes. The rash of primary HIV is of shorter duration and likely to be less clinically obvious than the rash of secondary syphilis, but is often accompanied by acute aphthous type ulcers in the mouth and sometimes on genital mucosa. Secondary syphilitic rashes are more variable and can mimic other skin conditions—psoriasis, pustular acne etc. These rashes are markers for the most highly infectious periods of HIV and syphilitic infection and so thinking of and making the diagnosis is extremely useful for public health, as well as the patient.

The rash of disseminated gonococcal infection is a little different to the first two generalised skin rashes, although accompanying systemic symptoms also commonly occur. It is seen on distal portions of the extremities as macules, papules, pustules, petechiae or ecchymoses, usually less than 30 in number. There is usually joint involvement with polyarthralgia and tenosynovitis as well. Sometimes there is frank arthritis. Accompanying fever and malaise is often quite mild.

Conclusion

The ideal time to diagnose an STI is before it manifests itself clinically. Testing patients for the presence of common STIs and perhaps less common but significant STIs like syphilis and HIV is now best practice. Every clinician in primary care should be opportunistic about STI testing, as well as optimistic about outcomes for patients and the public health when she or he embraces STI testing of asymptomatic but at-risk patients wholeheartedly. It is one area of primary care medicine which can make a real difference.

References:

1 Holland WW, Stewart S, Massera C. Policy brief – Screening in Europe. WHO European Centre for Health Policy 2006. [Online] [access April 2007]. Available from http://www.euro.who.int/Document/E88698.pdf

2 Garrow SC, Smith DW, Harnett GB. The diagnosis of Chlamydia, gonorrhoea, and trichomonas infections by self obtained low vaginal swabs, in remote northern Australian clinical practice. Sex Transm Infect 2002;78:278–81.

3 Ward B, Rodger AJ, Jackson TJ. Modelling the impact of opportunistic screening on the sequelae and public health care costs of infection with *Chlamydia trachomatis* in Australian women. Public Health 2006;120:42–9.

4 Walleser S, Salkeld G, Donovan B. The cost effectiveness of screening for genital Chlamydia trachomatis infection in Australia. Sexual Health 2006. 3:225–34.

5 Zenilman JM, Miller WC, Gaydos C, Rogers SM, Turner CF. LCR testing for gonorrhoea and Chlamydia in population surveys and other screenings of low prevalence populations: coping with decreased positive predictive value. Sex Transm Infect 2003; 79: 94–7.

6 Kent CK, Chaw JK, Wong W, Liska S, Gibson S, Hubbard G, Klausner JD. Prevalence of rectal, urethral and pharyngeal Chlamydia and gonorrhoea detected in 2 clinical settings among men who have sex with men: San Francisco, California, 2003. Clin Infect Dis 2005; 41: 67–74.

7 Corey L, Wald A, Celum CL, Quinn TC. The effects of herpes simplex virus-2 on HIV-1 acquisition and transmission: a review of two overlapping epidemics. J Acquir Immune Defic Syndr 2004; 35 (5): 435–45.

Talking about testing:
pre-test and post-test discussion

9

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Introduction

Pre- and post-test discussions are an integral part of testing for human immunodeficiency virus (HIV), hepatitis B virus (HBV), hepatitis C virus (HCV) and sexually transmitted infections (STIs). The aims of pre-test and post-test discussions are to provide information and support around the testing procedure, to minimise the personal impact of diagnosis, to change health-related behaviour and to reduce anxiety of the person being tested. Discussion thus requires the clinician to assess risk, to educate the patient regarding risk of transmission, to obtain informed consent, and to follow up and arrange referrals as indicated.

Changes to terminology

The 2006 National HIV Testing Policy[1] recommends that the term 'pre- and post-test discussion' replace 'HIV test discussion and post-test counselling'. This change recognises that the complexity of the discussion may differ significantly depending on testing context, patient experience of testing and assessment of risk factors.

Formal counselling is frequently required in the management of a person who has tested positive, or in the situation where a person who tested negative is continuing to participate in high-risk behaviours for HIV. This counselling is usually specialised and requires referral to an appropriate service or practitioner.

National Testing Policy

National HIV Testing Policy 2006

http://www.health.gov.au/internet/wcms/publishing.nsf/Content/health-pubhlth-strateg-hiv_hepc-hiv-index.htm#testing

National Hepatitis C Testing Policy 2007

http://www.health.gov.au/internet/wcms/publishing.nsf/content/phd-hepc-testing-policy-may07

Key points

- Pre-test discussion is essential for the patient to make an informed decision regarding HIV, HBV and HCV testing.
- Pre-test discussion provides the person with information about HIV, HBV and/or HCV, including modes of transmission and how to prevent infection. It helps the person to consider the implications of a positive result.
- Pre-test discussion should be adapted to a person's knowledge and cultural understandings as appropriate. Testing should not be avoided because pre-test discussion is 'too hard'.
- In positive people, post-test discussion explores support and resources available to the patient and provides education regarding the infection and how to minimise the risk of transmission.
- In negative people, post-test discussion provides information on safe sex and safe injecting and addresses risk behaviours that led to the possible exposure.
- Pre- and post-test discussion is no less important when testing or screening for other STIs, even though most of these are managed relatively easily.

The context of testing

Testing for HIV antibody has been available in Australia since October 1984. At that time, acquired immune deficiency syndrome (AIDS) was associated with high morbidity and mortality and an HIV diagnosis was highly stigmatised due to its association with marginalised social groups. HIV antibody testing was promoted primarily as a tool to enhance education and prevention initiatives. Since the mid-1990s, HIV treatment advances have reduced the number of AIDS-related diseases, AIDS notifications and AIDS-related deaths in Australia.[2]

The availability of antiretroviral therapy in the contemporary Australian setting has dramatically changed the medical context of HIV antibody testing; an HIV diagnosis now opens up the possibility of appropriate treatment and improved prognosis. However, despite treatment advances and changes in social perceptions, HIV infection remains a

stigmatised condition, and all people who are tested should be engaged in detailed and sensitive pre-test and post-test discussions.

Testing for HCV antibody has been available since 1990. As with HIV, HCV infection is stigmatised due to the association with injecting drug use. During pre-test discussion, questions may be asked about a history of injecting drug use that may be an unwanted reminder of a past phase of a person's life and may be resisted. However, a discussion of previous or present drug use provides an opportunity to educate the person about HCV transmission and the natural history of the disease. As with HIV, the benefits of testing include interventions and treatments to improve clinical outcomes and the facilitation of measures to prevent transmission.

Long-term management of HBV infection has changed due to the introduction of effective antiviral treatment and immunisation. The availability of HBV vaccination enables clinicians to take an active role in case-finding, leading to lower rates of transmission and identification of people with chronic HBV infection who may be suitable for treatment. Widespread community ignorance about the long-term complications of chronic HBV infection (Chapters 5, 7 and 11) still exists, and patients need to be appropriately educated.

Testing for other STIs is generally easily done and opportunistic screening in at-risk but asymptomatic people is a valuable part of best practice in primary care medicine. However, STIs too remain stigmatised conditions and clinicians should always provide information about STIs and discuss the issues with patients before arranging appropriate screening tests (see Chapter 8 on testing for STIs).

The discussion process

During the discussion process, information is exchanged and concerns explored. Coping strategies are developed that may be utilised in the event of a positive result. While discussion does not need to proceed according to any formula, key information areas need to be covered during the consultation with a person about testing (Table 9.1). Referring to a framework of key points ensures that the necessary information regarding blood-borne viruses is conveyed.

Both pre- and post-test discussion should be performed in a way that is relevant and appropriate to the person's gender, culture, behaviour and language[1]. That is, discussion involved and information emphasised for a high-risk man who has sex with men (MSM) in a major city will differ from a pregnant, remote Indigenous woman undergoing testing in a remote area of Australia.

TABLE 9.1 Summary of pre-test discussion

• Reason for testing and risk assessment
• Timing of risk and option of post-exposure prophylaxis (PEP)
• Need for other STI and blood-borne virus testing
• History of testing
• Confidentiality and privacy issues around testing
• Ensuring there is informed consent for the test
• Natural history and transmission information (if appropriate)
• Prevention of transmission and risk reduction through behaviour change
• Implication of a positive or indeterminate test result, including availability of treatment
• Implications of a negative test result
• Explanation of the window period
• General psychological assessment and assessment of social supports in the event of a positive result
• Logistics of the test: time taken for results to become available and the need to return for results

Reasons for testing

HIV, HBV and HCV antibody testing is indicated in the following circumstances:

- Patient request
- Identification of clinical symptoms or signs (Chapters 4, 5, 6, and 7)
- Identification of risk factors in the patient history (Chapters 2 and 3)
- Part of a screening process, e.g. pregnancy
- Presentation for post-exposure prophylaxis (PEP) after occupational or non-occupational exposure to HIV
- Diagnosis of another STI. People infected with an STI, especially an ulcerative STI, are at increased risk of acquiring HIV and should be offered testing

Risk factors from the patient history which would indicate HIV testing include:[1]

- MSM sexual contact. This is the most common mode of HIV transmission in Australia[2] and unprotected anal male-male sex is a clear indication for HIV testing, as well as testing for other blood-borne viruses
- Sharing of injecting equipment. This is also a strong reason for offering testing for blood-borne viruses
- Being the sexual partner of a person with HIV infection

- Being from a country or region with a high HIV prevalence, e.g. the Caribbean, Sub-Saharan Africa, South East Asia and Papua New Guinea
- Having recently travelled overseas; travellers may be at risk of HIV through unprotected sex, injecting drugs and medical procedures

Testing may relate to antenatal testing, pre-surgical testing (this is not routinely recommended), military requirements, correctional services, blood donation, and immigration or insurance requirements. Regardless of the reason for testing, pre-test discussion between the clinician and the patient and informed decision-making by the patient are important.

Patients who request testing may not reveal their full level of risk. In some situations, the clinician may assess the risk of infection as low but the patient's actual risk of infection may be high. For this reason, all patients requesting testing should be tested. Some patients, for example young people, may attend hoping to arrange an HIV, HBV or HCV test but are unable to state this request directly. In such cases, a request for a 'check-up' or 'blood tests' may prompt questioning by the clinician to elicit specific concerns (Case study 1).

CASE STUDY 1

An adolescent may request testing indirectly

Indirect requests for testing

Mary is a 16-year-old girl who presents for a check-up and reports feeling sick. Upon history and examination she is well but the clinician decides to perform a full blood count and iron studies. While the blood is being taken, Mary asks, 'By the way, doctor, does this test for AIDS?' Subsequent assessment indicates that Mary has had unprotected vaginal sex and is concerned about STIs. The clinician performs HIV pre-test discussion and conducts a full STI screen including an HIV test. A follow-up appointment is arranged and information provided about the local youth service which provides targeted health information.

Legal requirements

The Medicare Benefits Schedule (MBS) stipulates that a practitioner requesting an HIV test has ensured that a patient undergoing an HIV test has given informed consent, received adequate pre-test discussion and understands that further discussion may be necessary once the test result is available. Some States and Territories have specific legal regulations relating to pre-test and post-test discussion for HIV and viral hepatitis, which may be used as a guide for minimum standards of care. Clinicians should contact relevant State or Territory health departments for details.

Chapter 14 contains further discussion of legal responsibilities and highlights the need for full documentation of recommendations, counselling and follow-up undertaken by the clinician.

Pre-test discussion

Pre-test discussion has several objectives:

- To provide information about the implications of a positive or negative result
- To enable informed decision-making about testing
- To communicate the health benefits of testing
- To educate patients about modes of transmission, safe sex and risk reduction measures
- To prepare for a possible positive result.

History-taking and risk assessment

A non-judgemental approach is essential to facilitate honest answers to highly personal questions. Consideration of actual risk practices, rather than making assumptions based on the patient's perceived membership of a particular risk group, is the accurate way to perform a risk assessment. Chapter 3 addresses sexual and drug-use history-taking in detail, and Chapters 2 and 3 discuss risk assessment.

Issues to cover during pre-test discussion

Table 9.1 lists topics to be addressed during pre-test discussion. In particular, the key points to be discussed regarding an HIV, HCV, HBV test include:

- **Confidentiality**

Advise the person of the measures the service or practice takes to protect personal information, including results, as well as public health notification requirements (Chapter 14). Patients who do not wish to disclose their name or Medicare number should have access to coded testing (e.g. using the first two letters of surname and first two letters of given name plus date of birth).

- **Medical consequences of infection**

Provide information about the natural history and modes of transmission for HIV, HBV or HCV (Chapters 1 and 2 and Appendix 1–3).

- **Information about prevention**

Discuss the relative risks of transmission of HIV, HBV and HCV associated with various practices. Explore the person's ability to practise safe sex or safe injecting (Chapter 3).

- **The implications of a positive result**

Inform the patient that the presence of antibodies means viral infection has occurred. Discuss implications of chronic infection for sexual relationships, the existence of treatments and the emotional and social supports that people with an infection can access. The benefits of HBV immunisation for household members and sexual partners may be relevant. Some people may be reluctant to test even when the availability of

treatments has been explained to them. They may believe that it will be impossible to keep results private and they may hold well-founded fears of discrimination, social exclusion or personal violence that may follow disclosure of HIV or viral hepatitis infection.

- **Implications of an indeterminate result**

Prepare the patient for the possibility of an indeterminate result and the need to re-test.

- **The window period**

Explain this concept and its possible implications. The window period is usually defined as the period after which it is certain that the person being tested will not seroconvert following a given exposure. The true window periods of HIV and HCV antibody tests have improved greatly over the years. In Australia, the currently used HIV antibody tests (highly sensitive in themselves) are combined with an HIV antigen test and so can demonstrate reactivity as early as two to three weeks[3] after the infecting event. With older HIV antibody tests, a window period of three months since the time of exposure was standard. Three months is still usually quoted as the window period, although in practice in Australia, this is rarely the case. It is important to explain that someone who has recently acquired HIV is highly infectious during the window period.

For HCV and HBV, a longer time period post-infection (approximately 70 days)[3] is required before serology tests are able to reveal infection, due to a different time course of infection.

- **The implications of a negative result**

Explain that the absence of antibodies (the negative result) means either the person does not have the infection or that he or she is in the so-called 'window period' of infection, prior to the development of antibodies (see above section on the window period).

- **Coping with a positive result**

Previous ways of coping with crises may indicate how the person will cope with a positive test result. People with a history of depression or other psychiatric issues and those without self-perceived social supports are especially vulnerable following a positive diagnosis.

Assess the patient's psychiatric history and risk of suicide or self harm, and identify appropriate interventions in the event of a positive diagnosis. In cases where high-risk practices or clinical features are suggestive of infection, in-depth discussion of these issues may form the basis of a future management plan.

- **Referral**

The need for assistance from other agencies may arise during the pre-test discussion and clinicians need to have a low threshold for referral to specialist agencies. For example, when assessing patients with a history of injecting drug use, issues related to homelessness, poverty or drug and alcohol dependence may become apparent and referral may be indicated (Chapter 15).

- **Supporting the person while waiting for the result**

Ensure that follow-up appointments are booked at the pre-test assessment. Suggest that a trusted person be told about the test if the patient requires support while waiting for test results. In addition, the patient may be invited to bring a support person when returning for his or her result.

Summary

While pre-test discussion may seem time consuming, practice ensures that time is used efficiently within the primary care context. Clinicians will often develop their own style for discussing HIV and viral hepatitis, tailoring information and language to the needs of individual patients. Not all of the issues listed above may be relevant to every patient each time he or she presents for testing, but assumptions regarding the patient's level of knowledge should be avoided. While the process may seem unnecessary in low-risk patients, thorough pre-test discussion ensures that prevention measures are in place, the patient is prepared for his or her test results, and the clinician's ethical and legal obligations are met.

Post-test discussion

All HIV, HBV and HCV test results must be given in person. Ensure privacy and undertake the consultation in an area where you will not be interrupted. Further testing for other STIs and blood-borne viruses should be recommended as appropriate.

Giving a positive result

Key points to be discussed in relation to a positive HIV, HCV, HBV test include: (see Table 9.2):

- **Assess patient readiness to receive the result**

The person may be asked whether he or she has thought about the likely test result and its implications.

- **State the result clearly**

Some people confuse a 'positive result' with a good result. Ensure that the actual result is understood.

- **Seek consent to repeat the test for confirmation**

Mistakes in labelling at the surgery or in the laboratory are rare but they still do occur. It is important not to raise the patient's hopes too much over this issue, however.

- **Avoid information overload**

Give the patient time to process and react to the information. Listen and respond to the person's needs.

- **Reinforce commitment to health care**

The primary care clinician may reassure the patient that he or she will continue to be a partner in the patient's health care without discrimination.

- **Enlist available supports**

Help plan the person's next 24–48 hours. Arrange a follow-up appointment during the next two days and offer an after-hours phone contact number.

- **Discuss disclosure**

After a positive result, the patient may experience an urge to tell many people. The balance between disclosure and privacy can be difficult, and the clinician may caution the patient about widely disclosing his or her positive status during the first few days after diagnosis, due to the possibility of negative responses from some people.

- **Supply written material**

Supplying written material gives the person something to read outside of the consultation, reinforcing key messages that may not have been heard in the context of the shock of receiving a positive result. Information may address the medical and social consequences of HIV, HBV or HCV infection and provide details about local support services, including telephone information and support lines, AIDS Councils or Hepatitis C Councils (Chapter 15). The ASHM website (www.ashm.org.au) provides patient fact sheets including support services.

- **Reinforce prevention message including information about modes of transmission.**

This may form the basis of starting the contact tracing process.

- **Managing a positive result**

Much of the initial management of a new blood-borne virus diagnosis is psychosocial. Offering the patient the opportunity to return at any time to discuss concerns may help him/her to adjust to the diagnosis.

Chapters 10, 11 and 12 discuss the initial and ongoing assessment, monitoring and management of patients with HIV, viral hepatitis, and STIs.

Clinicians inexperienced in managing patients with BBV infections should collaborate with more experienced general practitioners and/or relevant specialists and specialist centres (Chapter 15 and the *ASHM Directory*).

Giving a negative result

Key points to be discussed in relation to a negative HIV, HCV, HBV test (Table 9.3)

- **Inform the patient of the result**

Tell the patient that he or she does not have the infection. If appropriate, discuss the window period and make an appointment for re-testing.

TABLE 9.2 Summary of post-test discussion: giving a positive result

First post-test consultation
• Establish rapport and assess readiness for the result
• Give positive test result
• Avoid information overload
• Listen and respond to needs (the patient may be overwhelmed and hear little after being told the positive result)
• Discuss immediate implications
• Review immediate plans and support
• Reassess support requirements and available services
• Arrange other tests and the next appointment
• Begin contact tracing process and discuss options available to facilitate this
Subsequent consultations
• Treatment options, diet and exercise
• Effect of diagnosis on relationships and prevention information
• Issues of disclosure
• Assessment of contact tracing process and difficulties encountered
• Access to life insurance may be affected
• Workplace implications
• Impact of other issues (eg. drug use, poverty, homelessness) on ability to access health care and treatments
• Referral for on-going counselling, social worker, medical specialist as appropriate

TABLE 9.3 Summary of post-test discussion: giving a negative result

• Explain the negative test result and the window period (if relevant)
• Reinforce education regarding safe behaviours
• Consider vaccination – for hepatitis B, hepatitis A (if indicated), and, for women aged between 9 and 26, human papillomavirus (HPV)
• Further discuss anxiety or risk behaviours
• Discuss testing for other STIs

- **Educate the patient about ongoing risk-taking**

Review safe sex and safe injecting practices. Discuss the role of drugs and alcohol in risk-taking, as well as how and where to access condoms and clean injecting equipment. Offer referral to local services as appropriate (Chapter 15).

- **Offer vaccination**

Hepatitis A and hepatitis B vaccination may be offered, plus one of the HPV vaccines in young women.

- **Address attitudinal barriers**

A negative result leaves time to explore important issues that may impact on infection risk. For example, a negative result after a high-risk encounter may reinforce a sense of invincibility among young people, especially young men. Such responses need to be addressed.

Indeterminate results

Occasionally, an equivocal or indeterminate result from HIV, HBV or HCV testing may occur. This can be a source of great uncertainty and anxiety for the patient. Clinicians may need to consult pathology laboratory staff or the National Serology Reference Laboratory for specialist advice in interpreting indeterminate results. Specific tests for each blood-borne virus have different types of equivocal results and differing rates of false positivity. In the case of HIV antibody testing, a positive ELISA and a single band on Western blot constitutes an indeterminate result.

A patient with an indeterminate result who has reported a recent high-risk exposure is regarded as being in the window period of infection and may require considerable support during this time to deal with the uncertainty. Further tests for viral antigens may be indicated to test for the presence of infection and should be performed in consultation with a specialist clinician. If reactivity in HIV or HCV antibody tests does not progress over approximately two weeks it is unlikely that a person is seroconverting.

The result is likely to remain 'indeterminate' due to the presence of non-specific reactivity in the test. Thus a clinician can draw a second sample soon after the first to determine the progression. However, to be sure and to address absolutely the fears of the person being tested or the healthcare worker's doubts, test results at approximately 12 weeks for HIV and six months for HCV should be obtained.

In populations of low seroprevalence of blood-borne viral infections, indeterminate results may be 'false positives'. Factors such as pregnancy, past blood transfusions, intercurrent viral infections, autoimmune diseases and malignancies may play a role in equivocal results. Upon re-testing at approximately two weeks, a second indeterminate result is regarded as confirmation of negative status.

Special considerations

Aboriginal and Torres Strait Islander People

The rates of HIV diagnosis per capita in the Indigenous and non-Indigenous populations are similar but there is evidence that Indigenous people are more likely to be diagnosed later in the course of the infection, and therefore have a higher AIDS disease diagnosis rate.[2] Higher prevalence of ulcerative and non-ulcerative STIs in this population may contribute to HIV transmission and STI testing should be offered. The primary objective of the *National Aboriginal and Torres Strait Islander Sexual Health and Blood-Borne Virus Strategy 2005–2008*[4] is to improve access to testing and medical care for HIV, blood-borne viruses and STIs among Aboriginal and Torres Strait Islander people. Facilitating this goal may involve:

- Understanding differing epidemiology of HIV in different local settings. For instance, higher rates of infection through heterosexual contact and intravenous drug use.[2]
- Addressing local and cultural issues, such as stigma and shame, associated with HIV and STI testing and diagnosis. Routine screening through antenatal clinics, adult health checks and community STI screening interventions may help reduce the stigma around testing.
- Local systems and policy to ensure confidentiality around STI and HIV testing.
- Specific programs to facilitate testing through collaboration and partnerships between Indigenous organisations and groups and specialist Sexual Health and HIV services. Local input to ensure the relevance and appropriateness of programs aimed at different subgroups, e.g. youth, MSM, sex workers.
- Pre- and post-test discussion may need to incorporate local patterns of transmission and modes of disease prevention. Education around the potential for blood-to-blood transmission in traditional ceremonial practices may be particularly relevant in some Indigenous settings and discussion should incorporate this information in an appropriate manner.
- Pre- and post-test educational resources such as videos or cassettes in Indigenous languages or plain English may assist to ensure informed consent and aid HIV and STI prevention education.
- Antenatal testing. As heterosexual transmission of HIV is more common in many Indigenous settings, antenatal testing may provide an important opportunity to inform, educate and test Aboriginal and Torres Strait Islander women for HIV.
- Consideration of the need for an interpreter. However, an interpreter may be closely connected with the patient's family and may create a fear regarding a possible breach of confidentiality.
- Testing for other STIs and blood-borne viruses. If HIV is detected, Aboriginal and Torres Strait Islanders should also be tested for HTLV-1 as this is more common in this population and may alter disease progression and management.[1,5]

Other cross cultural issues

Culture, language, literacy level, gender and age will affect how a person accepts and understands HIV, HBV and HCV testing, but this should not interfere with provision of pre-test and post-test discussion. Language barriers may be overcome by the use of an interpreter and language education resources such as leaflets, videos and multimedia.

HIV, HBV or HCV phobia

Occasionally the clinician will encounter a person whose fear of infection with HIV or viral hepatitis is out of proportion with the actual risk of infection. Such people, sometimes referred to as the 'worried well', may repeatedly request HIV or HCV tests after encounters that carry very low or no risk of transmission. Often these people are helped by emotional support or a discussion of the encounter and the provision of factual information about the risk of transmission. This may not be adequate for some people who may have co-existing psychiatric morbidity, such as undiagnosed obsessive compulsive disorder, and may need referral for specialist counselling or psychiatric assessment.

Testing and pregnant women

Why test pregnant women?

The risk of perinatal transmission of HIV and HBV can be significantly reduced with appropriate clinical care and interventions.

The basis for offering pregnant women HIV testing is the ability to prevent mother-to-child transmission. Several studies published in the mid-1990s demonstrated that azidothymidine (zidovudine) monotherapy reduced mother-to-child transmission from 25% to 8%.[6-8] The use of combination therapy plus planned caesarean delivery and bottle-feeding has reduced HIV transmission to less than 2%[9-12]. Mother-to-child transmission of HIV has fallen dramatically in countries where antiretroviral therapy is available to pregnant women.[13]

Interventions to prevent HBV infection are well established and reference to the National Health and Medical Research Council's Immunisation Handbook is advised.[14]

HIV testing during pregnancy

The 2006 National HIV Testing Policy recommends all pregnant women should be routinely offered HIV testing. Pregnancy is a time when women are in contact with clinicians, and it provides an opportunity for detection of previously undiagnosed infections. Previous policy suggested HIV testing in pregnancy if a risk assessment suggested possible HIV risk. However, many women diagnosed with HIV do not self-acknowledge risk factors, and therefore standard risk assessment may be inadequate to test and detect women with HIV infection.[15-17] Because prevention of mother-to-child transmission of HIV is highly effective if HIV is diagnosed antenatally, routine testing with informed consent is now the standard of care.

HIV discussion during pregnancy

The issues to be discussed during pre-test discussion listed in Table 9.1 remain relevant for pregnant women.

It is recommended that pre-test discussion in pregnancy should include a standard HIV risk assessment and discussion including informed consent. Pregnant women undergoing testing should be educated as to the benefits of HIV diagnosis and the management and prevention strategies in the case of a positive result.

Educational resources such as leaflets, videos and multimedia may be required in contexts where literacy or English understanding is poor. Interpreters and language resources may assist in these scenarios to ensure an understanding of the testing process and informed consent.

Discussion of an indeterminate result may also be considered, given that pregnancy may slightly increase the likelihood of an indeterminate result.

Post-test discussion of positive tests results should involve all of the points listed in Table 9.2. Antenatal women diagnosed with HIV should have the chance to consider all options regarding their current and future pregnancies with the correct information regarding transmission risk. If known teratogenic antiretroviral treatment is avoided, combination antiretroviral therapy is considered safe for the woman and foetus. Referral information to appropriate specialist HIV services should be facilitated.

Considerable anxiety and guilt may be associated with diagnosis during pregnancy. Special attention should be paid to the psychosocial aspects of receiving a positive test result during pregnancy.

CASE STUDY 2

A request for HIV testing may indicate anxiety not risk

HIV anxiety and sexual identity

Michael is a 39-year-old married man who presents for an HIV antibody test. During discussion, he reports mutual masturbation with a male acquaintance. Although sexual transmission of HIV is highly unlikely from this safe sexual encounter, Michael is convinced that he has HIV infection. On examination he is well and the antibody test comes back negative. In the meantime, Michael now thinks that he may be gay and needs to talk to someone about it. The clinician refers him to a counsellor but continues to offer psychosocial support, as well as HAV and HBV vaccination.

Discussion should include an assessment of the negative effects of diagnosis (e.g. discrimination, domestic violence, psychological difficulties) and should provide information on how to minimise these.

The clinician should evaluate an HIV-infected pregnant woman to determine her need for psychological and social services. Specialist counsellors or midwives with training in this area may be engaged during this process. The implications of the test result for both mother and child should be reiterated, as should treatment options and measures for preventing perinatal transmission so the woman can make informed decisions regarding her options.

- US guidelines can be found at http://www.aidsinfo.nih.gov
- The National HIV Testing Policy (2007) is available on the Commonwealth Department of Health and Ageing website at http://www.health.gov.au/internet/wcms/publishing.nsf/content/health-pubhlth-strateg-hiv_hepc-hiv-index.htm#testing (see Reference 1)
- Australian guidelines can be accessed through the ASHM HIV Models of Care database at http://www.ashm.org.au/moc/

HCV testing in pregnancy

At present no drug therapies are recommended to reduce the risk of mother-to-child HCV transmission which, providing the patient is not HIV co-infected, is low, at approximately 5%. No specific intervention at the time of delivery has been shown to reduce the risk of transmission and breastfeeding has not been shown to increase the risk of HCV transmission to the baby.

Routine screening of pregnant women is not recommended. Any woman identified as being at risk of, or personally concerned about, HCV infection should be offered testing.

Transmission from mother-to-child will not occur if the mother has spontaneously cleared the HCV infection, so all pregnant women who test positive for anti-HCV antibodies should be offered qualitative HCV RNA testing to determine if they are still viremic. Infants born to anti-HCV positive mothers will have passively acquired antibodies. In uninfected infants, seroreversion or loss of maternal antibodies will be seen within 18 months. Antibody testing should therefore only be carried out after the child reaches 18 months of age.[17]

Summary

Pre-test and post-test discussion for HIV and viral hepatitis (as well as for other STIs) provides the clinician with the opportunity to review and reinforce prevention and risk reduction messages. It also protects patient autonomy by ensuring informed consent regarding testing and helps prepare patients for positive test results. The benefits of early diagnosis, in terms of access to treatments and improved disease outcomes, should be highlighted when recommending testing. In the context of a positive result, post-test discussion and referral for counselling deals primarily with psychosocial issues, prevention of further transmission, contact tracing and information about on going monitoring and treatment.

ASHM can provide information and education resources on pre- and post-test discussion.

References

1. Department of Health and Ageing: National HIV Testing Policy 2006. [Online] [access 2007 April]. Available from URL http://www.health.gov.au/internet/wcms/publishing.nsf/Content/health-pubhlth-strateg-hiv_hepc-hiv-index.htm#testing
2. National Centre in HIV Epidemiology and Clinical Research. Annual Surveillance Report: HIV/AIDS, Hepatitis C and Sexually Transmissible Infections in Australia. Sydney: NCHECR;2006.
3. Busch MP. Kleinman SH, Nomo GJ. Current and emerging infectious risks of blood transfusions. JAMA 2003:289;959–62
4. National Aboriginal and Torres Strait Islander Sexual Health and Blood Borne Virus Strategy 2005-2008. Commonwealth of Australia, Department of Health and Ageing. Canberra, 2005.
5. 2006 Medical Management of HIV Infection. John Bartlett, Joel Gallant. John Hopkins University School of Medicine.
6. Connor EM, Sperling RS, Gelber R, et al. Reduction of maternal-infant transmission of human immunodeficiency virus type 1 with zidovudine treatment. N Engl J Med 1994;331:1173–1180.
7. Matheson PB, Abrams EJ, Thomas PA, et al. Efficacy of antenatal zidovudine in reducing perinatal transmission of human immunodeficiency virus type 1: the New York City Perinatal HIV Transmission Collaborative Study Group. J Infect Dis. 1995;172:353–358.
8. Aleixo LF, Goodenow MM, Sleasman JW, et al. Zidovudine administered to women infected with human immunodeficiency virus type 1 and to their neonates reduces pediatric infection independent of an effect on levels of maternal virus. J Pediatr 1997;130:906–914.

9 Thorne C, Newell ML. Treatment options for the prevention of mother-to-child transmission of HIV. Curr Opin Investig Drugs 2005;6(8):804–11

10 The International Perinatal HIV Group. The mode of delivery and the risk of vertical transmission of human immunodeficiency virus type 1 – a meta-analysis of 15 prospective cohort studies. N Engl J Med 1999:340(13):977–987.

11 Mandelbrot L, et al. Perinatal HIV-1 transmission, interaction between zidovudine prophylaxis and mode of delivery in the French perinatal cohort. JAMA 1998;280:55–60.

12 Parrazini F for The European Mode of Delivery Collaboration. Elective caesarean-section versus vaginal delivery in prevention of vertical HIV-1 transmission: a randomised clinical trial. Lancet 1999;353:1035–1039.

13 Royal College of Paediatrics and Child Health. Reducing mother to child transmission of HIV infection in the United Kingdom: Update report of an Intercollegiate Working Party. London; July 2006.

14 Barbacci MB, et al. Human immunodeficiency virus infection in women attending an inner-city prenatal clinic: ineffectiveness of targeted screening. Sex Trans Dis 1990;17:122–126

15 Fehrs LJ, Hill D, Kerndt PR, Rose TP, Henneman C. Targeted HIV screening at a Los Angeles prenatal/family planning health center. Am J Public Health 1991;81(5):619–22.

16 Lindsay MK, Peterson HB, Willis S, et al. Incidence and prevalence of human immunodeficiency virus infection in a prenatal population undergoing routine voluntary human immunodeficiency virus screening, July 1987 to June 1990. Am J Obstet Gynecol 1991;165(4 Pt 1):961

17 Department of Health and Ageing: National Hepatitis C Testing Policy 2007. [Online] [access 2007 October]. Available from URL: http://www.health.gov.au/internet/wcms/publishing.nsf/content/phd-hepc-testing-policy-may07

Primary care management of HIV disease

10

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Introduction

The course of HIV infection has been altered significantly in developed countries by the use of potent antiretroviral therapy and treatments for HIV-related opportunistic illnesses. In the era of combination antiretroviral therapy, many patients with HIV infection remain well ten years after their first AIDS-related illness. Nevertheless, HIV disease management remains a complex and evolving area of medicine which is constantly reshaped as new, scientific evidence emerges.

This chapter aims to provide the HIV non-specialist clinician with an update on the management of HIV disease and to describe the role of the primary care clinician in the shared management of patients with HIV infection. When managing patients with HIV disease, the primary care clinician often works in conjunction with a clinician, either a general practitioner or physician, who is able to prescribe antiretroviral drugs under Section 100 of the Pharmaceutical Benefits Scheme (PBS), as well as other services and agencies.

Key points

- HIV infection remains a complex disease and its management continues to evolve.
- The period of assessment and management of people living with HIV after diagnosis and before anti-HIV treatment is active for both patient and doctor. The role of the primary care clinician during this time is one of support, education, monitoring and referral.
- Knowledge of the conditions and illnesses associated with the stages of HIV immunodeficiency is necessary in the clinical monitoring of patients with HIV infection. Signs and symptoms of HIV disease are discussed in Chapter 6.
- Combination antiretroviral therapy is available for the treatment of HIV infection. Long-term suppression of HIV replication occurs in approximately 80% of people who commence triple combination therapy. Viral suppression produces strong immune recovery in most patients. Specialists and general practitioners who have completed HIV prescriber courses may prescribe antiretroviral therapy through Section 100 of the Pharmaceutical Benefits Scheme (PBS).
- The primary care clinician has a role in supporting adherence with patients who are taking antiretroviral therapy, as well as monitoring for adverse events and drug interactions.
- A focus on general health maintenance, psychosocial issues and support remains central to the care of patients with HIV infection in the era of combination antiretroviral therapy.

The challenges of managing patients with HIV infection

Management of HIV as a chronic disease

There are many challenges in the management of patients with HIV infection, some of which are common to the management of other chronic conditions. For example, the patient needs to be informed about the nature of the disease and potential treatments. Assistance in adherence to medication is particularly relevant in the management of HIV disease given the potential for drug resistance if doses are missed. The clinician also has a role in exploring a range of psychosocial and sexuality issues, and in encouraging a sense of hope through discussion of treatment options. Management of HIV infection as a chronic disease is shaped by the stigmatisation attached to HIV and the fear or anxiety patients may exhibit following diagnosis.

The quality of the doctor-patient relationship is central to the successful long-term management of HIV. Nurturing this long-term therapeutic relationship is a major task for the primary care clinician. The key characteristics of this relationship are honesty, accessibility, a demonstrated commitment to confidentiality and the privacy of the patient, and medical expertise. Offering frequent and long

consultations may be appropriate and provision of an after-hours contact number may be considered. The therapeutic relationship may be enhanced if the clinician demonstrates that he or she is comfortable with patients with HIV infection (e.g. by taking blood) and gay or bisexual patients (e.g. by openly discussing sexual matters).

The goals of the therapeutic relationship specifically in relation to patients with HIV include:

- Maintenance of an effective, collaborative, therapeutic relationship
- Thorough, ongoing assessment
- Education of the patient with regard to HIV infection, natural history, transmission and the effects of therapy
- Provision of information and referral regarding medical and psychosocial resources and services
- Facilitation of effective medical intervention to maximise the patient's health prior to and during treatment

Natural history and treatments

Following acute infection with HIV (Chapter 4), there is a stage of clinical stability where immunological and virological markers remain relatively stable. During this period, homeostasis exists between the amount of HIV produced and cleared each day, and the number of CD4 T-lymphocytes (CD4 cells) produced and destroyed each day. Subsequently, clinical stability may continue despite deterioration in laboratory markers as the immune system fails to control the amount of HIV produced (Chapter 1). At this time, the amount of HIV measurable in plasma (the viral load) may increase as the number of CD4 cells falls. The average time to progression to AIDS is about ten years but progression rates vary widely at the individual level. Determinants of the rate of disease progression include age and virological and host factors.

Constitutional symptoms (lethargy, fatigue, diarrhoea, weight loss and night sweats) may occur in the presence of a high viral load at any stage of the disease. Early symptoms of immune deficiency begin to appear when the CD4 cell count falls below normal levels (Figure 1.1, Chapter 1). As the CD4 cell count decreases to levels below 200 cells/μL, the patient is at greater risk of opportunistic infections.

An understanding of the natural history of HIV disease provides the basis for treatment decisions. Experts generally recommend commencement of therapy as surrogate markers deteriorate prior to onset of symptomatic disease, certainly prior to severe immune deficiency. However, the best time to commence antiretroviral therapy is yet to be established. See 'HIV treatment issues' on page 105 for more information.

Assessment and monitoring

Assessment and monitoring of the patient with HIV infection relates to general physical health, psychosocial wellbeing, as well as immune and virological status.

Initial assessment

During the initial consultations with a patient with HIV infection, a comprehensive medical and psychosocial assessment should be conducted. General discussion should include the impact of HIV on the patient and the availability of social support systems, as well as a discussion on issues of sexuality and transmission prevention. The patient's priorities with regard to HIV disease and his or her knowledge of HIV need to be established prior to discussion of the treatment options and transmission prevention. Ascertaining whether or not the patient sees an HIV specialist and whether a referral is sought may shape the consultation.

TABLE 10.1 Checklist: Initial assessment of the patient with HIV infection

• General assessment including medical history, family history, drug and alcohol history, smoking history, sexual history.
• Full psychosocial assessment.
• Targeted physical examination including weight, cardiovascular status, oral and dental health, skin, pelvic/anogenital examination and general systems examination.
• Sexual health review – tests for gonorrhoea and chlamydia (see Chapter 8 for sampling techniques), syphilis (RPR and a specific test e.g. TPPA), and hepatitis A, B and C (HAV IgG, HBsAg, anti-HBs, anti-HBc, HCV Ab [and HCV RNA if CD4 cells<200 cells/μL]*). Consider HSV type specific serology and anal smear tests (for detecting dysplasia); the role of regular anal Papanicolaou cytology tests and management of abnormal tests is currently unclear (see Chapter 8).
• Screens for infections such as toxoplasmosis (Toxoplasma IgG), tuberculosis (Quantiferon Gold or Mantoux test and chest X-ray), cytomegalovirus (CMV IgG).
• Blood tests, including HIV RNA viral load, CD4 cell count, CD4 cell percentage, fasting cholesterol, triglycerides and glucose, liver function tests, serum amylase, creatinine phosphokinase, urea and electrolytes and a full blood count (FBC).
• HIV resistance genotyping (can be conducted in consultation with a HIV-experienced clinician).
• Vaccination history needs to be noted and future vaccinations discussed. The patient should be offered HBV and HAV vaccination in the absence of established immunity or infection. Live vaccination should not be given to patients with HIV infection. Both Fluvax and Pneumovax are recommended as per NHMRC guidelines (available at www.ashm.org.au/position-papers/).[1]

*Patients with advanced HIV may lose anti-HCV reactivity, see page 112.

Initial medical assessment involves the establishment of the stage of HIV disease and assessment of potential co-morbidities. A comprehensive range of blood tests, serological tests and clinical examination should be conducted (Table 10.1).

Chapter 9 addresses how to deliver a positive HIV result to a patient and conduct early follow-up. In the context of a HIV diagnosis, the 'initial assessment' may take place over several weeks or months and psychosocial issues may take priority for the patient at this time.

Coinfection with viral hepatitis

Chronic liver disease commonly affects people with HIV infection and screening for viral hepatitis is recommended. Coinfection with either hepatitis B virus (HBV) or hepatitis C virus (HCV) is associated with greater risk of chronic liver disease and cirrhosis, increased hepatotoxicity from antiretroviral drugs and may affect survival. Viral hepatitis coinfections can impact on antiretroviral regimen choices as well as other lifestyle and health issues. The avoidance of alcohol and other potential hepatotoxins is important, as is the prevention of other hepatic infections. Vaccination against hepatitis A and hepatitis B is recommended for those who are not immune (Chapters 1, 5 and 11).

Markers of HIV disease: immunological and virological status

Immunological and virological status is evaluated by a general physical examination, T-cell subsets and viral load testing every three months. The CD4 cell count is the main measure of immune damage in people with HIV infection. The HIV RNA viral load (the number of viral copies per millilitre of blood plasma) is the key virological assay. In the absence of treatment, higher viral load is associated with faster CD4 cell decline and the development of AIDS-related conditions.

Data from the Multicenter AIDS Cohort Study (MACS) of HIV-infected men confirmed that both the CD4 cell count and HIV viral load are prognostic markers of likely disease progression and clinical illness in HIV disease.[2] As can be seen from Table 10.2, the proportion of men who progressed to an AIDS-defining illness was greatest for those with the highest viral loads and lowest CD4 cell counts. Within each stratum of CD4 cell count, prognosis was best for those with the lowest viral load.

Table 10.2 Surrogate markers and risk of progression to AIDS

CD4 cell count %	Viral load	% AIDS progression in men	
		over 3 years	over 9 years
<200 CELLS/ML	<10 000	14%	64%
	10 000 – 30 000	50%	90%
	>30 000	86%	100%
200-350 CELLS/ML	10 000	7%	66%
	10 000 – 30 000	36%	85%
	>30 000	64%	93%
>350 CELLS/ML	<10 000	7%	54%
	10 000 – 30 000	15%	74%
	>30 000	40%	85%

Adapted from multicenter aids cohort study[2,3]

CD4 cell count

In untreated HIV infection, progressive immune damage will occur, expressed as a loss of CD4 cells at an average rate of 60–80 cells/μL per year. Some patients may have a more rapid course, while others will remain stable for longer. There are levels of immune deficiency that are associated with greater risk of HIV-related conditions and opportunistic illnesses (Figure 1.1, Chapter 1). For example, when the CD4 cell count falls to between 200 and 500 cells/μL, oral hairy leukoplakia, skin conditions such as seborrhoeic dermatitis and psoriasis, recurrent varicella-zoster virus infection (shingles), and bacterial pneumonia may occur. CD4 cell counts below 200 cells/μL are associated with an increased risk of Pneumocystis jiroveci pneumonia (formally Pneumocystis carinii or PCP), cerebral toxoplasmosis, oesophageal candidiasis, Kaposi's sarcoma and cryptococcosis. Advanced immunodeficiency occurs at CD4 cell counts below 50 cells/μL, at which stage the individual is at risk of cytomegalovirus (CMV) retinitis, disseminated mycobacterium avium complex (MAC) infection, cryptosporidiosis and microsporidiosis, primary central nervous system lymphoma and HIV-associated dementia, and non-Hodgkin's lymphoma. Opportunistic infections are discussed in greater detail in Chapter 6.

The CD4 cell count is calculated by the percentage of CD4 cells in the lymphocyte component of the white cell count. The total number of CD4 cells will vary according to the white cell count and lymphocyte count. It is important to assess changes in the total CD4 cell count in the context of the percentage of CD4 cells and variability of the lymphocyte number secondary to intercurrent illnesses. A single measurement may be misleading because factors such as intercurrent infection, vaccination, menstrual cycle, and the time of day blood is taken can impact on results. Consequently, evaluation should focus on the trend in CD4 cell levels rather than a single result. A number of tests need to be performed over a period of time to provide an accurate picture of the patient's immune function. These test results enable the clinician to form an assessment of the course of a person's HIV disease and the rate of disease progression.

Viral load

Plasma viral load estimates provide the strongest long-term prognostic information for HIV patients. The plasma viral load is a measure of the balance between the amount of HIV produced each day and the amount of HIV cleared by the immune system.

Viral load (the amount of HIV RNA in the plasma) is measured by reverse transcriptase polymerase chain reaction (RT PCR). The laboratory will give results in both log number of copies/mL and absolute number of copies/mL. A significant change in viral load is an increase or decrease of greater than 0.5 log. Changes of less than 0.3 log are considered to be within the variability of the laboratory test performance (Table 10.3 and Case Study 1). The lower limit of detection of the assay is currently 50 copies/mL, and viral loads below this level are reported as undetectable; however this does not mean that there is no HIV present.[4]

Viral load is used to assist in making the decision to initiate antiretroviral therapy (along with the presence or absence of symptoms and the level of CD4 cells), to monitor the response to antiretroviral therapy and to identify treatment failure.

Monitoring HIV infection

There are a number of Models of Care for the clinical management of HIV infection from the USA, the UK and Europe. Online access to Models of Care can be obtained by consulting the ASHM website at: http://www.ashm.org.au/moc/.[5] Another source is *Clinical practice: Management of newly diagnosed HIV infection* by Hammer (2005).[6]

Patients will require more regular review and monitoring if they are immunocompromised (CD4 cells <350/μL) or receiving antiretroviral therapy. In general, the untreated, immunocompetent patient (CD4 cells >350/μL) should be reviewed every 3–6 months, while the patient with less than 350 CD4 cells/μL or receiving antiretroviral therapy needs review every 2–3 months (Table 10.4).[7]

Psychosocial assessment

Effective management of people with HIV infection involves an approach which addresses psychosocial as well as biomedical factors. In addition to psychosocial issues related directly to HIV infection, the social stigma and marginalisation experienced by groups most affected by HIV may compound the psychological, social and emotional impact of HIV infection.

Social, emotional and educational support is available through AIDS Councils and HIV-positive people's groups in each State and Territory (Chapter 15).

Psychosocial assessment and management involves consideration of the following issues:

- Self-esteem and body image
- Stigmatisation and discrimination
- Family and social relationships and supports
- Sexual relationships and related issues of disclosure and safe sex
- Depression and emotional issues (e.g. anger, denial, anxiety)
- Drug and alcohol use
- Issues around pregnancy and motherhood for women
- Compliance with drug therapy and related lifestyle issues
- Financial and employment situation
- Health care satisfaction

Most of these evaluations will take a number of consultations to complete, and ongoing assessment is recommended.

Key relationships and support systems are pivotal to the wellbeing of the patient. One of the most important support systems for many people is their biological family, therefore assessment of family relationships and social support should be conducted. Issues to consider include whether the family is aware of the patient's sexuality and HIV status, their reaction to this information and the patient's reasons for not telling them. Friends may also provide an invaluable support network.

TABLE 10.3 Significance of viral load changes

Biologically relevant changes in viral load (>0.5 log) and changes considered within the variability of the laboratory assay (>0.3 log)

Copy number	Log^{10}	Log^{10} change from 10,000 copies/mL	Fold change	Significant change from 10,000 copies/mL
5000	3.7	-0.3	0.5	No
10,000	4.0	0	1.0	–
20,000	4.3	+0.3	2.0	No
50,000	4.7	+0.7	5.0	Yes
100,000	5.0	+1.0	10	Yes

Other questions to ask are: is the patient in a relationship and what is the quality of that relationship? Does the partner know of the person's HIV status? How does the person's HIV status affect the relationship sexually or emotionally? Patients who lack supportive and trusting relationships may be isolated and vulnerable, and referral to community organisations or other services may be appropriate (Chapter 15).

Use of drugs and alcohol should be explored in a non-judgemental way. Substance abuse may be a form of self-medication for depression or may perpetuate denial and avoidant behaviours. Referral may be made to a treatment program or other specialist service. An accurate drug and alcohol assessment is essential prior to commencement of antiretroviral therapy due to the possibility of serious and life-threatening drug interactions.

For women with HIV infection, issues of family and children may be of particular concern. Fears about transmission or future care may influence a woman's desire for children, and full education and discussion is advised (Chapter 9). For a woman who already has children, there may be concerns that her children have HIV infection. Most infants with HIV develop signs of immune deficiency within the first year of life and antiretroviral therapies are available for children, although adherence to therapy can present difficulties. For women with HIV infection requiring support, referral to Positive Women's groups is recommended (Chapter 15).

In the era of combination antiretroviral therapy, patients may wish to address issues of returning to work, education or relationships in light of the improved prognosis. The demands of long-term adherence to therapy or the physical manifestations of drug toxicities may also give rise to other psychosocial concerns regarding body image, lifestyle and sexuality.

Psychological assessment[6]

Several Australian studies indicate a high prevalence of major depressive symptoms and dysthymia among people with HIV infection[8-10] with particularly high rates among patients with fewer social supports and lower income. Depressive symptoms may impact on the person's ability to maintain safe sexual practice or lead to suicidal ideation.

Psychological assessment should be conducted to identify and treat major psychiatric illness. Recent acquisition of HIV may indicate that the patient has participated in some sort of self-destructive behaviour, which may be related to depression or suicidal ideation, drug and alcohol dependence, post-traumatic stress disorder or a range of other problems. Depression in people with HIV infection may be influenced by factors such as social rejection, progression of HIV disease, lack of support networks or alcohol and drug use, and these factors should be identified and addressed.

Patients with significant immunosuppression may be at risk of developing organic brain disease and consideration should be given to the mental health implications of immune status. In addition, depressive, neuropsychological side-effects may be caused by antiretroviral agents, most commonly efavirenz.

CASE STUDY 1

When is a viral load change significant?

Viral load changes and adherence

Alex has regular monitoring of his viral load and CD4 cell count every six months. When his viral load reaches 48,990 copies/mL (4.69 log) and his CD4 cell count is 300 cells/μL, he commences combination antiretroviral therapy.

He has a good virological response to treatment, recording a viral load of 570 copies/mL (2.76 log) three months later. Over the first 12 months of therapy his viral load is measured at 800 and 1,000 copies/mL (2.90 and 3.00 log). No action is taken by the clinician, as these results are not significantly different from the nadir of 570 copies/mL (i.e. not greater than a 0.3 log difference from 2.76 log).

However, 18 months later his viral load is 6,500 copies/mL (3.81 log). This is a significant rise in viral load (>0.5 log), which prompts a discussion of his adherence to therapy and whether he has taken any new medication that may have interacted with his antiretroviral drugs. Alex says that he finds it difficult to remember to take his pills and admits missing doses.

The clinician explores strategies to assist Alex in taking his pills, such as keeping pills in highly visible locations (e.g. next to his bed, toothbrush or keys) or using a beeper.

Health promotion

Prevention

It is important that people with HIV infection have a clear understanding of HIV transmission so that they do not pass on the infection (Chapters 2 and 3, Appendix 1). A patient's knowledge of transmission, especially with regard to his or her own (possibly changing) behaviour, needs to be broached at regular intervals over the course of the therapeutic relationship. The risk of HIV transmission when the patient has undetectable or low viral load must also be addressed. Although viral load in the blood plasma often correlates with viral load in semen and vaginal fluids, this is not necessarily the case. Consequently, a person with undetectable virus in the blood may still be able to transmit HIV. The benefits of safe behaviours to the patient should be reiterated, such as prevention of sexually transmitted infections (STIs). Rates of STIs like syphilis, more

recently lymphogranuloma venereum (LGV) and possibly HCV remain high among people with HIV who have unprotected sex. Other STIs are also known to amplify the risk of HIV transmission to others. Unprotected sex between people with HIV infection may carry the risk of re-infection with a drug-resistant or more aggressive virus, which may accelerate disease progression. Condoms remain the best prevention tool for the sexual transmission of HIV.

TABLE 10.4 Assessment and monitoring of the patient with HIV infection

Three-monthly reviews in all patients with HIV infection	Additional monitoring for patients taking antiretroviral therapy
• Collection of history and symptom review	• Treatment-related monitoring is primarily conducted by the antiretroviral prescriber
• General physical monitoring	• Frequent review during the first month of treatment
• Weight, blood pressure, oral and dental checks	• Monitoring for severe side-effects (e.g. hypersensitivity, Stevens-Johnson syndrome, CNS toxicity)
• Full blood count	• Management of treatable side-effects (e.g. nausea, diarrhoea)
• Liver function tests and amylase	• Adherence monitoring and support. Tips to maximise adherence. Consideration of change of medication. Referral
• CD4 cells and percentage	**Three-monthly reviews**
• Viral load	• Assessment of potentially adverse effects of treatment (e.g. peripheral neuropathy, lipoatrophy, lipodystrophy)
• Psychosocial assessment and support	• Ongoing adherence monitoring and support
• Patient education (transmission prevention and treatment updates)	**Six-monthly reviews**
• Health promotion (alcohol avoidance for patients with HCV co-infection, smoking cessation, dietary adjustment)	• Fasting cholesterol (including HDL and LDL), triglycerides, insulin and oral glucose tolerance
Six-monthly reviews in all patients with HIV infection	• Monitoring of serum lactate, particularly in symptomatic patients, to detect lactic acidemia related to nucleoside analogue therapy (the utility of this monitoring in asymptomatic patients remains unclear)
• Ophthalmological assessment if CD4 cell count is below 50 cells/mL (rule out asymptomatic CMV retinitis)	**Annual reviews**
• Cervical cytology by Papanicolaou smear in women with previous evidence of cervical dysplasia. Anal smears are performed by some GPs but predictive value of subsequent anal carcinoma is unproven	• Physical assessment for lipodystrophy, including DEXA scan for assessment of fat and bone mineral density
• Syphilis serology (see guidelines[22])	• Assessment of cardiovascular risk factors (family history, smoking, hypertension, hyperlipidemia, insulin resistance)
Annual reviews for all patients with HIV infection	
• Assessment of immunity to hepatitis B	
• Vaccinations	
• Cervical cytology by Papanicolaou smear in women	
• STI screening for all sexually active men who have sex with men (see guidelines[23])	

Post-exposure prophylaxis – non-occcupational

In cases of exposure (e.g. through condom breakage), non-occupational post-exposure prophylaxis (NPEP) may help patients prevent transmission of HIV to their partners. NPEP involves taking antiretroviral medication within 72 hours of a high-risk exposure to HIV (see Chapter 4). Knowledge of this intervention can help to increase the confidence of people with HIV infection to be sexually active, particularly those in serodiscordant relationships, but must not be promoted as a stand-alone prevention strategy. National guidelines on the use of NPEP for non-occupational exposure are available (see Chapter 4 for details).

Education

The clinician may need to provide the patient with information about HIV disease, monitoring and treatment to facilitate patient participation in health and treatment decisions. Appendix 1 provides a summary of basic information about HIV infection, which may assist the clinician in educating the patient. As concepts are introduced and reviewed, many patients will come to a sophisticated understanding of their infection and natural history.

The clinician has a central role in interpreting test results and providing the patient with an understanding of his or her prognosis. The patient should be aware that CD4 cell counts and viral load can vary from test to test and that trends are more important than absolute numbers. Graphing results over time may be a helpful way of demonstrating the patient's position. While population-based studies have provided an overview of average rates of disease progression, the patient should know that there is no way of predicting the course of HIV disease in individual people. Patient education involves conveying the uncertainties of HIV disease, such as time to disease progression and response to therapy.

Patient education also involves provision of general dietary and lifestyle advice. A healthy, balanced diet, low levels of stress and regular exercise are recommended. Potential drug-related harms and drug interactions with antiretroviral therapy should be discussed.

Resources for health care professionals and positive people

There is a wide range of resources available to support clinicians and patients. ASHM distributes regular bulletins to members and has a website, which is regularly updated, providing information for clinicians and patients. Treatment information for patients is also available from community organisations (Chapter 15). Australian commentary to the locally adopted US DHHS *Guidelines for the Use of Antiretroviral Agents in HIV-1 infected Adults and Adolescents* can be found on the ASHM website : *http://www.ashm.org.au/aust-guidelines*

HIV treatment issues

The aim of antiretroviral therapy is to reduce HIV viral load, prevent HIV disease progression and produce immunological reconstitution. The primary marker of successful therapy is suppression of HIV viral load to undetectable levels.

The effect of potent combination therapy on immune function, survival, AIDS progression and hospitalisation has been dramatic.[11] The relationship between viral load and treatment benefit from antiretroviral therapy has been analysed in over 5000 patients enrolled in 18 clinical trials. These studies have shown that:[12]

- Reduction in viral load is associated with improved outcome, with each 1 log (10-fold) reduction reducing the risk of clinical progression by 65%
- Reduction in risk of disease progression or death is independent of baseline plasma HIV-1 RNA and CD4 cell count
- Benefit is independent of the increase in CD4 cell counts secondary to treatment
- Rates of mortality, illness and hospitalisation have fallen significantly

The treatment-induced reduction in viral load is determined by several factors, including the potency of the regimen. Viral load reductions of greater than 2.0 log are expected with first-line combination antiretroviral therapy regimens.

Initiating antiretroviral therapy

The decision to commence antiretroviral therapy is made on the basis of the risk-benefit analysis and the patient's readiness to take treatment. Antiretroviral treatment guidelines, based on expert opinion and available scientific evidence, have been developed to guide decisions about commencing and switching treatment. Australia follows the United States guidelines with an Australian commentary where local issues are relevant. These guidelines are on the ASHM website (www.ashm.org.au/guidelines/).[13-15]

Recommendations prior to 2001 were based on the amount of virus present (>10,000 copies/mL) or an abnormal CD4 cell count (<500 cells/μL).[15] However, the increased recognition of the risks of antiretroviral therapy in the form of long-term metabolic toxicities, combined with the realisation that eradication of HIV is unlikely to occur, has resulted in recommendations to delay the initiation of antiretroviral therapy until the CD4 cell count is around 350 cells/μL.

The following are indications to begin treatment with combination antiretroviral therapy:

- Symptomatic HIV infection
- Asymptomatic HIV infection with a CD4 cell count below 350 cells/μL

The question of when to commence antiretroviral therapy remains a topic of debate among expert physicians and GPs. Some may recommend therapy for a patient with a CD4 cell count greater than 350 cells/μL and a viral load greater than 100,000 copies/mL.

Table 10.5 Antiretroviral medications

**Drug information current at April 2007. See ASHM website (www.ashm.org.au) for updated information.*

Nucleoside/nucleotide analogue reverse transcriptase inhibitors (NRTI)

NRTI	Dose	Adverse effects	Comments
Abacavir (ABC)	300 mg bd or 600 mg qd	Hypersensitivity reaction	HLA B*5701 screening for abacavir hypersensitivity
Didanosine (ddI)	400 mg qd (>60 kg body weight) 250 mg qd (<60 kg)	Pancreatitis, peripheral neuropathy, nausea, diarrhoea	If used with tenofovir, reduce ddI dose to 250 mg/ 200mg qd
Emtricitabine (FTC)	200 mg qd	Skin discolouration, minimal adverse events	Renal excretion, adjust dose in renal failure
Lamivudine (3TC)	150 mg bd or 300 mg qd	Minimal adverse events, headache	Renal excretion, adjust dose in renal failure
Stavudine (d4T)	40 mg bd (>60 kg) 30 mg bd (<60 kg)	Peripheral neuropathy, pancreatitis, hepatic steatosis, lipodystrophy	
Tenofovir (TFV)	300 mg qd	Headache, nausea, vomiting, diarrhoea, renal insufficiency	
Zidovudine (AZT or ZDV)	250 mg bd	Headache, initial nausea, vomiting, malaise, anaemia, leukopenia, macrocytosis, lipodystrophy, hepatic steatosis, myopathy	

All nucleoside analogues have the potential to cause mitochondrial toxicity and a syndrome of chronic, low-grade lactic acidemia. In a small minority of individuals this may progress to life-threatening lactic acidosis.

qd: every day; bd: twice a day; tds: three times a day

Fixed-dose combination NRTI

Trade name	Component NRTI and doses in each tablet	Daily dose
Combivir	AZT 300 mg + 3TC 150 mg	1 bd
Trizivir	AZT 300 mg + 3TC 150 mg +Abacavir 300 mg	1 bd
Kivexa	Abacavir 300 mg + 3TC 300 mg	1 qd
Truvada	Tenofovir 300 mg + emtricitabine 200 mg	1 qd

Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTI)

NNRTI	Dose	Adverse effects	Comments
Delavirdine	400 mg tds	Rash, headache, abnormal liver function tests	Rarely used in Australia, because of high pill burden and tds dosing
Efavirenz	600 mg qd	Rash, insomnia, vivid dreams, other central nervous system effects, abnormal liver function tests	Contraindicated in pregnancy (potential teratogenicity)
Nevirapine	200 mg qd for first 14 days, then 200 mg bd	Rash (including Steven-Johnson syndrome), abnormal liver function tests to symptomatic hepatitis	Do not use as initial ARV therapy in men with CD4 cells >400 cells/μL and women with CD4 cells >250 cells/μL. Use with caution in those with cirrhosis

Table 10.5 *continued* **Antiretroviral medications**

Drug information current at April 2007. See ASHM website (www.ashm.org.au) for updated information.

Protease inhibitors (PIs)

PI	Dose	Ritonavir dose	Adverse effects	Comments
Atazanavir (ATZ)	300 mg qd	100 mg qd	Indirect hyperbilirubinemia, nausea, vomiting, diarrhoea	ATZ dose without ritonavir 400 mg qd (use only in naïve patients, or those not receiving tenofovir or efavirenz)
Darunavir (DRV)	600 mg bd	100 mg bd	Rash, diarrhoea, nausea, headache	
Fosamprenavir	1400 mg qd 700 mg bd	200 mg qd or 100 mg bd	Rash, nausea, vomiting, diarrhoea	qd dosing in PI naïve (fAPV) patients only
Indinavir (IDV)	800 mg bd	100 mg bd	Nephrolithiasis, nausea, vomiting, diarrhoea, hyperbilirubinemia	IDV can be dosed at 800 mg tds without ritonavir, but must have strict 2 hour windows around food consumption for each dose and must consume >2 litres water daily to prevent nephrolithiasis
Lopinavir/r (LPV)	2 x 200mg lopinavir/ 50 mg ritonavir tablets bd or 4 tablets qd	N/A co-formulated	Nausea, vomiting, diarrhoea, hyperlipidemia	If used in combination with efavirenz or nevirapine in ARV experienced patients – use 3 tablets bd
Nelfinavir (NFV)	1250 mg bd	Not used	Diarrhoea	
Saquinavir (SQV)	1000 mg bd	100 mg bd	Gastrointestinal intolerance, headache	
Tipranavir (TPV)	500 mg bd	200 mg bd	Hepatotoxicity, rash	
All protease inhibitors have the potential to cause hyperlipidemia, insulin resistance, lipodystrophy, abnormal liver function tests and hepatitis.				

Entry inhibitors

Entry inhibitor	Dose	Adverse effects	Comments
Enfuvirtide	90 mg bd SCI of bacterial pneumonia,	Injection site reactions, possible increased rate for treatment experienced rare hypersensitivity reactions	Can only be given subcutaneously, indicated patients only

Deferral is generally recommended if a patient's CD4 cell count is greater than 350/µL and viral load is lower than 100,000 copies/mL.

The final decision rests with the patient and clinician in consultation. In making the decision to treat, consideration must be given to the patient's commitment to therapy, his or her awareness of the importance of strict adherence to the regimen, and the potential for adverse effects. Advice regarding the decision can be obtained from the antiretroviral prescriber and a number of sources listed in Chapter 15.

Treatment regimens

There are four classes of approved antiretroviral medications: nucleoside analogue reverse transcriptase inhibitors (NRTIs), non-nucleoside reverse transcriptase inhibitors (NNRTIs), protease inhibitors (PIs) and entry inhibitors.

These antiretroviral drugs inhibit one of two viral enzymes—reverse transcriptase or protease or prevent entry of HIV into the CD4 cell. Anti-HIV medications and their side effects are summarised in Table 10.5.

Patients commencing treatment should be started on a combination of either three or four drugs.

Generally, a combination includes drugs from at least two different drug classes. In general, patients initiate treatment either with two nucleoside analogues and an NNRTI, or two nucleoside analogues and a PI. Treatment regimens are developed at the individual level based on dosing requirements, toxicity profiles and co-morbidities.

Assessment of response to therapy

For a patient on treatment, a significant increase in HIV RNA or failure to achieve undetectable viral load requires consideration of the following factors:

- The patient may show poor adherence and changes to the treatment regimen may be required.
- Drug levels may be too low to suppress HIV replication due to drug interactions or poor absorption, requiring dose adjustments or a change in regimen.
- Resistance to the antiretroviral drugs may have developed and resistance assays may be conducted by the antiretroviral prescriber

These tests must be interpreted in the context of the patient's antiretroviral history.

Side-effects and interactions

Side effects of antiretroviral therapy may be early (e.g. headache), persistent (e.g. diarrhoea) or long term (e.g. lipodystrophy).[16] Each antiretroviral drug has its own particular side effect profile with which the primary care clinician should be familiar (Table 10.5).

The patient should be supported through initial side effects, most of which are very common and usually short term (http://www.medscape.com/resource/hivantiretrovirals, or http://aidsinfo.nih.gov/Guidelines/). Some side effects are life-threatening and necessitate immediate cessation of the medication. These include acute hepatitis, severe rashes including the Stevens-Johnson syndrome (associated with the NNRTIs) and the abacavir-hypersensitivity reaction. This reaction occurs within six weeks of starting abacavir and symptoms include fever, nausea, vomiting, diarrhoea and malaise, with or without rash. Lactic acidosis is a rare adverse event associated with the nucleoside analogues, which may lead to organ failure and death. Usually the antiretroviral prescriber will be monitoring the patient very closely through this phase. If the patient presents to the primary care clinician with a problem, the antiretroviral prescriber should be directly consulted.

Protease inhibitors and nucleoside analogues have been associated with the lipodystrophy syndrome, which develops as a long-term toxicity of antiretroviral therapy. Lipodystrophy syndrome involves:

- Fat gain (particularly visceral abdominal fat)
- Peripheral subcutaneous fat loss in arms, legs, buttocks, face
- Increased serum lipids and insulin resistance

Chapter 6 includes a photograph of the clinical presentation of lipodystrophy (Figure 6.4).[17]

It is important to recognise the increased cardiovascular risk in patients with HIV infection, but also in those with insulin resistance and hyperlipidaemia. Appropriate management and attention to other risk factors, such as hypertension and smoking, is required. The Framingham risk evaluation should be carried out annually.

Drug interactions

The potential for drug interactions should also be considered. The PIs and the NNRTIs are metabolised by the hepatic cytochrome P450 3A4 enzymes. The PIs inhibit the P450 3A4 enzymes with varying potency and the NNRTIs can induce or inhibit the enzymes. It is no longer possible to remember all the drug interactions and there are several sources regularly updated that outline predicted interactions and known interactions. Useful websites include: www.hiv-druginteractions.org and http://www.tthhivclinic.com/

Always check one of the websites before introducing any new drugs. It is also known that some complementary medicines can cause reductions in PI concentrations (e.g. St John's Wort, garlic pills). The recreational drug ecstasy may also interact with PIs to produce very high levels of ecstasy in the blood and extreme caution should be advised regarding use of recreational drugs by people taking PIs.

Drugs contraindicated with concomitant use of PIs because of potential life-threatening reactions are:

- Terfenadine, astemizole – non-sedating antihistamines (use loratidine as an alternative)
- Cisapride – prolongation of the Q-T interval, torsade de pointes arrhythmias
- Lovastatin – rhabdomyolysis
- Midazolam, triazolam – prolonged sedation

(It is important to inform anaesthetists about antiretroviral therapy because of the impact on procedures such as endoscopy or bronchoscopy. Propofol is recommended as an alternative.)
Additional contraindications and cautions apply in the case of the PI ritonavir.

Adherence issues

Medication must be taken properly to be effective in the long term. If the patient is regularly missing doses, not following dosing recommendations or has commenced a new medication or complementary medicine which affects the metabolism of the drugs, the reduced concentration of drug allows for the selection of drug-resistant HIV and 'failure' of the antiretroviral regimen.[18] Unfortunately, there is often significant cross-resistance within the same class of antiretroviral drugs[19] and resistance to one drug may undermine response to subsequent regimens. If the patient reports poor adherence, discussion with the HIV prescriber may be appropriate to consider simplification of the antiretroviral regimen to a once- or twice-daily regimen to make adherence easier. Management of side effects may also improve adherence.

In consultation with the patient's antiretroviral prescriber, consider referring the patient for adherence counselling. The AIDS Councils, specialist HIV units and domiciliary nursing organisations conduct adherence counselling.

Immune-based therapies

Immunomodulators are another form of therapy for HIV infection currently under investigation. Subcutaneous interleukin-2 is known to induce significant rises in CD4 cells, but treatment cycles are associated with often incapacitating, short-term side effects.[20] The current trials are investigating whether this rise in CD4 cells translates to a clinical benefit in terms of improved survival and reductions in disease progression to AIDS-defining illnesses. Other approaches to immunomodulation under investigation include therapeutic HIV vaccination.

Prophylaxis

When the CD4 cell count falls below 200 cells/μL, there is an increased risk of opportunistic infections and prophylaxis is recommended to prevent some common opportunistic infections. Table 10.6 contains the prophylactic regimen of choice and an alternative prophylactic regimen in the event of intolerance or drug allergy, and the CD4 cell count at which prophylaxis is recommended.[21] For patients who have instituted prophylaxis and then experience immune reconstitution after combination antiretroviral therapy, prophylaxis may be discontinued safely if the CD4 cell count remains above 200 cells/μL for at least six months. However, prophylaxis should be recommenced if the CD4 cell count falls below that level again.

AIDS-related illness

Symptoms in the patient with HIV infection should be interpreted in the context of the patient's current and past immune function, current therapy and recent changes in medication or complementary therapy. In patients with normal CD4 cell levels, symptoms may represent community-acquired infections or medication side effects.

Patients who initiate therapy at low CD4 cell counts (less than 100–200 cells/μL) may present with 'immune reconstitution' illness. Fever, lymphadenitis, sweats and fatigue may be related to localisation of Mycobacterium organisms to the lymph nodes by a reconstituted immune system. Other common forms of 'immune reconstitution' illness are discussed in Chapter 6.

In immunocompromised patients (CD4 cell count less than 200–250 cells/μL), certain symptoms and signs should raise alarm bells and trigger investigation of an HIV-related infection or malignancy. Signs or symptoms which warrant further investigation include: persistent constitutional symptoms of unexplained weight loss, fatigue, malaise, fever, sweats, diarrhoea; skin conditions such as seborrheic dermatitis and eosinophilic folliculitis; respiratory complaints of dry cough and dyspnoea; neurological symptoms of headache, seizure, weakness, numbness, visual disturbances and psychiatric changes including the development of depression, sleep disturbances, memory problems and slowed reaction times or hypomania. If the patient develops unexplained symptoms or signs in the setting of immunodeficiency, it is important to contact an infectious diseases or HIV specialist for referral and guidance on investigation and management.

Summary

Given the long period of clinical latency typically seen in HIV disease, primary care management of HIV disease is often highly appropriate despite the increasing complexity of antiretroviral management. Monitoring of disease progression should focus on clinical, immunological or virological markers of disease progression. Referral to a specialist HIV antiretroviral prescriber (GP or physician) should be made when signs of disease progression occur. Psychosocial management, safe sex education and provision of information and referral are key features of HIV primary management.

TABLE 10.6 Recommended prophylaxis during HIV infection

Opportunistic infection	First-line prophylaxis	Alternative	CD4 cell count
Pneumocystis jiroveci pneumonia	cotrimoxazole 1 tablet qd	dapsone nebulised pentamidine	200 cells/μL
Toxoplasmosis	cotrimoxazole 1 tablet qd	dapsone/pyrimethamine	200 cells/ μL
Mycobacterium avium complex	azithromycin 1200 mg weekly	rifabutin 300 mg qd	50 cells/μL
CMV retinitis	ophthalmological review 6 monthly		50 cells/μL
Pneumococcal pneumonia	Pneumococcal vaccine		500 cells/μL
influenza	influenza vaccine annually		any
tuberculosis (Mantoux positive)	isoniazid 300 mg/pyridoxine for 9 months		any

References

1 Kent SJ, Pierce A. Routine vaccinations for HIV-1-infected adults. Position Paper. Australasian Society for HIV Medicine; February, 2001.

2 Mellors JW, Rinaldo CR, Gupta P, White RM, Todd JA, Kingsley LA.. Prognosis in HIV-1 infection predicted by the quantity of virus in plasma. Science 1996;272:1167-70.

3 Mellors JW, Munoz AM, Giorgi JV. Plasma viral load and CD4+ lymphocytes as prognostic markers of HIV-1 infection. Ann Intern Med 1997;126:946-54.

4 Saag MS, Holodniy M, Kuritzkes DR, O'Brien WA, Coombs R, Poscher ME, et al. HIV viral load markers in clinical practice. Nat Med 1996;2:625-9.

5 ASHM Australian Models of Care Database. [Online] [access April 2007]. Available at http://www.ashm.org.au/moc/

6 Hammer SM. Clinical Practice. Management of newly diagnosed HIV infection. N Engl J Med 2005;353;1702-10.

7 Adapted from material originally submitted by G. Rogers et al, Chapter 6.

8 Komiti A, Hoy J, Judd F, Mijch, A., Hoy, J., Williams, B., et al. Depression in HIV infected patients attending general practice clinics. 12th Annual Conference of the Australasian Society for HIV Medicine: 2000 12-14 Oct; Melbourne. Abstract P32.

9 Rogers G, Curry M, Oddy J, Beilby J. Serious health disadvantage evident in a cohort of HIV positive and HIV negative gay men: baseline health characteristics of the care and prevention programme cohort. 12th Annual Conference of the Australasian Society for HIV Medicine: 2000 12-14 Oct; Melbourne. Abstract P56.

10 Grierson J, Bartos M, de Visser R, McDonald K. Futures II: The health and well-being of people with HIV/AIDS in Australia. Monograph Series Number 17. Melbourne: Australian Research Centre in Sex, Health and Society, La Trobe University, 2000.

11 Palella FJ Jnr, Delaney KM, Moorman AC, Loveless MO, Fuhrer J, Satten GA, et al. Declining morbidity and mortality among patients with advanced human immunodeficiency virus infection. HIV Outpatient Study Investigators. N Engl J Med 1998;338:853-60.

12 Marschner IC, Collier AC, Coombs RW, D'Aquila RT, DeGruttola V, Fischl MA, et al. Use of changes in plasma levels of human immunodeficiency virus type 1 RNA to assess the clinical benefit of antiretroviral therapy. J Infect Dis 1998;177:40-7.

13 US Department of Health and Human Services Panel on Clinical Practices for Treatment of HIV Infection. Guidelines for the Use of Antiretroviral Agents in HIV-infected Adults and Adolescents. January 2008. http://www.hivatis.org

14 British HIV Association Writing Committee. Draft British HIV Association (BHIVA) guidelines for the treatment of HIV-infected adults with antiretroviral therapy. 2001. http://www.aidsmap.com

15 Carpenter CC, Cooper DA, Fischl MA, Gatell JM, Gazzard BG, Hammer SM, et al. Antiretroviral therapy in adults. Updated recommendations from the International AIDS Society – USA Panel. J Am Med Assoc 2000;283:381-90.

16 Carr A, Cooper DA. Adverse effects of antiretroviral therapy. Lancet 2000;356:1423-30.

17 Carr A, Miller J, Law M, Cooper DA. A syndrome of lipoatrophy, lactic acidemia and liver dysfunction associated with HIV nucleoside analogue therapy: contribution to protease inhibitor-related lipodystrophy syndrome. AIDS 2000;14:F25-32.

18 Chesney MA. Factors affecting adherence to antiretroviral therapy. Clin Infect Dis 2000;30(suppl 2):S171-S176.

19 Condra JH, Petropoulos CJ, Ziermann R, Schleif WA, Shivaprakash M, Emini EA.. Drug resistance and predicted virologic responses to human immunodeficiency virus type 1 protease inhibitor therapy. J Infect Dis 2000;182:758-65.

20 Emery S, Capra WB, Cooper DA, Mitsuyasu RT, Kovacs JA, Vig P, et al. Pooled analysis of 3 randomized, controlled trials of Interleukin-2 therapy in adult human immunodeficiency virus type 1 disease. J Infect Dis 2000;182:428-34.

21 USPHS/IDS. Guidelines for the prevention of opportunistic infections in persons infected with human immunodeficiency virus. MMWR 1999:48:1-67.

22 Australasian Chapter of Sexual Health Medicine RACP 2004. Clinical guidelines for the management of sexually transmissible infections among priority populations. [Online] [access April 2007]. Available from http://www.racp.edu.au/public/SH_clinical_guidelines.pdf

23 Sexually transmitted infections in gay men action group (STIGMA) 2005. Sexually transmitted infection testing guidelines for men who have sex with men. [Online] [access April 2007]. Available from http://www.racp.edu.au/public/SH_MSMguidelines.pdf

Primary care management of chronic viral hepatitis

11

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Introduction

A primary care role in the management of chronic viral hepatitis involves the provision of information, support and referral as well as initial and ongoing clinical assessment and monitoring. The primary care clinician may undertake tasks such as specific diagnosis and initial assessment of the severity of disease, counselling the patient about the current understanding of the disease process and potential complications, as well as general issues of diet, mental health, lifestyle, transmission and vaccination.[1,2] With recent advances in the treatment of hepatitis B and C, the primary care clinician has an important role in presenting the patient with specific treatment options and potential side effects.[3] This chapter focuses on the primary care management of chronic hepatitis C, with some consideration of treatment options for chronic hepatitis B.

Clinical evaluation and diagnosis

The initial approach of the clinician must include consideration of the non-viral and viral aetiologies for hepatitis (Table 11.1). Elevated liver enzymes are often a trigger for consideration of viral hepatitis.

The most common causes of abnormal liver function tests (LFTs) seen in clinical practice include fatty liver, alcoholic liver disease and drug toxicity (usually transient) as well as chronic viral hepatitis.

A diagnosis of chronic hepatitis requires persistently abnormal liver function tests for a period of six months. Thus, the strict definition is one of duration rather than severity (Chapters 5 and 7).

The majority of patients with chronic viral hepatitis will be asymptomatic or have non-specific symptoms such as fatigue and lethargy, and only some will have signs of compensated or decompensated cirrhosis.

Key points

- Patients with active chronic viral hepatitis should be monitored every six months. Liver biopsy is the definitive investigation to assess the degree of hepatic inflammation, fibrosis and cirrhosis.
- Effective antiviral therapy is available for chronic hepatitis B and C in many patients.
- For patients with chronic hepatitis C, the rate of progression to cirrhosis is usually very slow and antiviral treatment may not be indicated in all cases.
- Most patients with adult-acquired chronic hepatitis B infection will not suffer long-term sequelae, but approximately 25% of people with chronic hepatitis B from infancy develop cirrhosis or hepatocellular cancer (HCC). Antiviral treatment is indicated in many patients with active chronic replicative hepatitis B.
- Depending on viral genotype and other cofactors, 30–70% of patients have a sustained response to currently approved HCV treatments.
- A course of antiviral treatment for HBV can induce sustained HBeAg seroconversion in 30–40% of patients, as well as clinical improvements and survival benefits. Potential benefits of antiviral therapy for chronic hepatitis B include 'e' antigen seroconversion, improved liver function, improved liver histology and reduced progression to cirrhosis and its complications.
- Primary care management of chronic viral hepatitis includes education and counselling, psychosocial support and dietary and lifestyle advice. It also involves monitoring the disease process and identifying if and when referral to a specialist is required.
- Prevention education and vaccination against other hepatitis viruses are important in the management of chronic viral hepatitis.

Chapter 7 contains a detailed discussion of the clinical presentation of chronic viral hepatitis.

A sound understanding of modes of transmission, risk behaviours and epidemiology should permit a detailed risk assessment in patients with suspected hepatitis of unknown aetiology (Chapters 1–3). In cases where clinical and risk assessment suggest the possibility of chronic viral hepatitis, viral serology should include hepatitis B surface antigen (HBsAg), hepatitis C virus (HCV) antibody (anti-HCV) and human immunodeficiency virus (HIV) antibody (anti-HIV), as appropriate, following pre-test discussion and informed consent (Chapter 9). Patients with advanced HIV infection may lose anti-HCV reactivity. Therefore, serum HCV RNA should be assessed if acute or chronic HCV infection is suspected in HIV patients with negative antibody results. Further considerations are dependent upon whether the patient has chronic HCV or chronic HBV infection.

Hepatitis C

Initial assessment

A detailed history should include an estimation of the duration of exposure, age at infection and whether there are important contributing factors to hepatic fibrosis. These factors may include a history of significant alcohol consumption, obesity and diabetes, which are risk factors for non-alcoholic fatty liver disease. Concomitantly, the patient should be evaluated for ongoing risks, such as injecting drug use and ongoing, excessive alcohol consumption.

Initial assessment of a patient with hepatitis C should address whether or not the patient has active disease, inactive disease or has cleared infection, as well as their likelihood of having significant fibrosis. Patients are more likely to have significant fibrosis if they have had a long duration of infection (>20 years), have a history of significant alcohol use (which may be remote), or have been overweight or obese. Chapter 7 discusses virological markers, liver function tests, liver imaging, liver biopsy and other investigations which form the basis of this assessment.

Patients should have liver enzymes monitored every one to two months for several months to establish whether enzymes are persistently abnormal, persistently normal, or fluctuating. It should be kept in mind that while patients with persistent elevation of alanine aminotransferase (ALT) levels are at higher risk of significant liver damage and disease progression, even patients with normal liver enzymes may be at risk of progressive disease.

TABLE 11.1 Important causes of chronic hepatitis

Aetiology	Diagnostic test
Fatty liver (incl. non-alcoholic steatohepatitis)	Risk factors, imaging ± biopsy
Alcohol	History ± biopsy
Viral Hepatitis B Hepatitis C (Hepatitis D)	Viral serology (Tables 10.3, 5.3 and 5.4)
Metabolic Haemochromatosis	Iron studies, HFE gene test
Wilson's disease	Serum copper, caeruloplasmin, 24-hour urinary copper
Alpha-1-antitrypsin deficiency	Serum alpha-1-antitrypsin
Autoimmune hepatitis	Anti-nuclear antibody(ANA), anti-smooth muscle antibody (SMA), immunoglobulins and biopsy
Drugs	History ± biopsy
Cryptogenic	

Patients with positive anti-HCV and persistently normal ALT levels should be evaluated for the presence of viraemia with an HCV RNA (qualitative) test, as some may have cleared infection spontaneously. The HCV RNA test is rebatable under Medicare for this indication.

Patients found to be HCV RNA negative should be reassured that while they have probably been exposed to HCV in the past, they have apparently cleared infection. It is recommended that patients with normal liver function and no detectable HCV RNA have their liver enzymes checked one year after initial evaluation; if HCV RNA remains negative and liver enzymes are normal, no further follow-up is necessary.

Patients with normal or abnormal ALT levels and detectable HCV RNA may be considered for antiviral therapy; however, if they choose not to be treated at the time they should be followed every six to 12 months. Regular follow-up of patients with hepatitis C allows for monitoring of flares of activity, assessment of disease progression and discussion of current therapies.

See Table 11.2 for a summary of serological and virological markers.

TABLE 11.2 Interpretation of HBV, HCV and HDV serology

Virus	Marker	Significance
***Hepatitis B (HBV)**	HBsAg	Persistent infection
	anti-HBs	Past infection (natural immunity) or vaccination (acquired immunity)
	HBeAg	Highly infectious (absence may indicate mutant form)
	anti-HBc IgM	Acute infection*
	anti-HBc IgG	Current or past infection
	HBV DNA	Circulating virus
Hepatitis C (HCV)	anti-HCV	Current or past infection
	HCV RNA	Circulating virus** indicating current infection
Hepatitis D (Delta) (HDV)	anti-HDV	Current or past infection (only in HBsAg-positive patient)

Ag = antigen; s = surface; c = core; anti = antibody.
*May be only indicator of infection in 'window period' between disappearance of sAg and appearance of sAb.
**May be useful in high-risk HCV antibody-negative patient.

Ongoing monitoring of patients with chronic hepatitis C

The aims of follow-up in patients with chronic hepatitis C are to:

- Reinforce the need for lifestyle changes
- Decide which patients are appropriate for antiviral therapy
- Determine appropriate timing of referral to a specialist
- Monitor patients with cirrhosis for complications, such as hepatic decompensation and hepatocellular carcinoma (HCC)

For patients with chronic hepatitis C, ongoing monitoring is recommended every six to 12 months, unless there are specific reasons for more frequent monitoring (e.g. encouraging behaviour change). Tests to be conducted may include:

- Liver enzymes
- Full blood count
- Prothrombin time or international normalised ratio (INR)
- Hepatic ultrasound to screen for HCC in patients with cirrhosis
- Serum alpha-fetoprotein (AFP) to screen for HCC in patients with cirrhosis

Assessment for antiviral therapy

Previously in Australia, antiviral therapy was funded only for patients at highest risk of histologic progression. However, with increasing data to support the efficacy of antiviral therapy, it is now available to any previously untreated patient 18 years or older with compensated liver disease. Any patient with chronic hepatitis C should be advised of the potential benefits of antiviral therapy, and much of the assessment should be related to appropriate timing of therapy. Patients at highest risk of histologic progression (those with significant cofactors, long duration of infection, haematologic or biochemical markers of fibrosis such as low platelet count or aspirate aminotransferase [AST] higher than ALT, moderate or severe fibrosis on liver biopsy) should be encouraged to consider therapy as soon as practicable. For other patients, timing of treatment can be based on other lifestyle issues such as work, social circumstance, control of substance abuse, and desire for pregnancy.

When evaluating current disease severity and risk of progression to fibrosis and cirrhosis, clinical examination should be conducted (Chapter 7) and the investigations listed above should be performed. The finding of an elevated ALT level indicates the presence of necroinflammatory activity but is not predictive of cirrhosis or significant fibrosis. Thrombocytopenia, prolonged INR or hypoalbuminaemia all suggest the presence of cirrhosis with some degree of hepatic decompensation and portal hypertension. However, patients with well-compensated cirrhosis due to hepatitis C may have a completely normal platelet count, INR and serum albumin level for many years. Hepatic ultrasound may show features of cirrhosis or fatty infiltration but is commonly normal.

Liver biopsy remains a very useful procedure for confirming or excluding significant fibrosis. However, a number of non-invasive fibrosis tests are currently under evaluation and may eventually replace liver biopsy in the majority of patients. Despite the removal of a mandatory liver biopsy to access antiviral therapy, it remains useful for guiding a patient's decision, particularly if they are ambivalent about therapy.

Liver biopsy is a relatively safe procedure. It is usually performed as a day-stay procedure, under ultrasound guidance using local anaesthetic only. Patients commonly experience some minor abdominal discomfort and right shoulder tip pain but severe pain is unusual. There is a small risk of significant bleeding (1:300) and death (1:10,000).

There are several systems in use for recording the degree of fibrosis in a liver biopsy. Most of these systems use a scoring system ranging from 0 (no fibrosis) to 4 (definite cirrhosis). The finding of minimal disease activity and no fibrosis (stage 0) suggests a very low likelihood of disease progression. Consequently, the patient may be reassured, and toxic and expensive therapy may be avoided.

Patients with stage 1 fibrosis may be offered antiviral therapy if there is associated moderate to severe inflammation, while patients with stage 2–4 fibrosis should be offered antiviral therapy, provided no contraindications are present.

Consideration of duration of infection is also important in the assessment of disease severity, rate of progression and need for treatment. For example, patients who have stage 1 fibrosis after three years of infection may have greater need for treatment than a person with stage 1 fibrosis after ten years.

Viral genotype impacts on length of treatment and likely response and, as discussed in the treatment section, genotype testing may assist the patient in making the decision to start treatment. Alternatively, genotype testing may be delayed until the patient sees a specialist.

In determining whether a patient is appropriate for antiviral treatment, the primary care clinician may also consider the patient's social support and whether he or she is likely to adhere to treatment.

Local hepatitis C councils or drug user groups may provide information and peer support for people considering treatment (Chapter 15).

Shared care and referral

The primary care clinician has an important role in assessing which patients with chronic hepatitis C should be referred for specialist review. Such patients include those who wish to undergo antiviral treatment, those with persistently elevated ALT levels, those with clinical or laboratory features suggestive of cirrhosis, and those who request specialist evaluation. Liver clinics usually offer additional services that may be of benefit to patients. Such services include clinical nurse consultants, psychologists, psychiatrists, social workers and dieticians.

TABLE 11.3 Pre-referral investigation checklist

• Liver enzymes (usually three tests are conducted over six months)
• HCV serology (anti-HCV)
• HBV serology (HBsAg, anti-HBs, HBeAg, HBV DNA)
• HIV serology (if indicated)
• FBC, electrolytes, creatinine, coagulation studies (INR/APTT)
• Alpha-fetoprotein
• Liver ultrasound

Table 11.3 outlines investigations to conduct prior to referral. Referral to a liver clinic or hepatologist, which can be made at any time, is necessary for specialist pre-treatment assessment. Ongoing support and management of the patient on treatment may be conducted by primary care clinicians and specialists in a shared-care setting.

Monitoring for complications of liver disease

Patients with HCV-associated cirrhosis should be monitored for deteriorating liver function and for the development of HCC. Often a specialist is involved in the care of a patient with cirrhosis but frequently the patient will attend his or her general practitioner when new symptoms develop. Concerning features include:

- Falling serum albumin levels
- Prolongation of prothrombin time
- Development of jaundice
- Development of other clinical signs (e.g. peripheral oedema, ascites, muscle wasting)

Patients with these features should be considered for referral to a liver transplant unit.

HCC is becoming a major clinical problem in patients with HCV-associated cirrhosis. The current recommendations regarding screening for HCC include ultrasound and AFP levels every six months, to detect small lesions that may be amenable to curative treatment.

Hepatitis B

Initial assessment

The natural history of HBV infection varies according to age at acquisition of infection, mode of transmission and ethnic background. In people with the infection since infancy, hepatitis B proceeds through fairly predictable stages: a prolonged immunotolerant phase; a phase of attempted immune-mediated clearance, and then a quiescent phase. Not all patients pass through the immune clearance phase, and some can continue to have hepatic flares for many years, particularly if an HBeAg-negative (pre-core) mutant emerges (Chapter 1).

The aim of the initial evaluation of a patient with chronic hepatitis B is to assess the stage and severity of disease. Full viral serology and other investigations to be conducted during initial assessment are discussed in detail in Chapter 7. Serology results (Table 11.2) should be assessed in the context of liver function and the age of the patient. For example, a patient aged less than 20 years who is positive for surface and 'e' antigen (HBsAg+ and HBeAg+) and has normal liver enzymes does not require antiviral therapy. However, this patient should be told that he or she has a high likelihood of developing flares of hepatitis over subsequent years. Follow-up should be recommended so that hepatitis flares can be identified and antiviral treatment given at an appropriate time.

Patients over 20 years with abnormal liver function tests should have HBeAg status checked. If HBeAg+, they have active infection with wild-type HBV. If HBeAg is negative, they have a high likelihood of infection with an HBeAg-negative mutant. In this situation, HBV DNA should be performed to determine if viraemia is present. If HBV DNA is <104 copies/mL, and the patient has abnormal LFTs, alternative diagnoses should be considered.

HBsAg+, HBeAg-negative and anti-HBe+ patients with normal liver enzymes are in a relatively inactive phase of disease, although they may already be cirrhotic.

Ongoing monitoring of patients with chronic hepatitis B

All HBsAg+ patients should be followed, regardless of their apparent virologic status at initial evaluation. The six-monthly review of patients with chronic hepatitis B includes:

- A check for signs of chronic liver disease or decompensation
- Serum liver enzymes, FBC, coagulation studies and AFP
- Liver ultrasound if cirrhotic or family history of HCC

HBsAg+, HBeAg-negative women with no evidence of active liver disease are generally at low risk of progression and require only yearly check-ups to make sure that their status has not changed. For reasons that remain unclear, men with the same serologic status, particularly those with infection since infancy, remain at risk of HCC development regardless of the presence or absence of cirrhosis. They should be seen twice a year for review.

Patients with known cirrhosis should undergo serum AFP testing and ultrasound every six months to screen for HCC. Because non-cirrhotic patients are also at risk of HCC, screening is recommended by some physicians but this policy is not universally adopted.

Patients with active liver disease (that is, with abnormal liver enzymes) should be closely monitored and considered for antiviral therapy. In HBeAg+ patients, the long-term response to antiviral therapy is significantly better if treatment is initiated during a hepatitic flare (ALT>twice normal) rather than when enzymes are normal or only mildly elevated (ALT<twice normal).

Patients with HBeAg-negative disease (pre-core mutant) and elevated ALT levels should be considered for liver biopsy with a view to antiviral therapy as they have a high likelihood of significant fibrosis. Patients with known cirrhosis without decompensation should also be considered for antiviral therapy as there is evidence of reduced progression to decompensated liver disease and HCC.

General management issues for patients with viral hepatitis

Discussion about routes of viral transmission

Patients with viral hepatitis will commonly be concerned about the risks of transmitting the infection to others. Issues regarding sexual transmission, mother-to-child transmission, blood-borne transmission and casual contact transmission should all be discussed.

Hepatitis C is transmitted primarily through blood-to-blood contact. The sharing of grooming tools that can cause skin abrasion (such as razors, toothbrushes and tweezers) should be avoided.

Injecting drug users must be encouraged to use sterile water, needles and syringes, as well as new injecting equipment such as spoons, filters and tourniquets each time they inject (Chapter 3 and Appendix 4).

Patients may be concerned about sexual transmission of HCV. There appears to be a very low risk of sexual transmission of HCV, although sexual behaviours that potentially involve exposure to HCV-infected blood may pose a more significant risk. There is conflicting evidence concerning an increased risk

of HCV transmission during anal intercourse and condoms may be recommended in this context. A recent increase in cases of acute hepatitis C among HIV-positive men who have sex with men (MSM) has been reported from a number of countries.[4] These cases seem to be associated with sexual (permucosal) transmission rather than injecting drug use but whether this relates to biological factors (e.g. higher HCV viral loads in HIV co-infection) or behavioural factors is as yet unclear.

There clearly is a risk of transmitting HCV from mother to child, although the risk is low (approximately 5%).[5] This risk is significantly higher if the mother has HIV-HCV co-infection.

Currently, there is no indication for elective caesarean section in mothers with HCV infection.

However, it should be noted that there is some evidence that prolonged rupture of membranes and use of invasive foetal monitoring may increase the risk of mother-to-child transmission of HCV,[6] and decisions about intervention may need to be made on a case-by-case basis. Breastfeeding is not generally considered to present an additional risk of HCV transmission. However, breastfeeding should be suspended if the nipples are cracked or if the baby has cuts in or outside the mouth.

In Australia, many people with HBV infection are migrants who contracted infection as infants.

With universal HBV vaccination of neonates and administration of hepatitis B immunoglobulin to infants of mothers with HBV infection, there are very few new cases of vertically acquired HBV in Australia. Most cases are acquired sexually or through direct blood-to-blood contact. People with HBV infection should ensure the safety of sexual partners by recommending vaccination and using safe sex methods.

Any patient who is HBsAg+ may transmit HBV sexually. Other recommendations to prevent blood-to-blood HBV transmission are as for prevention of HCV transmission.

Risk of transmission and infection is discussed in detail in Chapter 2. Communication of safe sex and safe injecting messages is covered in Chapter 3 and Appendix 1-3.

Lifestyle issues

The possibility of lifestyle modification needs to be discussed with the patient, particularly in relation to alcohol consumption and recreational drug use.

Alcohol intake should be minimal. There is no doubt that excessive alcohol consumption (>50 g/day) leads to disease progression and a poorer response to treatment in chronic HCV. A drink containing 10 grams of alcohol, such as a can of medium-light beer (3.5% alcohol) or a nip (30mL) of spirits, is regarded as a 'standard drink'. A can of regular beer (4.9% alcohol) equals 1.5 standard drinks (15 grams alcohol). A bottle of wine (9.5–13% alcohol) equals about seven to eight standard drinks (70–80 grams alcohol).[7] Australian guidelines published by the Digestive Health Foundation recommend that people with viral hepatitis should drink alcohol infrequently or at low levels, and should consider not drinking at all. Specific strategies are set out in Table 11.4. People with cirrhosis should be encouraged to stop drinking alcohol completely.

TABLE 11.4 How to reduce alcohol consumption

• Plan at least two alcohol-free days per week
• Switch to low alcohol or alcohol-free drinks
• Avoid situations where there will be pressure to drink, e.g. rounds at the pub
• Alternate non-alcoholic and alcoholic drinks
• Drink a daily maximum of two drinks

People who continue to inject drugs are of particular concern. Those using in a chaotic manner, particularly in an unsafe environment, are less at risk from chronic hepatitis C infection than from major overdose, acquisition of other viral infections, and other health concerns. In such patients, these areas should be addressed first rather than treatment for chronic hepatitis B or C. Referral to treatment programs and support groups may be appropriate. In people who inject only occasionally, or who are on stable drug dependency programs, treatment for hepatitis C and B can be carried out successfully. All people should be counselled regarding the risk of HCV re-infection after successful viral clearance if risk behaviour continues.

Nutrition

There is considerable, unsubstantiated dietary information and advice directed at people with chronic viral hepatitis. In November 2000, the Dietitians' Association of Australia supported dietary advice for people with hepatitis C. This advice strongly warns against restrictive diets which recommend exclusion of all dairy foods, red meat, caffeine-containing drinks, and food containing added sugar, artificial colours and preservatives.[8] Instead, a well-balanced diet is recommended. For most people with hepatitis C, dietary recommendations are the same as for the general population (encouraging: grilled rather than fried food; lean meats and fish; reduced-fat products; wholemeal bread; vegetables and fruit; pasta; minimisation of fat for spreading and cooking). People with advanced liver disease, or other conditions such as coeliac disease or diabetes may be referred to a specialist dietitian for further advice.

Overweight or obese patients should be advised of a gradual weight-reduction program, particularly as there is increasing evidence of interaction between HCV, obesity and type 2 diabetes in accelerating progression to fibrosis. Those who may have fatty liver need to avoid a precipitous drop in weight as this can induce deterioration in liver function.

Many people with active hepatitis C report nausea and intolerance to certain foods and drinks. Referral to a dietitian may be appropriate to ensure the patient is consuming necessary vitamins and minerals.

Patients with advanced liver disease who develop protein-calorie malnutrition should be seen by a specialist dietitian. Such patients often require protein supplementation, and should be encouraged to eat high-energy foods frequently throughout the day. Very few, if any, patients with advanced liver disease should be subjected to protein restriction. This is a change from the previous doctrine that all patients with hepatic encephalopathy should be protein restricted.

Fatigue and other symptoms

People with chronic hepatitis C may report fatigue, malaise, headache, rash and aching muscles and joints. Consideration should be given to specific food and drinks that may be triggering symptoms, as well as work, family or other commitments, which may exacerbate stress and fatigue. Patients may benefit from planning rest periods during the day or incorporating light-to-moderate exercise into their routines to reduce fatigue.

For reasons that are unexplained, patients with chronic hepatitis B infection seem to experience less fatigue than patients with chronic hepatitis C, unless they are having a hepatitic flare.

Vaccination

Co-infection with more than one hepatitis virus may be associated with more severe liver disease.

Superinfection with hepatitis A infection (HAV) in a patient with chronic hepatitis B or C, or acute hepatitis B in a patient with chronic hepatitis C may precipitate the development of acute liver failure. In the long term, patients with HBV and HCV co-infection tend to be more likely to progress to cirrhosis and to develop HCC. Thus, HAV and HBV vaccination should be offered to all patients with chronic hepatitis C, and HAV vaccination should be offered to chronic hepatitis B patients (Chapter 5).

Psychosocial support

Patients may experience social isolation, anxiety or discrimination related to infection with viral hepatitis, which may be compounded by physical symptoms. The primary care clinician can begin by listening to the patient and demonstrating sensitivity to linguistic and cultural differences, which may impact on an individual's response to viral hepatitis. Provision of verbal and written information relating to transmission or disease natural history may allay fears (Chapter 15). Referral to counselling or support services may be indicated for patients with complex emotional, family and relationship or disclosure issues. All patients should be made aware of services such as counselling and support groups, telephone helplines and community organisations.

Information about services is available from any teaching hospital unit or the local hepatitis C council (Chapter 15).

Complementary therapies

There is little evidence that herbal medicines have a profound antiviral effect despite many patients reporting some symptomatic improvement and the ability of some agents to induce a fall in ALT.[9,10]

Most preparations are safe but some have reported hepatotoxicity and should be avoided (e.g. mistletoe, valerian, heliotropium, kombucha tea). Close monitoring of liver biochemistry is recommended at the commencement of any herbal medicine.

Steroids, chemotherapy and viral hepatitis

Severe flares of hepatitic activity may be seen following a course of corticosteroids or other immunosuppressive or cytotoxic therapy, particularly in patients with chronic hepatitis B. Such flares may be fatal. For instance, HBsAg+ patients receiving chemotherapy have a 5% mortality from acute liver failure. All patients undergoing chemotherapy or other immunosuppressive treatments should be screened for HBsAg and if positive should be commenced on prophylactic antiviral therapy. People with HCV infection may also have mild flares of activity in such circumstances. However, acute liver failure does not occur.

Antiviral therapy for viral hepatitis

Aims of treatment

There are a number of aims of antiviral therapy in chronic viral hepatitis. These include:

- Eradication of infection
- Prevention of disease progression
- Improvement in histologic markers
- Improvement of symptoms
- Improved survival

All these aims can be achieved in a significant proportion of patients with hepatitis C or hepatitis B with currently available therapies.

Antiviral therapy – hepatitis C

The major aim of treatment is to achieve viral eradication. In hepatitis C, viral eradication is defined by the achievement of a sustained virological response (SVR); that is, negative HCV RNA by a

TABLE 11.5 Treatments for hepatitis B and C. Section 100 Highly Specialised Drugs Program of the PBS*

LAMIVUDINE (ZEFFIX) 100 mg daily taken orally (except in patients with HIV co-infection – the dose is 300 mg daily)

Condition	Criteria	Caution
Chronic hepatitis B	• Histological evidence of chronic hepatitis B on liver biopsy** • Abnormal serum ALT levels • HBeAg positive and/or HBV DNA positive • Absence of pregnancy and lactation • Female patients using effective contraception • Persons with advanced liver disease should have their treatment discussed with a transplant unit prior to initiating therapy	The development of lamivudine resistance in patients with cirrhosis or who are immunosuppressed may be associated with a severe flare of hepatitis and progression to liver failure.

INTERFERON ALFA-2A (ROFERON-A)
INTERFERON ALFA-2B (INTRON A) 5–10 million units subcutaneously 3 times weekly for 16–24 weeks

Condition	Criteria	Caution
Chronic hepatitis B	• Chronic hepatitis B on liver biopsy** • HBeAg+ and/or HBV DNA+ • HBV infection >6 months abnormal ALT • Absence of class B or C cirrhosis (ascites, variceal bleeding, encephalopathy, albumin <30 g/l, bilirubin >30 mmol/l • Absence of pregnancy and lactation • Female patients using effective contraception	Pegylated interferon alfa has been associated with depression and suicide. Patients with a history of mental illness should be warned of the risks. Psychiatric status must be monitored during therapy.

PEGYLATED INTERFERON ALFA-2A PLUS RIBAVIRIN (PegasysRBV Combination Therapy)
PEGYLATED INTERFERON ALFA-2B PLUS RIBAVIRIN (Pegatron Combination Therapy)

Dosage variable. Refer to relevant product information. For patients with genotype 2 or 3 without cirrhosis or bridging fibrosis the treatment course is limited to 24 weeks. For patients with genotype 1, 2, 3, 4, 5 or 6 with cirrhosis or bridging fibrosis, treatment course is limited to 48 weeks. Patients with genotype 1, 4, 5 or 6 who are eligible for 48-week treatment may only continue treatment beyond 12 weeks if HCV RNA is negative or viral load has dropped by at least 2 logs (a second HCV RNA assay is not necessary at week 24). Patients with genotype 1, 4, 5, or 6 who are HCV RNA positive at week 12 but have attained at least a 2-log drop in HCV viral load may only continue treatment after 24 weeks if plasma HCV RNA is negative at week 24. Patients with genotype 2 or 3 with cirrhosis or bridging fibrosis may only continue treatment after 24 weeks if HCV RNA is negative at 24 weeks.

Condition	Criteria	Caution
Chronic hepatitis C in patients 18yrs or older, with compensated liver disease, and with no prior interferon or peg-interferon.	• Abnormal ALTs plus anti-HCV+ and HCV RNA+ • Absence of pregnancy and lactation in women (including partners of male patients) • Patient (male or female) and his/her partner must use effective forms of contraception (one for each partner)	As for interferon above ribavirin is a teratogen (category X – drugs with a high risk of causing permanent damage to the foetus) and must not be given to pregnant women. Pregnancy in women taking ribavirin and in the female partners of men taking ribavirin must be avoided during treatment and for 6 months following treatment. N.B. Even though liver biopsy is no longer mandatory, many hepatologists will still recommend it for staging of liver disease.

ADEFOVIR DIPIVOXIL 10mg daily taken orally. Patients may receive treatment in combination with lamivudine for the first 3 months only of PBS-subsidised adefovir dipivoxil therapy (patients who are immunocompromised may receive the same treatment for 12 months). Thereafter, PBS-subsidised adefovir dipivoxil must be used as a monotherapy.

Condition	Criteria	
Patients with chronic hepatitis B who have failed lamivudine therapy.	• Absence of pregnancy and lactation in women • Female patient and her partner must use effective forms of contraception (one for each partner) • Repeatedly abnormal ALTs (>1.2 x upper normal limit) while on concurrent antihepadnaviral therapy of 6 months or more in conjunction with anti-HBe+ and/or HBV DNA+	

Continued overleaf

TABLE 11.5 Treatments for hepatitis B and C. Section 100 Highly Specialised Drugs Program of the PBS*

PEGYLATED INTERFERON ALFA-2A MONOTHERAPY (PEGASYS) 180 micrograms subcutaneously once weekly

Condition	**Criteria**
Monotherapy in patients with chronic hepatitis B and compensated liver disease who satisfy all of the following criteria:	(1) Histological evidence of chronic hepatitis on liver biopsy (except in patients with coagulation disorders considered severe enough to prevent liver biopsy) (2) Abnormal serum ALT levels in conjunction with documented chronic hepatitis B infection (HBe antigen positive and/or HBV DNA positive) (3) Have received no prior peginterferon alfa therapy for the treatment of hepatitis B (4) Female patients of child-bearing age are not pregnant, not breast-feeding, and are using an effective form of contraception (5) Are not persons with Child's class B or C cirrhosis (ascites, variceal bleeding, encephalopathy, albumin less than 30g per L, bilirubin greater than 30 micromoles per L) Treatment is limited to 1 course of treatment for a duration of up to 48 weeks.

ENTECAVIR MONOHYDRATE 0.5mg daily

Condition	**Criteria**
Patients aged 16 years or older with chronic hepatitis B who satisfy all of the following criteria:	(1) Histological evidence of chronic hepatitis on liver biopsy (except in patients with coagulation disorders considered severe enough to prevent liver biopsy) (2) Abnormal serum ALT levels in conjunction with documented chronic hepatitis B infection (HBe antigen positive and/or HBV DNA positive) (3) Female patients of child-bearing age are not pregnant, not breast-feeding, and are using an effective form of contraception Persons with Child's class B or C cirrhosis (ascites, variceal bleeding, encephalopathy, albumin less than 30g per L, bilirubin greater than 30 micromoles per L) should have their treatment discussed with a transplant unit prior to initiating therapy. Note: PBS-subsidised entecavir monohydrate must be used as monotherapy.

ENTECAVIR MONOHYDRATE 1.0 mg daily

Condition	**Criteria**
Patients aged 16 years or older with chronic hepatitis B who have failed lamivudine therapy and who satisfy all of the following criteria:	(1) Repeatedly elevated (greater than 1.2 times the upper limit of normal) serum ALT levels while on concurrent antihepadnaviral therapy of greater than or equal to 6 months duration in conjunction with documented chronic hepatitis B infection (HBe antigen positive and/or serum HBV DNA positive) (2) Female patients of child-bearing age are not pregnant, not breast-feeding, and are using an effective form of contraception Persons with Child's class B or C cirrhosis (ascites, variceal bleeding, encephalopathy, albumin less than 30g per L, bilirubin greater than 30 micromoles per L) should have their treatment discussed with a transplant unit prior to initiating therapy. Note: PBS-subsidised entecavir monohydrate must be used as monotherapy. Patients should have undergone a liver biopsy at some point since initial diagnosis to obtain histological evidence of chronic hepatitis. Patients with Child's class B or C cirrhosis should have their treatment discussed with a transplant unit prior to initiating therapy. No Caution section for these last treatments.

*Details correct at July 2007.
**Patients with severe coagulation disorders not required to undergo biopsy. Monotherapy with interferon alfa-2a and -2b is no longer the standard for HCV therapy. The longer-acting pegylated interferons have replaced them except where the patient is intolerant to ribavirin.

sensitive qualitative test six months after the completion of six or twelve months of therapy.

The most effective therapy for hepatitis C is a combination of once-weekly subcutaneously administered pegylated interferon plus twice-daily oral ribavirin. Such treatment is available in Australia under Section 100 of the Pharmaceutical Benefits Scheme (PBS). Refer to Table 11.5.

The combination of pegylated interferon and ribavirin produces an overall SVR of greater than 50%,[11,12] a significant improvement over the SVR rates achieved with interferon monotherapy (<10%) or standard interferon (given three times a week) plus ribavirin (40%).

The likelihood of response is much higher in patients infected with genotype 2 or 3 (80% SVR rate after six months of combination pegylated interferon and ribavirin) than genotype 1 or 4 (50% SVR rate after 12 months of therapy). While HCV genotype is the most powerful predictor of response, other predictors of SVR include low viral load, minimal hepatic fibrosis, female gender and age (younger than 40 years). Recently the rapidity of on-treatment response has emerged as a major factor in predicting sustained virologic response.

By monitoring on-treatment response, patients can be counselled as to their likelihood of viral eradication. Patients who have a greater than 2 log (100-fold) reduction in viral load by week 12 (termed an early virologic response) have an approximately 70% chance of sustained virologic response.[13] Conversely, patients with genotype 1 who fail to achieve a greater than 2 log drop in viral load at week 12 should have their treatment ceased as there is a negligible chance of viral eradication. Additionally, patients with genotype 1 who achieve undetectable HCV RNA at week 4 of therapy (termed a rapid virologic response) have a 90% chance of viral eradication and may even be able to shorten their treatment duration.[14] There is currently significant effort being directed at determining whether measurement of early on-treatment virological responses may allow some patients to have treatment duration shortened, and whether other patients may benefit from longer duration of therapy.

The benefits of achieving an SVR include a reduced risk of progression for patients at all stages of disease and probably a lower incidence of HCC development.

In addition, there have been reports of significant regression of fibrosis, even in cirrhotic patients. Patients who have failed to respond to either interferon monotherapy or combination interferon plus ribavirin are not eligible for further treatment under current Section 100 guidelines but may pay for their own treatment or may be able to access combination pegylated interferon plus ribavirin through compassionate-use protocols.

Therapy may be for six or 12 months duration, depending on HCV genotype.[15] When discussing the benefits and risks of treatment, the GP can request genotype testing.

Medicare funding covers genotype testing. This information may help to guide a patient who is ambivalent about having treatment. In particular, patients with genotype 2 or 3 can be counselled that they have a high chance of eradicating the virus with six months of treatment.

Patients with genotype 1 infection can also be informed of their likelihood of eradicating infection. While this rate is lower, it should not dissuade patients from attempting treatment but remains an important discussion point. These discussions may take place before specialist referral.

There are significant numbers of patients with hepatitis C who respond poorly to therapies or have contraindications to therapy. Decisions about therapy in these individuals are made on a case-by-case basis by the specialist. These include patients with HCV and HBV co-infection, HCV and HIV co-infection, chronic renal failure, cryoglobulinaemia and with HCV recurrence after liver transplantation.

HIV and HCV co-infection

HIV and HCV co-infection is associated with higher HCV viral load and an accelerated rate of HCV disease progression.[16] There is no fundamental difference in the management of HCV in the presence of HIV although certain antiretroviral agents (e.g. didanosine, zidovudine) are contraindicated or should be avoided if possible. Patients with HIV and HCV co-infection who either have stable CD4 cell counts on antiretroviral therapy, or who do not require antiretroviral therapy may be considered for combination pegylated interferon plus ribavirin. Management of such patients may be difficult, particularly in patients already taking multiple medications, as side-effects, drug interactions and poor tolerability are common and therapy should be carried out by a specialist experienced in this area.[17]

Who should be treated for hepatitis C?

Antiviral therapy is currently reimbursed for patients who are 18 years or older with:

- Anti-HCV positivity
- Detectable serum HCV RNA
- Compensated liver disease
- No prior treatment with interferon alfa or pegylated interferon alfa

In the past, to access reimbursed antiviral therapy, patients have required abnormal liver enzymes and a liver biopsy showing at least a moderate degree of fibrosis. Neither of these features are now required.

Table 11.5 details who can receive treatment for hepatitis C through Section 100 of the PBS. The major contraindications to therapy include:

- Decompensated liver disease
- Major psychiatric conditions, particularly severe depression
- Autoimmune disease
- Significant cardiac disease
- Pregnancy (ribavirin is a teratogen – patients and their partners must avoid pregnancy during therapy and for six months after cessation of treatment due to the possibility of birth defects)

Although interferon is contraindicated in people with depression it may be used safely in patients with controlled depression and anxiety disorders or controlled seizure disorders. If the patient is being treated by a psychiatrist or neurologist, discussion with the specialist is recommended before the initiation of interferon therapy.

Side effects

Side effects are common but do not usually require discontinuation of treatment. However, patients do require significant support and encouragement throughout treatment. Adverse effects of therapy include flu-like symptoms, irritability, weight loss, insomnia, vomiting, depression and anxiety, mild hair loss, rash, cough, myelosuppression and induction of autoimmunity, particularly thyroid disease.

Ribavirin treatment always induces a degree of intravascular haemolysis, which results in a fall in haemoglobin in most patients. This anaemia may result in tiredness, shortness of breath and precipitation of myocardial ischaemia in at-risk patients. Depression may occur as a result of serotonin depletion caused by interferon, and SSRIs may be considered for management or prophylaxis.

Given the wide range and potential seriousness of side effects, patients must be closely monitored during therapy. Currently, most treatment is provided through public hospitals and patients have ready access to nurse specialists to advise and support them through therapy. In general, patients on therapy are seen once a week for the first month, and then each month until the end of treatment, with blood counts and biochemistry evaluated at each visit. Dose modification guidelines are followed when side-effects or laboratory changes require intervention.

The decision to treat

Given the likelihood of significant side effects, decisions about whether to treat and when to treat are often difficult. When discussing therapy with a patient, issues and commitments such as work, study, relationships, substance abuse and pregnancy should be considered.

The shift to primary care

While most treatment is based in public hospitals at present, there is an important trend towards treatment in the community. This will involve primary care clinicians taking on a greater role in the support and monitoring of patients on therapy. Many hospitals have put together shared-care packages with specific information and guidelines about management during therapy. In addition, a small number of GPs in NSW and ACT have been approved to prescribe combination therapy as part of a Section 100 (PBS) community prescribing pilot project. To ensure the highest chance of achieving viral eradication, it is important to support patients through a complete course of therapy.

Antiviral therapy – hepatitis B

Until recently the only treatments available for patients with chronic hepatitis B were interferon alfa and lamivudine (see Table 11.5). In the last few years, a number of new agents have been approved for the treatment of patients with chronic hepatitis B.[18] These include the nucleoside analogue entecavir, and the immunomodulator pegylated interferon alfa 2a. Both are subsidised through Section 100 of the PBS.[19,20] In addition a nucleotide analogue, adefovir dipivoxil, is also approved although only subsidised in patients with lamivudine-resistance. Another nucleoside analogue, telbivudine, is also approved but not yet subsidised.

The choice between these agents is based on a number of factors. A four- to six-month course of standard interferon is associated with HBeAg loss in 30–40% of patients and, in early trials, approximately 10% lost HBsAg.[21,22] Long-term benefits include improved survival and a reduction in the incidence of HCC. Interferon is of particular benefit in those patients with high ALT and low HBV DNA levels. Interferon may be hazardous to those with advanced liver disease and is associated with significant side-effects. Recently, pegylated interferon alfa 2a given weekly for 48 weeks has been shown to be effective in both HBeAg positive and HBeAg negative disease.[23,24]

Lamivudine (100 mg daily) is well tolerated and highly effective in suppressing HBV replication and improving liver histology. It is very effective against HBeAg negative mutant HBV and is useful in both compensated and decompensated cirrhosis. The rate of HBeAg seroconversion in HBeAg positive patients after 12 months of lamivudine therapy, however, is less than that with Pegylated interferon and cessation of lamivudine treatment is frequently associated with virological and biochemical relapse. Unfortunately, lamivudine therapy is also associated with the emergence of resistant strains (YMDD variants), and the incidence of mutations increases with duration of treatment. Although not usually associated with clinical deterioration, these variants may induce a severe hepatitis and liver

failure in cirrhotic or immunosuppressed patients. Lamivudine is also of benefit in patients with HIV/HBV coinfection, as it is effective against both viruses. However, such patients have a high likelihood of developing lamivudine-resistant HBV, which may be associated with rapidly progressive disease.

Adefovir is a nucleotide agent with anti-HBV activity. Addition of adefovir dipivoxil in HBV mono-infected patients with lamivudine resistance is effective.[25] Adefovir is available via Section 100 for patients who have failed lamivudine and have elevated serum ALT (>1.2 times the upper limit of normal) and are HBeAg and/or HBVDNA positive. Continuation of lamivudine when adefovir is added appears to prevent the development of adefovir resistance[26] but currently dual agent therapy is subsidised for only three months on the PBS in immunocompetent individuals. Adefovir monotherapy may be associated with emergence of drug-resistant mutants and a clinical flare of hepatitis.

Entecavir is approved and reimbursed via Section 100 for, and is effective in, both therapy naïve patients and patients with evidence of lamivudine resistance. In clinical trials it has been proven to be superior to lamivudine in naïve patients with both HBeAg positive and HBeAg negative disease.[27,28] It has a very low rate of resistance in naïve patients. Whilst entecavir is still active in lamivudine resistant disease, the entecavir resistance rate in this setting is much higher. Telbivudine is another nucleoside agent which has been recently approved, but is not yet available through PBS-subsidy. Telbivudine is well tolerated, and very potent against hepatitis B, but is associated with some emergence of drug resistance, particularly in those patients that fail to rapidly suppress HBV DNA to undetectable levels. It is ineffective in individuals with lamivudine resistance.

Tenofovir is a nucleotide analogue with dual HIV and HBV activity. It is currently licensed for HIV therapy but not for use in HBV mono-infected patients. In HIV/HBV coinfected patients it is highly effective against HBV in both treatment naïve and lamivudine experienced patients.[29] It is well tolerated and has a very low rate of HBV resistance. It is likely to become licensed for use in HBV mono-infection in the near future.

Who should be treated?

In compensated patients with chronic HBV, antiviral therapy is indicated where there is:

- active viral replication (HBeAg+ and/or HBV DNA positive)
- persistently elevated ALT levels
- histological evidence of chronic injury

The initial aim of treatment is to suppress viral replication as indicated by HBeAg seroconversion (loss of HBeAg and appearance of anti-HBe) and loss of HBV DNA. Optimal duration of therapy is unknown but the current recommendation is to continue therapy for at least 6–12 months after seroconversion occurs. Once therapy has stopped, at least 15% of patients will undergo seroreversion (i.e. they become HBeAg+ again).

Patients with HBeAg-negative infection should also be considered for therapy although the optimal duration of therapy is not known and patients may need to continue treatment indefinitely.

Patients who are HBeAg-negative with abnormal LFTs should have an HBV DNA performed to identify pre-core mutant disease. If HBV DNA is positive, then liver biopsy and treatment with an antiviral agent should be discussed, particularly for patients with moderate or marked hepatic fibrosis.

Liver transplantation in viral hepatitis

Chronic hepatitis C and hepatitis B are the leading indications for liver transplantation in Australia.

Patients should be referred to a transplant unit when they develop signs of hepatic decompensation, such as ascites, encephalopathy, bacterial infections (particularly spontaneous bacterial peritonitis), muscle wasting or worsening fatigue. It is best to try to identify subtle signs of impending liver failure (Chapters 5 and 7), so that early referral can be made. Liver transplantation is also indicated in some patients with HCC. Detailed management of end-stage liver disease is beyond the scope of this publication.

Summary

Chronic hepatitis poses challenges of diagnosis, general management, selection for treatment and care during treatment. It is important that a patient's concerns be addressed by the provision of information about the disease and access to counselling and psychosocial support. The primary care clinician has a vital role in the assessment and monitoring of patients with chronic viral hepatitis. Shared care is the preferred model of care for patients with chronic viral hepatitis and effective communication between GPs, specialists and referral centres is required for optimal patient management.

References

1 Farrell GC, editor. Hepatitis C. A management guide for general practitioners. Aust Family Physician 1999;28:SI3–88.

2 Farrell GC, Liaw Y-F, McCaughan GW, editors. Consensus statements on the prevention and management of hepatitis B and hepatitis C in the Asia-Pacific region. J Gastroenterol Hepatol 2000;15:815–41.

3 Schiff ER, Hoofnagle JH, editors. Update on viral hepatitis. Hepatology 2000;32:SI 1–199.

4 Danta M, Brown D, Bhagani S, Pybus O, Sabin C, Nelson M, et al. for the HIV and Acute HCV (HAAC) group. Recent epidemic of acute hepatitis C virus in HIV-positive men who have sex with men linked to high-risk sexual behaviours. AIDS 2007;21(8):983–91.

5 Conte D, Fraquelli M, Prati D, Colucci A, Minola E. Prevalence and clinical course of chronic hepatitis C virus (HCV) infection and rate of vertical transmission in a cohort of 15,250 pregnant women. Hepatology 2000; 31:751–5.

6 Gibb DM, Goodall RL, Dunn, DT. Mother-to-child transmission of hepatitis C virus: evidence for preventable peripartum transmission. Lancet 2000;356 (9233):904–07.

7 National Health and Medical Research Council (NHMRC). Australian Drinking Guidelines: Health risks and benefits. Canberra: NHMRC, October 2001.

8 Albion Street Centre. Nutrition and hepatitis C: information for health care workers. 2000. Available at:www.sesahs.nsw.gov.au/albionstcentre

9 Batey RG, Batey RG, Bensoussan A, Fan YY, Bollipo S, Hossain MA. Preliminary report of a randomized, double blind placebo-controlled trial of a Chinese herbal medicine preparation CH-100 in the treatment of chronic hepatitis C. J Gastroenterol Hepatol 1998;13:244–7.

10 Parés A, Planas R, Torres M, Caballería J, Viver JM, Acero D, et al. Effects of silymarin in alcoholic patients with cirrhosis of the liver: results of a controlled, double-blind, randomized and multicenter trial. J Hepatol 1998;28(4):615–21.

11 Manns MP, McHutchison JG, Gordon SC, Rustgi VK, Shiffman M, Reindollar R, et al. Peginterferon alfa-2b plus ribavirin compared with interferon alfa-2b plus ribavirin for initial treatment of chronic hepatitis C: a randomised trial. Lancet 2001;358:958–65.

12 Fried MW, Shiffman ML, Reddy KR, Smith C, Marinos G, Gonçales FL Jr, et al. Peginterferon alfa-2a plus ribavirin for chronic hepatitis C virus infection. N Engl J Med. 2002;347:975–82.

13 Davis GL, Wong JB, McHutchinson JG, Manns MP, Albrechtr J. Early virologic response to treatment with pegylated interferon alfa-2b plus ribaviron in patients with chronic hepatitis C. Hepatology 2003; 38:645–52.

14 Jensen DM, Morgan TR, Marcellin P, Pockrus PJ, Reddy KR, Hadziyannis S, et al. Early identification of HCV genotype 1 patients responding to 24 weeks peginterferon -2a(40kd) ribaviron therapy, Hepatology 2006; 43:954–60

15 McCaughan GW, Strasser SI. Emerging therapies for hepatitis C virus (HCV) infection: importance of HCV genotype. Aust NZ J Med 2000;30:644–6.

16 Benhamou Y, Bochet M, Di Martino V, Charlotte F, Azria F, Coutellier A, et al. Liver fibrosis progression in human immunodeficiency virus and hepatitis C coinfected patients. Hepatology 1999;30:1054–8.

17 Soriano V, Rodriguez-Rosado R, Garcia-Samaniego J. Management of chronic hepatitis C in HIVinfected patients AIDS 1999;13:539–46.

18 Keeffe EB. Marcellin P. New and emerging treatment of chronic hepatitis B. Clin Gastroenterol Hepatol 2007;5(3):285–94.

19 Strasser SI, McCaughan GW. Therapies for chronic hepatitis B: emerging roles for nucleoside analogues. Aust NZ J Med 2000;30:556–8.

20 Torresi J, Locarnini S. Antiviral chemotherapy for the treatment of hepatitis B infection. Gastroenterology 2000;118 (suppl):S83–S103.

21 Niederau C, Heintges T, Lange S, Goldmann G, Niederau CM, Mohr L, Häussinger D. Long-term follow-up of HBeAg-positive patients treated with interferon alfa for chronic hepatitis B. N Engl J Med 1996;334:1422–7.

22 Perrillo RP, Schiff ER, Davis GL, BodenheimerHC, LindsayK, Payne J, et al. A randomized, controlled trial of interferon alfa-2b alone and after prednisone withdrawal for the treatment of chronic hepatitis B. The Hepatitis Interventional Therapy Group. N Engl J Med 1990;323:295–301.

23 Marcellin P, Lau GK, Bonino F, Farci P, Hadziyannis S, Jin R et al. Peginterferon alfa-2a Alone, Lamivudine Alone, and the Two in Combination in Patients with HBeAg-Negative Chronic Hepatitis B [Multicenter Study. Randomized Controlled Triall].

N Engl J Med 2004;351(12):1206–17.

24 Lau GK, Piratvisuth T, Luo KX, Marcellin P, Thongsawat S, Cooksley G, et al. Peginterferon Alfa-2a, Lamivudine, and the Combination for HBeAg-Positive Chronic Hepatitis B [Multicenter Study. Randomized Controlled Trial]. N Engl J Med 2005;352(26):2682–95.

25 Schiff ER, Lai CL, Hadziyannis S, Neuhaus P, Terrault N, Colombo M, et al. Adefovir Dipovoxil Study 435 International Investigators Group. Adefovir dipivoxil therapy for lamivudine-resistant hepatitis B in pre- and post-liver transplantation patients. Hepatology 2003:38;1419–27.

26 Rapti I, Dimou E, Mitsoula P, Hadziyannis SJ. Adding-on versus switching-to adefovir therapy in lamivudine-resistant HBeAg-negative chronic hepatitis B. Hepatology 2007;45(2):307–13.

27 Chang TT, Gish RG, de Man R, Gadano A, Sollano J, Chao Y-C, et al. for the BEHoLD AI463022 Study Group. A comparison of entecavir and lamivudine for HBeAg-positive chronic hepatitis B. N Engl J Med 2006;354(10):1001–10.

28. Lai CL, Shouval D, Lok AS, Chang T-T, Cheinquer H, Goodman Z, et al. for the BEHoLD AI463027 Study Group. Entecavir versus lamivudine for patients with HBeAg-negative chronic hepatitis B. N Engl J Med 2006;354(10):1011–20.

29 Schmutz G, Nelson M, Lutz T, Sheldon J, Bruno R, von Boemmel F, et al. Combination of tenofovir and lamivudine versus tenofovir after lamivudine failure for therapy of hepatitis B in HIV-coinfection. AIDS 2006;20(15):1951–4.

Primary care management of STIs

12

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Introduction

Sexually transmitted infections (STIs) are a diverse group of infections whose most common feature is sexual transmission. This group embraces the blood-borne viruses (BBVs)—hepatitis B virus (HBV), hepatitis C virus (HCV) (very rarely) and human immunodeficiency virus (HIV)—as well as other well known STIs such as gonorrhoea, syphilis, and genital chlamydia infection.

This chapter aims to provide an update on the management of STIs for primary care practitioners and other specialist clinicians who may be relatively unfamiliar with STIs, and to describe the role of the primary care clinician in the diagnosis and treatment of patients with STIs.

In the first part of the chapter the emphasis will be on general principles of management. The second part of the chapter will look at the individual management of the eight STI syndromes outlined in Chapter 8.

The challenge of managing patients with STI infection

There are many challenges in the management of patients with STIs or patients who are at risk of STIs. Misconceptions about STIs are rife in the community and patients are generally less well informed about common STIs than they are about HIV. Only a minority know how common genital chlamydia infection is in the community, how silent it can be and how it is associated with pelvic inflammatory disease (PID) and later infertility in women. Providing simple information about STIs and their potential for harm is a vital role for the primary care clinician. Management of all STIs is shaped by the stigma attached to these infections and the fear or anxiety patients may have about the necessary investigations, the treatments involved and exactly what the diagnosis means to them, their regular sexual partner and other current or future partners. Women almost inevitably think about the possible effect of the diagnosis on their fertility and their ability to give birth to healthy children.

Key points

- In their early stages, STIs are generally simple infections, capable of rapid assessment and on-the-spot single dose treatment.
- Some STIs (e.g. chlamydia, herpes simplex, human papillomavirus) are amongst the most common infections encountered in everyday practice, so clinicians need to be familiar with their management and know how to talk with and inform their patients about these conditions.
- Although single-dose treatment is favoured for STIs, there are some situations (PID, epididymo-orchitis) where more prolonged treatment is necessary. If the patient is regularly missing doses, treatment failure may result.
- STIs and fear of STIs introduce a range of psychosocial and sexuality questions in patients; the clinician has a vital role in providing an opportunity for patients to talk about and explore these uncertainties.
- Contact tracing (partner notification) is an integral part of the treatment of almost all STIs. All treating clinicians have a clear responsibility to help achieve successful outcomes in contact tracing.
- All ano-genital ulceration in Australia and New Zealand is due to genital herpes until proven otherwise, but clinicians should always ask themselves 'could this be syphilis?'
- Once the clinician has excluded pregnancy in a patient with pelvic pain, if the sexual history is suggestive, she or he should treat immediately for STI-related PID, pending results of tests and response to therapy.
- Think of primary HIV infection in any patient diagnosed with a recently acquired STI, as well as in any patient with a flu-like illness.
- Not all ano-rectal symptomatology is surgical or routinely medical. Ask yourself, and not just in gay men, 'could this be an STI?'
- Treating genital warts can be tedious and time-consuming but it is difficult to overstate the psychological impact of their presence on a patient's sense of wellbeing.

Clinicians must be sensitive to these issues and must be prepared to discuss them frankly.

The doctor-patient relationship is central to the successful management of STIs. Establishing, from the very first visit, friendly and open rapport and then nurturing this ongoing relationship is a major task for the primary care clinician. The qualities clinicians need to maintain such a relationship are demanding, but not unlike qualities needed to manage other conditions. They are empathy, honesty, sensitivity to the patient's feelings and needs, accessibility, a firm and practical commitment to confidentiality and the privacy of the patient, and medical knowledge and expertise. In addition the clinician needs to be able to show by body language, attitude and spoken word, that she or he is comfortable talking about sex without reserve or shame and is ready and able to deal helpfully with patients with possible STIs. Finally, the clinician needs to be able to set aside personal feelings, moral beliefs and any long-held attitudes towards sex and sexual diversity so that the patient does not feel judged or belittled.

Natural history

When managing and treating STIs, it's useful to understand the natural history of the specific STI you're dealing with; this is especially important where no curative treatments are available—as is the case with the viral STIs. It's also useful to know where there are gaps in medical knowledge, e.g. with genital human papillomavirus (HPV) infection.

Assessing the patient with a possible STI

The initial assessment

Patients requiring assessment are those who present with symptoms that are consistent with an STI being present, those who declare that they are concerned about STIs and that they may be at risk for an STI, as well as those who accept opportunistic STI screening at the clinician's suggestion.

There are several things the clinician will want to know about the patient:

- The nature of the symptoms: are they one of the eight STI syndromes (see Table 12.1). Could these symptoms be due to something not STI-related such as torsion of the testis or ectopic pregnancy?
- Any previous history of STIs or tests for STIs: have there been previous sexual health check-ups?
- The sexual history: what is the patient's risk? For example, numbers of partners in last three months and 12 months, gender(s) of partners, types of sex (vaginal, oral, anal), type of protection used if any (condoms, contraception), partners' sexual risks (overseas travel, injecting drug use, sex worker or client of sex worker, possible same sex contact).
- The patient's level of knowledge about STIs, including BBV

TABLE 12.1 STI syndromes

• Urethral discharge
• Vaginal discharge
• Ano-genital ulcer disease
• Ano-genital lumps and bumps
• Ano-rectal syndromes
• Pelvic pain syndrome in women
• Scrotal swelling
• Skin rash – genital and generalised

- General health and past medical history including vaccinations: hepatitis A virus (HAV), hepatitis B virus (HBV), and human papillomavirus (HPV); drug allergies
- Recent medications, both systemic and topical, prescribed or over the counter: has the patient been using any antimicrobial agents in the last few days?
- Psychosexual history: is the patient comfortable with sexuality? Is the patient able to cope well with problems of everyday life? Is there any psychiatric history?

Establishing a good rapport with your patient takes practice, but it should be possible to gain the required information within a reasonable time frame and in such a way that the patient feels involved and a contributor to the process. Assessing sexual risk requires a collaborative approach between clinician and patient. The clinician is also able to impart a lot of useful information to patients while taking a sexual history.

Co-infection with HIV

HIV infection is an STI, so almost by definition people with an STI, or at risk of STIs, are at some risk of HIV, although the precise level of risk will depend on the type of sexual activities, the gender of the patient's partner or partners and the prevalence of HIV infection in the region, city or country where the patient's sexual contact(s) took place.

The interaction between HIV and other STIs is complex and cumulative (see Chapter 1). HIV, on the one hand, interferes with the clinical manifestations and severity of some STIs and, on the other hand, some STIs increase the viral load of HIV in bodily fluids, enhance HIV viral shedding from genital sites and can alter the natural history of HIV infection.[1]

People living with HIV today are generally well and continue to be sexually active. Their treating clinicians would not want them, nor advise them to become celibate, but they do exhort them to

adopt safer sex practices to avoid contracting other STIs and to prevent ongoing transmission of HIV. Standard safe sex practices which advocate condoms for all penetrative vaginal and anal sex still allow unprotected oral sexual activities to continue. Several STIs are transmitted by oral sex, so all clinicians now advise regular screening of people with HIV infection for other STIs and appropriate guidelines are available (see Chapters 4 and 9).[2,3]

Primary HIV infection (the seroconversion illness) in Australia and New Zealand occurs most commonly after an unsafe sexual contact. Unsafe sexual contacts sometimes result in the patient contracting another STI in addition to HIV. The STI may be symptomatic or the patient may be diagnosed with an STI after undergoing a routine opportunistic screen on the clinician's recommendation (see Chapter 8). In either case, primary HIV infection can be recognised first in primary care practices (including emergency departments and sexual health clinics)[4] as often the reason the patient attends is for intercurrent flu-like illness (see Chapter 8). The take-home message is:

- Think of primary HIV infection in any patient diagnosed with a recently acquired STI, as well as in any patient with a flu-like illness (Case Study 1).

Physical examination

When patients have symptoms consistent with a STI, clinicians should examine with a good light source the anogenital region very carefully as well as any other relevant areas (mouth and throat, lymph nodes, palpation of abdomen and pelvis) to avoid the possibility of missing pathology. The clinician should take the time to explain why a genital examination is necessary, what it involves and, most importantly, what measures she or he proposes to minimise embarrassment (a covering sheet, presence of a nurse of the same gender as the patient). If an internal vaginal or a proctoscopic examination is required, the clinician should show first time patients the equipment which will be used. It is a matter of clinician preference what position the patient should be placed in for a vaginal speculum examination or proctoscopy: the left lateral position is good for ano-rectal examination, and lithotomy is most preferred for vaginal speculum examination, but patient comfort and being able to see what is being done are the main considerations. If a Papanicolaou smear is to be done or swabs are to be taken during the course of an internal examination, the clinician should explain briefly what will be done and why, assuring the patient that such testing causes little if any discomfort. It is preferable to have everything ready (specimens labelled and swabs within easy reach) before the examination begins. The aim is to perform the anogenital examination smoothly, painlessly and with minimal psychological discomfort. It is an art, so it takes practice.

CASE STUDY 1

Barbara is a 22-year-old university student and lives in an inner city suburb of Sydney. About six months ago she formed a relationship with a 25-year-old male student from Cambodia. Barbara has had an Implanon implant in situ for one year and has been amenorrhoeic until this episode.

Barbara developed mild pelvic pain of 10 days duration three months ago and irregular vaginal bleeding over the previous month. Her clinician strongly suspected PID and commenced appropriate treatment immediately, with good initial resolution of symptoms. A cervical swab showed a positive PCR test for chlamydia and all other STI tests, including HIV antibody, were negative. Her boyfriend attended the Student Health Service (SHS) and also had a positive PCR test for chlamydia on a FCU specimen. The doctor at the SHS treated him with azithromycin. Ten days into her treatment for PID Barbara woke up one morning with nausea, vomiting, fever, headache and painful mouth ulcers. She had developed a mild macular erythematous rash on her chest and abdomen. Her boyfriend took her to the local emergency department and the doctor who assessed her admitted her to the gynaecology ward, as she still had mild tenderness in her lower abdomen.

The presumptive diagnosis was an exacerbation of PID with a possible allergic reaction to either doxycycline or metronidazole. Her treatment was changed to an intravenous regimen of clindamycin plus gentamycin. Over the course of the next two weeks she slowly improved. Now, three months later, she returns to her usual clinician for follow-up STI tests. Her clinician is concerned to see that Barbara has lost 7kg in weight since her last visit and is even more concerned when the laboratory rings to say Barbara's HIV antibody test is now positive.

Taking tests

Patients can be asked to collect tests themselves, which is ideal and the preferred method for screening, but not ideal for testing symptomatic patients: such tests are first catch urine (FCU), mid-stream urine (MSSU), high vaginal swabs (HVS) and blind anorectal swabs. Throat swabs are taken by a clinician to sample the oropharnyx rather than the roof of the mouth or the tongue. In patients with symptoms, clinicians should examine and collect tests during the course of examination of the external anogenital region, the vagina and cervix or the anal canal and rectum. If on a first visit the patient is excessively shy and uncomfortable, she or he can self-collect specimens of discharge, or swab a genital lesion: the clinician might succeed in doing an examination at the next visit, but this is a second best option. Some clinicians refer all their clients to a pathology laboratory for ano-genital testing. This is acceptable if the clinician knows that the local laboratory staff are experienced in their work and sensitive in their dealings with shy and embarrassed patients with a possible STI.

Serological testing

Serological tests are available for HIV antibody (combined in Australia with a p24 antigen test which allows earlier detection of HIV infection); syphilis (specific antibody tests and a non-specific but useful test, the rapid plasmin reagin test [RPR]), herpes (type specific tests for antibody to herpes simplex virus HSV-1 and HSV-2), chlamydia (antibody: readily available but only useful for the diagnosis of lymphogranuloma venereum [LGV]), hepatitis A (IgM and IgG antibody), hepatitis B (surface antigen, surface antibody and core antibody) and hepatitis C (antibody). Syphilis and HIV are relatively rare infections in the Australian and New Zealand populations generally, but both are serious infections and early diagnosis is important for the individual patient and for the public health. For this reason, after appropriate pre-test discussion, it is good practice to encourage all patients at risk for STIs to have a serological test for HIV and syphilis. Syphilis is still endemic in Indigenous communities, in neighbouring countries in Asia and around the Pacific rim, and among men who have sex with men (MSM). HIV is a definite risk for MSM in both Australia and New Zealand, so the recommendation for HIV and syphilis testing is even stronger in MSM and Indigenous patients, as well as in travellers who have had sexual contacts in countries where syphilis and HIV are prevalent. Serological testing for herpes is only useful in certain specific clinical situations, one of which may be screening MSM and especially HIV-positive MSM[3] (see Chapter 8). However, in general, screening for HSV serologically is not helpful for individual patient care at the present time.

On a first visit, testing for previous exposure to HBV (generally HBcAB, but HBsAb if the patient believes they have been vaccinated already) and, in the case of MSM, to HAV (HAV IgG) is a prelude to offering vaccination if testing shows the patient is not immune.

Making a quick psychosocial assessment

The clinician must take into account psychosocial as well as biomedical factors. This is more the case with some STIs than others. For example, the diagnosis of potentially long-term genital infections like genital herpes and genital HPV is much more likely to have a significant psychological, social and emotional impact on the patient than the diagnosis of an infection like gonorrhoea or chlamydia, which is easily cured with the correct dose of an appropriate antibiotic. While individuals vary greatly in their perception of what an STI diagnosis means for them, there is still a strong undercurrent of stigma and opprobrium in the community about STIs, and it is a rare patient who is not affected by this very negative response. Sometimes patients feel disproportionate shame and loss of self-worth even when they have a very minor STI (e.g. pubic lice). They say they feel dirty, soiled, 'used' and betrayed by their sexual partner. It is clear that the diagnosis of an STI may bring underlying conflicts and varying degrees of guilt about sex and sexuality to the surface for the first time. In these situations the treatment of the STI may constitute only a small part of the necessary overall management of the patient. The diagnosis of genital herpes may precipitate a grief and loss reaction because the patient may believe this particular condition renders them sexually unattractive, a continual risk to any future sexual partner and that they will never be able to contemplate pregnancy and parenthood.

It's essential, therefore, that the clinician makes a quick assessment, at the time of the initial consultation, of the psychological strengths and weaknesses of the patient and their psychosocial situation. Consideration of the following issues (many of which are identical to the ones suggested in Chapter 9 in the assessment of patients with HIV) may be helpful:

- Self-esteem and self worth
- Perception of stigma associated with STIs
- Family relationships and supports for adolescents
- Past or present sexual abuse or risk
- Sexuality and patient's comfort with it
- Compulsive sexual behaviour
- Sexual relationships and related issues of disclosure and safe sex
- Depression and emotional issues (e.g. anger, denial, anxiety, obsessional ideas)
- Drug and alcohol use, especially associated with sex
- Issues concerning pregnancy and motherhood for women
- Beliefs about drugs (antibiotics in particular)
- Network of friends who may be supportive

An underlying theme likely to be uppermost in the patient's mind if they have a regular sexual partner is: how will this STI affect my relationship sexually or emotionally? Exploring and helping the patient deal with this issue is a very important part of STI management.

Making a diagnosis and giving treatment

Presumptive diagnosis

It's generally true that STIs, in their early stages, are simple infections that lend themselves to presumptive diagnosis on the basis of the history of symptoms, the sexual history, the clinician's knowledge of local STI prevalence and the examination. When patients present with symptoms consistent with one of the STI syndromes, clinicians should always do the appropriate tests, but they should aim to prescribe treatment for the patient immediately as a result of their careful clinical appraisal. The rationale for this is to relieve the patient's symptoms expeditiously and to render the patient non-infectious as soon as possible. The one disadvantage of this approach is that some patients will be over-treated, but this is a small price to pay for

benefiting the public health and gaining a relieved and grateful patient. On the return visit for results, the clinician is able to give the patient the confirmed diagnosis.

Giving treatment and considering contact tracing

Effective single-dose therapy exists for uncomplicated gonorrhoea, uncomplicated genital chlamydia infection, trichomoniasis, early syphilis, vulvovaginal candidiasis and bacterial vaginosis. Treatment for scabies and pubic lice is essentially single-dose topical treatment, although one follow-up treatment several days later may be optimal therapy. Clinicians should use single-dose therapies wherever possible, and should remember every single time they prescribe STI treatment that the task is only partially complete until the patient's sexual partner(s) is (are) also treated.

Therapy for viral STIs is much less satisfactory and providing a general standardised treatment approach for viral infections is impractical, so for more details readers should consult the management outline below for specific STI syndromes.

Contact tracing (partner notification) is part of the management of almost all STIs. It should not be left to subsequent visits but should be dealt with at the time of handing out the initial prescription for treatment. If the clinician has taken a good sexual history at the time of testing or screening, contact tracing becomes much easier, rather than attempting to raise the issue for the first time when handing out treatment. It is relatively easy to say: 'earlier you told me you had three partners in the last three months; are you able to contact them and tell them about the infection or do you need my help?' All treating clinicians have a clear responsibility to play a part in achieving successful outcomes in contact tracing. Involving patients in shared responsibility for the management of their sexual partners improves outcomes—this was the clear finding of a recent systematic review,[5] which concluded that assisting patients in disclosing their diagnosis to partners is the biggest priority in STI management. ASHM has produced a publication on contact tracing and readers should make themselves familiar with its recommendations.[5]

Avoiding sex is obviously wise until treatment has proved effective. With infections capable of easy cure with single-dose therapy, the patient will be rendered non-infectious within 24 hours (gonorrhoea, trichomoniasis and syphilis) and 72 hours (chlamydia serovars D to K). Advising abstinence from sex for three days after treatment is good practice; longer (seven to 14 days) if the STI is complicated (PID). With viral STIs, patients need more detailed advice about reducing risk of passing on infection.

Compliance with treatment regimens

Although single-dose treatment is favoured for STIs, there are some situations (PID, epididymo-orchitis) where more prolonged treatment is necessary. Medication must be taken properly to be effective in the long term. If the patient is regularly missing doses or not following dosing recommendations, or is taking other complementary medicine which may affect the metabolism of antimicrobial drugs, treatment failure may result. If the patient reports poor adherence, the clinician might consider modifying the recommended regimen (see suggestions under sections on PID and epididymoorchitis).

Vaccination

In non immune individuals, clinicians should offer hepatitis B vaccine to all patients at risk of STIs, and hepatitis A vaccine to all MSM. The new quadrivalent recombinant HPV vaccine (Gardasil) and the bivalent HPV vaccine (Cerverix) are now available for use in women—readers should check the 9th edition of the *Immunisation Handbook* for recommendations for their use.

Health promotion

Clinicians have a pivotal, often unrealised role in promoting sexual health. Health promotion for STIs consists of information giving about the diagnosed infection (or the likely diagnosis), tips on future prevention, education about STIs in general, including HIV/AIDS, and handing on printed resources about STIs, which in this day and age should include addresses of reliable and medically accurate websites (see Chapter 15).

Information giving

This is relatively simple if the patient understands English and medical concepts well; it may not be so simple when the patient is an adolescent, comes from a culturally or linguistically different background or when the consultation is being carried out with the help of an interpreter. In plain and simple language the clinician should tell the patient what the diagnosis most likely is, or what tests have proven it to be. She or he should briefly explain some facts about the infection, how common it is, how it is most often transmitted, what its complications may be and what the treatment options are. If it can be cured, then the clinician should stress that fact. If it can't be cured and must be managed, as in the viral infections, then the patient requires key facts about the STI on the day of diagnosis and treatment, and an appointment for a further visit(s) where she or he can learn more and receive extra support. The clinician should offer simply written brochures, if possible in the patient's most easily understood language. Brochures are always an additional resource, never a substitute for an interactive and informative conversation between clinician and patient.

Tips on prevention

It is important that people diagnosed with an STI have a clear understanding of STI transmission for two reasons: so that they know how to reduce the risk of passing their infection on to others, if their STI is not capable of rapid cure; and so that they can avoid contracting the same or another STI in future. This is easy to state in theory; it is not so easy to explain how to put theory into practice. Let's start from first principles using what we know from evidence based studies, with practical comments:

- Avoid sexual intercourse and you'll never catch an STI – true, but impractical in the long term for 99.9% of the sexually active population. In the short term it may have merit.
- Get vaccinated against hepatitis A, hepatitis B, and now if you're a woman under 27, HPV – good advice and highly protective against those hepatitis viruses and four common genital HPV types.
- Find and stick to one monogamous sexual partner after she or he has been exhaustively tested for all known STIs – true in theory; a little less reliable in practice. It still isn't possible to screen someone for every known STI, and even monogamous sexual partners may prove unreliable in the long term.
- Use a condom every time for all penetrative vaginal and anal sex – there's a good deal of evidence to support this advice.[7] It certainly works very reliably for HIV, hepatitis B, trichomoniasis, cervical and rectal gonorrhoea and chlamydia. There's the issue of oral sexual activities where syphilis, HSV, HPV, gonorrhoea, chlamydia and, extremely rarely, hepatitis B and HIV might be transmitted. It is sensible to recommend the use of condoms and dental dams during all forms of oral sex for sex workers and others who have multiple sex partners.
- Have a regular STI check-up at least for the treatable STIs – it's good advice and overcomes the problem of oral STIs (gonorrhoea, chlamydia and syphilis), which are often asymptomatic but are amenable to simple easy treatment. There is also some evidence of benefit, at least in limiting the complications of chlamydia in women in communities where screening programs are operational.
- Talk with your partner about sex; communicate; be honest and open; look at the problem of STIs together and try to reach some risk-limiting solutions that work for you – admirable advice that takes account of more than the mechanics of sex. There are no studies yet to show the impact this has on STI prevention, though.
- Be as hygienic as you can, i.e. if male, wash under your foreskin daily with soap (or a soap substitute) and water and rinse well afterwards; for both sexes, keep your anogenital area as clean and dry as possible and always wash before sex and as soon as possible after sex (including under the foreskin if male). People need to reach a happy medium as over-enthusiastic washing of the genital area, especially with soap, leads to itching and scratching and may increase the risk of recurrent bacterial vaginosis in women. Offer sound advice to young patients on how to steer a safe course between maintaining genital hygiene and not irritating the skin with too much soap. Recent evidence from African studies indicates that male circumcision is protective against acquisition of HIV: it reduces risk by at least 50%.[8]

Education – imparting general knowledge about STIs

The clinician will need to provide the individual patient with information about all the STIs relevant to that patient's situation. The gender of the patient's partners, the patient's pattern of sexual behaviour, her or his willingness to use protection, as well as the local prevalence of STIs, will provide some guide. Generally, in Australia and New Zealand, urban exclusively heterosexual patients need detailed information about HPV, chlamydia, genital herpes and bacterial vaginosis because they are common, and brief information about HIV, gonorrhoea and syphilis because of the real threat they pose to health. MSM need detailed information about all of these STIs (except bacterial vaginosis) as well as hepatitis A, B and the LGV strains of chlamydia. Indigenous heterosexual patients need information about HPV, chlamydia, genital herpes, gonorrhoea, syphilis, bacterial vaginosis and trichomoniasis. Women who have sex with women (WSW) need the same information as heterosexual women, with clear explanation that any sexual contact with men places them at the same risk as exclusively heterosexual women.

Resources for health care professionals and people with, or at risk of, STIs

There is a wide range of resources available to support clinicians and patients. All State and Territory health departments have printed information about all individual STIs, as do major sexual health clinics (see Chapter 15 for links to online information). ASHM distributes the *Contact Tracing Manual* which includes a good summary of all the STIs[6] and has a website providing information for clinicians and patients which is regularly updated (http://www.ashm.org.au).

Management of specific STI syndromes

Table 12.1 lists the eight specific STI syndromes.

1. Urethral discharge

Description and causes

Urethral discharge denotes the existence of urethritis. A gram-stained smear of urethral discharge will show varying numbers of leucocytes on microscopy. For all practical purposes, any discharge from the urethra is abnormal and signals the presence of an STI. Thick purulent and profuse discharge with some dysuria is usually due to gonorrhoea. Thin,

scant, clear or mildly mucopurulent discharge with slight urethral irritation is often due to chlamydia. A similar discharge with marked dysuria sometimes means there's a primary herpetic urethritis, but this is rare. *Trichomonas vaginalis* mostly causes entirely asymptomatic urethritis but sometimes initiates a very slight mucopurulent discharge. Unprotected anal intercourse on occasions causes a urethritis in the insertive partner, from which enteric coliforms can be cultured, but this too is uncommon.

Some other sexually transmissible microbial agents cause urethritis (Table 12.2), of which Mycoplasma genitalium is probably the most significant, but there are no laboratory tests available as yet for this bacterium. Non-specific urethritis (NSU) is an unhelpful term because it is poorly defined. It means there is a urethritis present but all available tests are negative—e.g. it is a non-gonococcal, non-chlamydia, urethritis. Fortunately most urethritis seen in practice is due to chlamydia or gonococcus. If not due to either bacterium, most remaining urethritis responds to antichlamydial treatment or gets better on its own. If it fails to do so, the clinician should reassess the patient carefully.

Differential diagnosis

There is no non-STI differential diagnosis for urethral discharge, except perhaps the very rare situation where a gastro-intestinal infection triggers urethritis as part of the triad of urethritis, conjunctivitis and arthritis in Reiter's syndrome.

Diagnostic tests

Where a discharge exists, collect some on cotton tipped swabs. If there is insufficient discharge to sample, the patient should produce an FCU specimen for NAATs (nucleic acid amplification tests) for chlamydia (and for gonorrhoea in areas where it is prevalent). There is never a need to insert swabs into the urethral meatus.

The recommended tests are for gonorrhoea and chlamydia (see Table 12.3). The clinician should only consider additional tests (trichomoniasis, HSV, adenoviruses etc.) if symptoms fail to respond to initial treatment.

Initial treatment of urethral discharge

Patients with urethral discharge should be treated on the initial visit, only after tests have been taken. Azithromycin 1g orally as a single dose is the recommended initial treatment. In addition, a single dose of ceftriaxone 500mg intramuscularly should be given in the following situations:

- Where a partner is known, or likely to have a gonococcal infection
- In areas and communities where gonorrhoea is highly prevalent (e.g. remote Indigenous communities)
- When the patient has recently had sex with a local person in an overseas country where gonorrhoea is highly prevalent (e.g. South East Asia)
- When the patient gives a history of male-to-male sex (oral or anal)
- When the discharge is purulent, profuse and accompanied by dysuria

Treat or arrange treatment with azithromycin with or without ceftriazone for male or female sexual partner(s).

TABLE 12.2 STI causes of urethral discharge (in order of frequency)

• *Chlamydia trachomatis* (serovars D–K)	• Adenoviruses
• *Neisseria gonorrhoeae*	• Herpes simplex virus types 1 or 2
• Mycoplasma genitalium	• Neisseria meningitidis
• Ureaplasma urealyticum	• Enteric bacteria
• *Trichomonas vaginalis*	

TABLE 12.3 STI causes of vaginal discharge (in order of frequency)

• Bacterial vaginosis
• Vaginal candidiasis
• *Chlamydia trachomatis* serovars D–K, cervicitis or urethritis
• Herpes simplex virus types 1 and 2, cervicitis or vaginal ulcerations
• *Neisseria gonorrhoeae* cervicitis or urethritis
• *Trichomonas vaginalis* cervicitis and vaginitis
• *Mycoplasma genitalium* cervicitis or urethritis

Treatments for specific STIs causing urethral discharge

See Table 12.4 for treatments for specific STIs. For urethral discharge these are treatments for:

- Gonorrhoea
- Chlamydia
- Trichomoniasis
- Herpes simplex

For all other causes of urethral discharge consult a textbook of sexual health medicine[10] or seek advice from a sexual health physician.

Follow-up – see Table 12.5.

2. Vaginal discharge

Description and causes

There is a normal physiological discharge from the vagina which varies in character and consistency during the course of the menstrual cycle. Some women may not notice the gradual development of a less normal discharge unless it is accompanied by itch, odour or colour change.

An abnormal vaginal discharge may come:

- From the endometrial lining associated with endometritis – this is uncommon except after childbirth or following some gynaecological procedures (insertion of an intrauterine device (IUD), dilatation and curettage (D & C), termination of pregnancy)
- From the cervical canal – herpetic and trichomonal cervicitis are possible causes but gonorrhoea and chlamydia are usually the cause; studies show that in fact chlamydia rarely causes a vaginal discharge; there has to be a profuse purulent or mucopurulent exudate from the cervix before a noticeable change is perceived in the vaginal discharge
- From the vagina itself where the three common causes are trichomoniasis, candidiasis or bacterial vaginosis; bacterial vaginosis is by far the commonest cause. Rarely, herpetic vaginal ulceration may cause a discharge
- From the female urethra – discharge from the urethra is not often detectable as an abnormal vaginal discharge

More than one condition might cause an abnormal vaginal discharge; any combination of two or more STIs may be present at one time (Table 12.5). This fact explains why the classic textbook descriptions of vaginal discharge are rarely encountered in routine practice. Discharge associated with gonococcal cervicitis may be frankly purulent; discharge caused by trichomoniasis may be heavy green and frothy; discharge due to candidiasis may be like cottage cheese accompanied by vulval erythema, oedema and itching; and discharge due to bacterial vaginosis is usually thin, white-grey and slightly frothy. If any of these STIs coexist with another condition, the actual vaginal discharge produced can look quite non specific.

Differential diagnosis

Apart from STIs and bacterial vaginosis, other causes of abnormal vaginal discharge are:

- Leucorrhoea (increase in quantity of normal vaginal discharge) – may be associated with hormonal changes, hormone replacement therapy
- Other infections – e.g. group B streptococcal infection (discharge then often resembles the discharge seen with *Trichomonas vaginalis*), Staphyloccocus aureus (toxic shock syndrome)
- Retained foreign bodies (condoms, tampons etc) – resulting often in a foul smelling discharge
- Neoplastic disease (carcinoma of endometrium, cervix, urethra, vagina) – these usually cause a blood-stained discharge

Diagnostic tests

In the presence of an abnormal vaginal discharge, the clinician should undertake an internal examination using a vaginal speculum and take tests at the same time. If a first time patient is shy and apprehensive, put off the examination until a subsequent visit, providing the clinician duly records the fact that the examination has been postponed and needs to be followed up.

During the internal examination, the clinician should take high vaginal swabs (HVS) for bacterial vaginosis, trichomoniasis and candidiasis and swabs from the endocervical canal for gonorrhoea and chlamydia.

In cases of recurrent candidiasis, request culture on an HVS as it is useful to identify the species of Candida and its sensitivity to antifungal agents. A cervical test for herpes can be taken if there is a relevant history of possible exposure, evidence of herpes externally, or if the cervix looks ulcerated. On the first visit, if the clinician postpones an internal examination, the patient can self-collect HVS for bacterial vaginosis, trichomoniasis and candidiasis and provide a FCU for chlamydia and gonorrhoea (if appropriate).

The clinician should also arrange other serological tests as appropriate, after discussion with the patient, (HIV, HBV, HCV, syphilis), a throat swab for gonorrhoea (if appropriate) and a Papanicolaou smear when due. (See Table 12.5).

Initial treatment of vaginal discharge

Abnormal vaginal discharge is an uncomfortable symptom. Clinicians should treat the symptom at the initial visit, but only after they have taken the appropriate tests.

The following is a guide for an initial treatment plan:

1. If the sexual history indicates risk for a significant STI (age 15 to 25, recent partner change, multiple partners), whatever the nature of the discharge:

- Azithromycin 1g orally as a single dose (safe in pregnancy B1*)
- Ceftriaxone 500mg intramuscularly as a single dose to be added, if infection acquired in an area where gonorrhoea is prevalent (safe in pregnancy B1)

2. If the discharge has an unpleasant odour:

- Tinidazole 2g orally (B3) as a single dose or metronidazole 2g orally (B2) as a single dose (metronidazole preferred in pregnancy, rather than tinidazole)

3. If the discharge is accompanied by vulval erythema, swelling or itch:

- Fluconazole 150mg orally as a single dose (not in pregnancy D), with or without a topical vaginal anti-candidal preparation.

* Categories of drugs in pregnancy[9]

Treat or arrange treatment for male or female sexual partner(s) as appropriate.

Treatments for specific STIs (and bacterial vaginosis) causing vaginal discharge

Consult Table 12.4 for a list of treatments for specific STIs. For vaginal discharge these are treatments for:

- Gonorrhoea
- Chlamydia
- Cervical herpes
- Trichomoniasis
- Bacterial vaginosis
- Candidiasis

Follow-up – see Table 12.5

3. Ano-genital ulcer disease (GUD)

Description and causes

Ulceration in the ano-genital region, genital ulcer disease (GUD), is a less common STI presentation than urethral or vaginal discharge. Ulceration may be accompanied by inguinal lymphadenitis; palpation of both groin areas is an integral part of the examination of all GUD. Trauma is a frequent cause of short-lived genital ulceration, but a number of STIs can present as ulceration in the ano-genital region. These include genital herpes, primary and secondary syphilis, LGV (due to *Chlamydia trachomatis* serovars L1–L3), chancroid (due to Haemophilus ducreyi) and donovanosis (due to Klebsiella granulomatis). GUD can be painful (herpes and chancroid) or painless (syphilis, LGV and donovanosis). In Australia and New Zealand, LGV, chancroid and donovanosis are rare. There are two exceptions: LGV is an infection seen now in Australasia in some MSM but in this group, LGV mostly manifests as an acute proctitis rather than as GUD; donovanosis still occurs (but now rarely) in remote Indigenous communities in northern and central Australia. As a rule of thumb, all GUD in Australia and New Zealand is due to genital herpes until proven otherwise, but clinicians should always ask themselves: 'could this GUD be syphilis?'

Differential diagnosis

Other causes of ano-genital ulceration are:

- Trauma
- Scratched scabies lesions on the genitals
- Anal fissures and fistulae
- Herpes varicella zoster lesions involving the anogenital region
- Other uncommon infections, e.g. cutaneous amoebiasis, leishmaniasis, mycobacterial infections
- Neoplastic lesions: precancerous lesions (Bowen's disease), squamous cell carcinoma, basal cell carcinoma

Diagnostic tests

The recommended tests for any ulceration in the ano-genital region are swabs of the lesion for HSV (NAAT) and (if available) for syphilis. Few laboratories now perform dark field microscopy for syphilis. There are now NAATs for *Treponema pallidum* for use on swabs from ulcerative lesions and some pathology laboratories have access to them. Some are part of a 'multiplex' NAAT for GUD which tests for HSV, Haemophilus ducreyi and *Treponema pallidum* (and in some parts of remote Australia, for Klebsiella granulomatis) on the one specimen. Clinicians should use these tests if they are available and if syphilis is a reasonable possibility. If, from the history, there are grounds for believing GUD may be due to chancroid, LGV or donovanosis, the clinician should discuss the case with the local laboratory and a sexual health physician.

Serological tests for syphilis (RPR plus a specific test to improve sensitivity) should be arranged for any patient with ano-genital ulceration.

The clinician should arrange other serological tests as appropriate, after discussion with the patient (HIV, HAV, HBV, HCV), a throat swab for gonorrhoea culture and sensitivity, rectal swabs for gonorrhoea culture and sensitivity and NAAT for chlamydia (if appropriate) and a Papanicolaou smear when due (female patients). See Table 12.3.

Initial treatment of ano-genital ulcer disease

HSV-1 or HSV-2 causes most GUD either on the penis, on the vulva, around the introitus or perianally. Primary and initial outbreaks of herpes are painful as are some recurrences. Both local and systemic analgesics as well as frequent bathing with luke-warm physiological (normal) saline are helpful adjuncts to more specific treatment.

Early treatment with an antiviral agent relieves symptoms, decreases risk of transmission to sexual partners, and reduces the length of the outbreak. Clinicians should treat at once on clinical suspicion if lesions are causing the patient discomfort. Recommended initial treatment, pending results of NAAT, is:

- Valaciclovir 500–1000mg orally twice a day (B3) for 5–10 days or famciclovir 250mg orally three times a day (B1) for 5–10 days; equally effective

Add treatment for early syphilis (see Table 12.4) in the following situations:

- In communities where syphilis is highly prevalent
- Where the GUD is a single painless indurated ulcer with enlarged non-tender inguinal nodes
- In MSM who have GUD which is not typical of herpes

Treat or arrange treatment for male or female sexual partner(s) as appropriate.

TABLE 12.4 Treatments for specific STIs[2,16]

Bacterial vaginosis:
- Tinidazole 2g orally (B3) as a single dose or metronidazole 2g orally as a single dose; metronidazole (B2) preferred in pregnancy (equally effective)

For recurrent attacks: metronidazole 400mg twice a day orally for 5 days (B2)

Candidiasis:
- Fluconazole 150mg orally as a single dose (don't use in pregnancy D); and/or a topical vaginal anti-candidal preparation for vulvovaginitis and a topical anti-candidal cream for balanoposthitis. Recurrent vulvovaginal candidiasis may need treatment for longer periods

Chancroid:
- Ceftriaxone 500mg intramuscularly as a single dose (B1)

Chlamydia – *Chlamydia trachomatis* serovars D–K
- Azithromycin 1g orally as a single dose; (B1)

Alternative:
- Doxycycline 100mg twice a day orally for 7 days (don't use in pregnancy D); single dose treatment should always be used in preference to this regimen

Donovanosis:
- Azithromycin 1g orally as a single dose. Repeat at weekly intervals for 4–6 weeks (B1)

Enteritis:
- Treat appropriately for the specific agent isolated i.e. for giardiasis, amoebiasis, shigellosis

Gonorrhoea:
- Ceftriaxone 500mg intramuscularly as a single dose; (B1) NB: 250mg is an adequate dose for gonorrhoea but is no longer available in retail pharmacies in Australia

Alternatives:
- Ciprofloxacin 500mg orally as a single dose (don't use in pregnancy B3). Ciprofloxacin will NOT be effective if local strains of *Neisseria gonorrhoeae* are resistant, as is the case in many capital cities in Australia

OR
- Gatifloxacin 400mg orally as a single dose (don't use in pregnancy B3). Expensive and not yet listed on the Australian PBS

NB: Always treat for *Chlamydia trachomatis* as well when treating for gonorrhoea

Herpes:
Initial therapy, herpetic urethritis and cervicitis or a moderately severe outbreak:
- Valaciclovir 500–1000mg twice a day orally (B3) for 5–10 days or Famciclovir 250mg three times a day orally (B1) for 5–10 days; equally effective

Suppressive therapy (continuous):
- Valaciclovir 500mg orally daily (B3) or Famciclovir 250 twice a day orally (B1); equally effective

LGV – *Chlamydia trachomatis* serovars L1–L3
- Doxycycline 100mg twice a day orally for a minimum of 21 days (do not use in pregnancy D)

Pubic Lice:
- Benzyl benzoate 25% lotion – apply to all affected hairy areas at bed time. Avoid direct contact with scrotum. Wash off next morning. Repeat in five days

Scabies:
- Permethrin 5% cream – apply in a single application at bed time topically to whole body except head. Wash off next morning

Syphilis (primary or secondary)
- Benzathine penicillin 1.8g (2.4 million international units) intramuscularly as a single dose

OR
- Procaine penicillin 1.5g intramuscularly daily for 10 days (both probably equally effective and safe in pregnancy [A], but the procaine penicillin course of treatment is preferred in HIV-positive patients as single dose therapy has been found to be less successful in this client group)

Alternative:
- Doxycycline 100mg twice a day orally for 10 days (do not use in pregnancy D)

NB: If patient is a pregnant woman allergic to penicillin, consult a sexual health physician for advice

Trichomoniasis:
- Tinidazole 2g orally (B3) as a single dose or Metronidazole 2g orally as a single dose (metronidazole preferred in pregnancy B2); equally effective

* Treatments are based on the Australasian Chapter of Sexual Health Medicine's *Clinical guidelines for the management of sexually transmissible infections among priority populations* and the Centres for Disease Control (USA) *Sexually transmitted diseases treatment guidelines 2006*;2:15.

TABLE 12.5 Diagnostic tests for STIs

Ano-rectal junction
- Anal cytology for people living with HIV and MSM (if available – currently only in specialist centres)

Blood culture
- For culture and sensitivity for *Neisseria gonorrhoeae*

Cervix
- Sample from ectocervix and endocervical canal for cytology (Papanicolaou smear) (in accordance with NHMRC guidelines – usually two years after sexual debut and then regularly every two years)

Endocervical canal
- Swab smeared onto a slide for gram-stain microscopy for inflammatory cells and diplococci
- Swab in transport medium for culture and sensitivity for gonorrhoea
- Swab for NAAT for chlamydia
- Swab for NAAT for herpes simplex (only if there is a relevant sexual history, other evidence of herpes externally, or if cervix looks ulcerated)

Faeces
- Stool samples (X2) for microscopy for leucocyctes, red cells, ova, cysts and parasites (including concentrate microscopy and permanent stains and Cryptosporidium/Giardia antigen test), plus culture and sensitivity (X1)

High vaginal swab (HVS)
- Swab smeared onto a slide for gram-stain microscopy for number of leucocytes, presence of clue cells (bacterial vaginosis), spores and hyphae (candidiasis)
- Swab for NAAT for trichomoniasis (if available)

High vaginal swab (HVS) *continued*
- Swab in transport medium for culture and sensitivity (for candidiasis and for bacteria; if no NAAT test for trichomoniasis, a wet preparation can be made from this swab to look for motile trichomonads)

Joint aspirate
- Sample of aspirate for microscopy, culture and sensitivity for *Neisseria gonorrhoeae*

Rash (ano-genital)
- Swab from affected area (e.g. vulva, perianal area or under the foreskin) smeared onto a slide for gram-stain microscopy for spores and hyphae (candidiasis)
- Swab from affected area in transport medium for culture and sensitivity (for candidiasis and for bacteria)
- HVS swab for NAAT for trichomoniasis if vulval rash (if no NAAT test available, send swab in transport medium; a wet preparation can be made from this swab to look for motile trichomonads and culture is also possible)
- Microscopy for scabies mite or pubic louse (if appropriate)
- Punch biopsy for histology if diagnosis is uncertain

Rectal mucosa
- Swab collected by direct vision smeared onto a slide for gram-stain microscopy for inflammatory cells and diplococci (not a useful test if swab has been taken blind)
- Swab for NAAT for chlamydia (preferably by direct vision, otherwise blind) – routine tests are for D–K serovars; some specialist laboratories are able to test for L1–L3 serovars

Treatments for specific STIs causing ano-genital ulceration

See Table 12.4 for treatments for specific STIs. For ano-genital ulceration these are treatments for:
- Herpes
- Syphilis
- LGV
- Chancroid
- Donovanosis

Follow-up – see Table 12.5.

Patients treated for syphilis require a repeat RPR test at 3 months, 6 months, 12 months and 24 months to check RPR titre is falling. Patients diagnosed with ano-genital herpes may require referral for ongoing counselling.

4. Ano-genital lumps and bumps

Description and causes

There only two STIs causing lumps and bumps in the ano-genital region (apart from the lumps or nodules characteristic of scabies when burrows occur in the soft skin of the penis or labia; itch is still the major symptom in this infestation). The two STIs are genital warts (due to HPV, usually types 6 and 11) and molluscum contagiosum (due to the Molluscipoxvirus). Molluscum contagiosum have a characteristic smooth round igloo shape often with central indentation. They have a yellowish waxy colour. They favour the skin of the supra-pubic region, the inner thighs, shaft of the penis and hair-bearing areas of the vulva. Warts can occur anywhere at all on the skin and mucous membrane of the ano-genital region, especially under the foreskin, on the

TABLE 12.5 Diagnostic tests for STIs *(continued)*

Rectal mucosa (continued)
- Swab in transport medium for culture and sensitivity for gonorrhoea (preferably by direct vision, otherwise blind)
- Swab for NAAT for HSV if pain is a feature (preferably by direct vision, otherwise blind)

Ulcers or lesions in ano-genital region
- Swab for NAAT for HSV
- Swab for NAAT for *Treponema pallidum* (if available), OR
- Swab for multiplex test for NAAT for HSV, Haemophilus ducreyi and *Treponema pallidum* (if available)

Serology
- Hepatitis A – HAV antibody IgG (past infection), IgM (current or recent infection)
- Hepatitis B – HBcAb (exposure to HBV), HBsAg (recent or chronic infection), HBsAb (immune following vaccination or previous infection)
- Hepatitis C – HCV antibody (exposure to HCV)
- HIV antibody (with p24 antigen in Australia) – HIV infection
- LGV – microfluorescent antibody test for chlamydia serovars L1–L3 (if available) or chlamydia antibody complement fixation test (high titre consistent with LGV)
- Syphilis – RPR (non specific antibody test, but quantitated with a titre 1:2, 1:4 etc.), plus TPPA or EIA or FTA ABS (all specific tests)

Urethra (if discharge present and can be sampled painlessly)
- Swab of discharge smeared onto a slide for gram-stain microscopy for inflammatory cells and diplococci (i.e. gonococci)
- Swab of discharge in transport medium for culture and sensitivity for gonorrhoea
- Swab of discharge for NAAT for chlamydia
- Swab of discharge for NAAT for HSV or NAAT for trichomoniasis (only in unresponsive urethritis)
- Swab of discharge for viral culture (e.g. adenoviruses), only in unresponsive urethritis
- Swab of discharge for NAAT for Mycoplasma genitalium, only in unresponsive urethritis (not yet widely available)

Throat i.e. oro-pharyngeal mucosa (if patient gives a history of performing fellatio where there is a high prevalence of gonorrhoea)
- Swab in transport medium for culture and sensitivity for gonorrhoea (microscopy not helpful from throat due to other resident diplococci)

Urine
- First catch urine specimen (FCU) for NAAT for gonorrhoea, chlamydia and (if available) trichomoniasis (the latter only useful in areas of high prevalence for trichomoniasis, i.e. outside urban practice)
- Mid stream specimen of urine (MSSU) for microscopy, culture and sensitivity

inner surfaces of the labia minora, in the fourchette, and perianally. Warts vary greatly in morphology, ranging from small flat plaques to filiform lesions to large highly keratinised papules. There may be only one or two warts or large warty colonies. They are unsightly and uncomfortable psychologically, if not usually physically, for the patient.

Differential diagnosis of ano-genital lumps and bumps

Non-STI causes of lumps and bumps are usually anatomical variants such as pearly penile papules, Fordyce spots, Tysons glands, lymphocoeles and angiokeratomas. The reader should consult a good sexual health[10] or dermatology text to familiarise themselves with these common lesions. Papular and nodular neoplasms also cause lumps in the ano-genital region. In the perianal area, the condylomata lata of secondary syphilis, haemorrhoids, thrombosed external piles, perianal abscesses and sentinel piles are all part of the differential diagnosis. See Figure 12.1 (angiokeratomas) and Figure 12.2 (pearly penile papules).

Diagnostic tests

Clinicians mostly diagnose ano-genital warts and molluscum contagiosum purely on their characteristic appearance and behaviour. When lesions look atypical, behave atypically or fail to respond to usual forms of treatment, it is wise to do an excision or punch biopsy for histological diagnosis. The diagnosis of asymptomatic HPV infection is usually dependent on cytological techniques Papanicolaou smear (cervical or anal cytology).

Serology for syphilis is always important in patients with extensive molluscum or ano-genital warts to exclude condylomata lata. It's good practice on the initial visit to advise a Papanicolaou smear in women (unless it has been performed within the

recommended time period according to NHMRC guidelines) and testing for other common STIs. Recommended tests are for chlamydia by FCU, gonorrhoea (according to local prevalence), swabs from appropriate sites and other relevant serological tests (HIV, HAV, HBV and HCV) after discussion with the patient. (See Table 12.5).

Initial treatment for ano-genital lumps and bumps

Heavy growths of warts in places like the introitus or around the anus become irritated, smell offensive and can be extremely difficult to live with. Heterosexual men may feel a sense of shame if they have developed extensive perianal warts without ever having had receptive anal intercourse (Case study 2).

The aim of treatment of warts and molluscum contagiosum is to remove the unsightly and uncomfortable lesions for the patient's psychological wellbeing, as well as the possibility that treatment will stimulate local immune defences which may reduce the likelihood of recurrence and the length of time during which the patient remains infectious to sexual partners. There is no evidence for this, but there is no doubt that earlier treatment provides peace of mind for the patient. No matter what form of treatment is used, there is a recurrence rate of about 40%.[11] Warts tend to be less responsive to treatment in people who are immunosuppressed (e.g. in people with HIV infection). With all patients with warts, start treatment as soon as possible.

Clinicians should review male and female partners for the presence of hidden warts and to check on cervical screening history in women.

Treatments for specific STIs causing ano-genital lumps and bumps

Ano-genital warts

These are the available treatments for ano-genital warts:

- Excision: simple surgical under local or general anaesthesia; safe in pregnancy
- Ablative; using various modalities: cryotherapy using liquid nitrogen, CO2 slush, or a cryotip and nitrous oxide (usually with local anaesthetic cream such as xylocaine or emla etc); diathermy under local or general anaesthesia; laser therapy under local or general anaesthesia; and application of trichloracetic acid (only suitable for single small warts); all safe in pregnancy
- Antimitotic agents: podophyllotoxin cream or paint (lends itself to patient application according to manufacturer's instructions); 5-fluorouracil cream (should only be applied by the clinician and should be washed off after four hours); neither treatment to be used in pregnancy

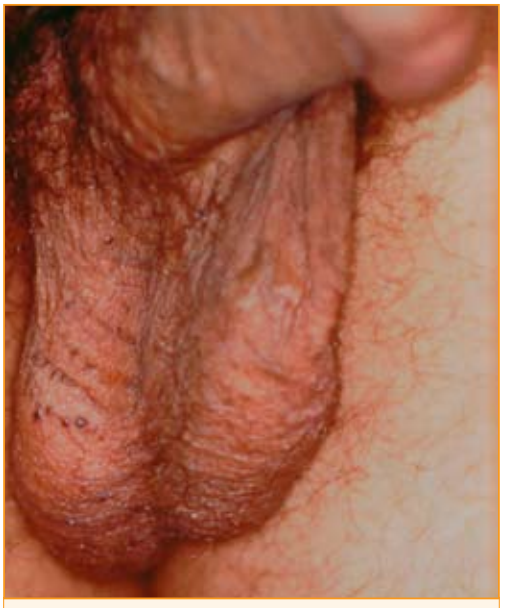

FIGURE 12.1 Angiokeratomas

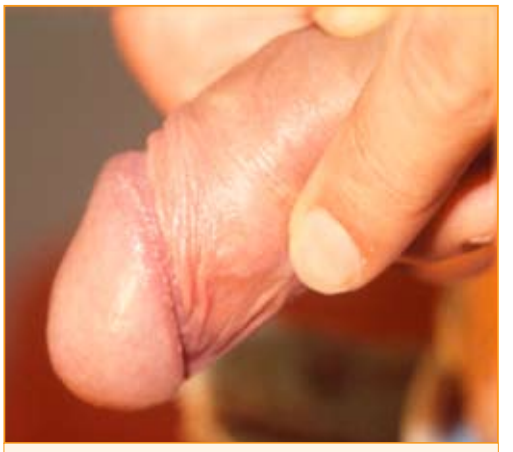

FIGURE 12.2 Pearly penile papules

- Immunomodulatory agent: imiquimod cream (apply three times weekly at bed time, wash off in the morning, for a minimum of four weeks); not useful for long-standing highly keratinised warts; not to be used in pregnancy

No treatment is entirely satisfactory or completely effective; recurrences can occur after any treatment. Quitting smoking is a very important part of treatment if warts are proving recalcitrant. However, except in the severely immunosuppressed patient (HIV, and sometimes in pregnancy), with patience and persistence all warts will regress eventually.

Mollusca contagiosa

There is generally a better early success rate treating mollusca than treating warts. These are the available treatments:

- Deroofing the individual lesion accompanied by squeezing out the firm cheese-like contents (ideal if there are only a few lesions; it's easy to teach patients to do this themselves)
- Ablative therapies as for warts (all work fairly well for mollusca)

Treatment is only a problem in the severely immunosuppressed, when mollusca can sometimes grow quite large and remain fairly unresponsive to usual treatments.

Follow-up – see Table 12.5.

5. Ano-rectal syndromes

Description and causes

An ano-rectal syndrome is present when a patient reports anal symptoms (i.e. itch, pain, discomfort or irritation) or disturbed bowel function and there's a possibility the symptoms are related to anal sexual activities. Many other conditions, both medical and surgical, can also cause such symptoms.

Many STIs affecting the ano-rectum are asymptomatic, at least for the first few days or weeks of infection. Here are some possible sexually transmissible agents associated with STI-related ano-rectal syndromes, in order of their frequency in practice:

- HSV types 1 or 2 – causes ulceration and proctitis, often asymptomatic, but can cause anal pain and constipation, anal discharge and sometimes bleeding, especially in an initial outbreak
- *Chlamydia trachomatis* serovars D–K – generally asymptomatic, causes mild proctitis, so sometimes causes anal discomfort and irritation
- HPV all genital types – generally asymptomatic, types 6 and 11 may cause warts
- *Neisseria gonorrhoeae* – often asymptomatic; causes a moderate proctitis; astute patients may notice purulent discharge around their bowel motions; can cause anal discomfort or mild pain
- *Treponema pallidum* – often asymptomatic but anus may be site of a painless primary chancre (ulcer), and anorectal mucosa may be affected by snail-track ulcers in secondary syphilis. Condylomata lata (flat warty or skin tag-like moist excrescences around the anus) also occur in secondary syphilis
- *Chlamydia trachomatis* serovars L1–L3 (LGV) – usually causes a moderate to severe proctitis characterised by deep anal pain, increased frequency of bowel action and passage of muco-purulent discharge, plus systemic symptoms
- Enteric micro-organisms – there are a variety of which the commonest are Shigella sp, Giardia duodenale, Entamoeba histolytica and hepatitis A virus (HAV). HAV causes pale stools and hepatitis; all other enteric agents cause diarrhoea of varying severity. The key factor is that the patient has acquired the infection by ingesting faecally contaminated material during sex, either on fingers, from a condom, from handling a sex toy or by direct oro-anal contact. In immunosuppressed patients with HIV, a number of other enteric infections may occur (cryptosporidiosis, microsporidiosis, MAC complex), not usually sexually acquired (Chapter 10)

Differential diagnosis

Here is a list of some non-STI causes of symptoms which mimic the STI ano-rectal syndrome:

Medical

- Enteric infections acquired in conventional rather than sexual modes
- Crohn's disease
- Ulcerative colitis

Surgical

- Traumatic lesions of anus and rectum
- Retained foreign bodies (dildoes)
- Ano-rectal benign and malignant neoplasms
- Fissures, fistulae, thrombosed external piles and haemorrhoids

The take-home message is that not all ano-rectal symptomatology is surgical or routinely medical. Ask yourself, and not just in gay men: 'could this be an STI?'

Diagnostic tests

The patient with the ano-rectal syndrome needs a careful examination of the anal and perianal area. Ideally tests can be taken at the same time.

If the clinician suspects an enteric infection because the predominant symptom is diarrhoea or loose bowel actions, then the patient should collect the usual stool specimens for microscopy for ova, cysts and parasites (OCP) and faecal culture. Medicare pays for two samples for OCP examination and one sample for culture within a seven-day period; current guidelines recommend two stool OCP exams (including concentrate microscopy and permanent stains and Cryptosporidium and Giardia antigen test) plus one faecal culture. If results are negative, it is recommended to test again over one week later.

If proctitis is suspected, the rectal mucosa should be viewed directly through an anoscope or proctoscope; sometimes this is not possible because of anal pain. The clinician should examine for traumatic lesions and the possibility of a retained foreign body. The recommended tests are swabs from lesions or ulcers for HSV NAAT and (if available) for syphilis; swabs from the rectal mucosa (preferably collected through a proctoscope by direct vision unless too painful) for gonococcal culture, HSV NAAT and chlamydia NAAT. If LGV is suspected, the clinician should discuss the possibility of testing for LGV serovars with the local laboratory; in addition she or he should request a

serological test for LGV. Anyone with an STI-related ano-rectal syndrome may be at risk for syphilis and hepatitis A; serology for HAV will determine the patient's HAV immune status and the presence of HAV IgM will indicate recent infection. Serology for syphilis should include both RPR and a specific test.

Finally the clinician should arrange other serological tests as appropriate after discussion with the patient (HIV, HBV, HCV), a Papanicolaou smear, if not already screened appropriately, for women and (if available) an anal cytology test for MSM. The clinician should take a throat swab if the patient has a history of performing fellatio and there is a high local prevalence of gonorrhoea (see Table 12.5).

Initial treatment of ano-rectal syndromes

After tests have been taken, the clinician must provide treatment to relieve the patient's symptoms. If pain is the overriding symptom, with or without peri-anal ulceration, and both trauma and a retained foreign body have been eliminated as causes:

- The diagnosis is ano-rectal herpes until proven otherwise. Treat for an initial outbreak of genital herpes

If there is a mild proctitis (as demonstrated by mild pain or discomfort) and only mildly inflamed mucosa seen on proctoscopy:

- Treat for chlamydia (D–K serovars)

If there is a proctitis (with mild to moderate pain) but a more inflamed looking mucosa with obvious purulent material lying on the mucosal surface (as seen by proctoscopy):

- Treat for gonorrhoea and chlamydia (D–K serovars)

If there is severe proctitis (considerable pain) and very inflamed mucosa with systemic symptoms:

- Treat for gonorrhoea
- Treat for an initial outbreak of herpes
- Treat for LGV

If there is an enteritis (diarrhoea):

- Treat symptomatically as for any other enteric infection with fluid replacement and loperamide pending results of tests
- Treat or arrange treatment for male or female sexual partner(s) as appropriate

Treatments for specific STIs causing ano-rectal syndromes

See Table 12.4 for a list of treatments for specific STIs. For ano-rectal syndromes these are treatments for:

- Herpes proctitis and perianal herpes
- Chlamydia proctitis (serovars D–K)
- Gonococcal proctitis
- Early syphilis (primary or secondary) including condylomata lata:
- LGV chlamydia proctitis (serovars L1–L3)
- Enteritis

Follow-up (see Table 12.5)

TABLE 12.6 Follow-up after treatment

Clinicians should always ask patients to return for follow-up in 7–14 days so she or he can:

- Give the results of tests, so that the patient knows what STIs are present
- Check the response to initial treatment has been successful; in the case of ano-genital warts, mostly further treatments will be necessary
- Check adherence to medication (if necessary)
- Check whether sexual contacts have been contacted and treated appropriately
- Provide further information and education; essential in the case of both ano-genital herpes and syphilis and often with HPV infection
- Arrange further visits to check progress (LGV proctitis, enteritis) or to arrange further serology, e.g. syphilis (if necessary)
- Arrange for a further STI screen in three months

Clinicians should ask patients who are unwell, as may be the case with gonococcal, herpetic and LGV proctitis, to return in three days for review.

6. Pelvic pain syndrome in women

Description and causes

Pelvic pain in women is a common presenting symptom. Urinary tract infections, gastro-intestinal conditions, as well as a variety of gynaecological conditions can present with either acute or chronic pelvic pain. A number of sexually transmissible agents (*Chlamydia trachomatis* serovars D–K and *Neiserria gonorrhoeae* mostly, but probably also ureaplasmas and mycoplasmas) may be responsible. After a period of silent cervical infection, these STIs can ascend, often around the time of menstruation, through the endometrium causing infection initially in the mucosa of the fallopian tubes (salpingitis), with subsequent spread through the wall of the tube causing infection in surrounding structures—ligaments, serosa and ovaries (PID). Pelvic pain due to PID varies greatly in severity, ranging from asymptomatic to extremely mild (chlamydial PID) to quite severe, accompanied by systemic symptoms (gonococcal PID). Initially, STI-related salpingitis and PID is an infection caused by one or two STIs; however, once the cervical barrier has been breached, very quickly other micro-organisms ascend from the vagina in the wake of the STIs, causing a mixed aerobic and anaerobic infection.

Differential diagnosis

The differential diagnosis of female pelvic pain is too wide for this monograph. The main diagnosis not to miss is an ectopic pregnancy. For this purpose, the menstrual history is vital, including the date of onset of the last normal period, plus details of any intermenstrual bleeding or spotting or post-coital bleeding. A good sexual history is also essential, including the precise date of the last unprotected sex

with a male partner. It is relatively simple to diagnose non-STI causes of PID, e.g. history of recent delivery and post-partum endometritis, gynaecological procedures or surgery, and PID secondary to an acute appendicitis. To assist accurate diagnosis, here are some common characteristics of STI-related PID, and some common clinical features which would suggest another diagnosis:

Common characteristics of STI-related PID[12]:
- Recent risk factors for contracting an STI
- Patient under 35 years of age
- Past history of STIs
- Gradual onset of pain
- Ill defined pain: few or no systemic symptoms
- Deep dyspareunia
- Abnormal vaginal discharge, irregular menstrual bleeding
- No associated gastrointestinal tract symptoms
- No urinary tract symptoms or only very mild ones (slight dysuria)
- Tender lower abdomen on palpation with adnexal or cervical motion tenderness on bimanual examination

Clinical features suggesting another diagnosis:
- Sexual history non-contributory, or indicates little or no risk
- History of recent child-birth or gynaecological procedure
- Pregnancy
- Sudden onset of pain – (ruptured ectopic pregnancy or torsion of an ovarian cyst)
- Recent missed period – (ectopic pregnancy)
- No indication of cervical infection – no discharge
- No dyspareunia
- Possible GIT symptoms (anorexia, constipation, diarrhoea, flatulence, nausea, vomiting etc.)
- Possible urinary tract symptoms (marked dysuria and frequency)
- Lower abdomen tender or non-tender on palpation, but bimanual pelvic examination non-contributory and no cervical motion or adnexal tenderness elicited

The take-home message is:
- Once the clinician has excluded pregnancy, if the sexual history is suggestive, treat as STI-related PID pending results of tests and response to therapy

Diagnostic tests

The clinician should organise the following tests before and during the course of the examination:
- Pregnancy test (a urine pregnancy test may remain negative for up to 21 days after an episode of unprotected sexual intercourse)
- FCU for gonorrhoea and chlamydia
- MSSU
- HVS – microscopy on HVS is sometimes useful if it shows a greater than normal number of leucocytes (indicating a cervicitis) or the presence of many clue cells (bacterial vaginosis) as PID is more likely in the presence of cervicitis or bacterial vaginosis

CASE STUDY 2

Andrew is a 27-year-old trawler fisherman who lives in Weipa on the Gulf. He presents to the local GP with extensive perianal warts, but is otherwise asymptomatic. He is highly embarrassed and stresses to the doctor that he has never engaged in any anal sexual activities. He believes he noticed a wart on the shaft of his penis about a year ago which he succeeded in scratching off over the space of a few days. It never re-appeared but about a month later he began to notice small lumps around his anus. They have continued to grow and now he constantly feels uncomfortable especially after sweating at work, or after going to the toilet.

Recently he has noticed some blood on the toilet paper when he wipes himself. He had a steady girlfriend up to eighteen months ago and when she broke it off he felt very upset for some time. He has had sex with about eight different girls since that time, all very casual, usually on a Saturday night after a few drinks at the local pub. He admits he is a bit of a binge drinker. He says he uses condoms about 60% of the time. In the last two months, however, the anal problem has put him off sex. His general health is good although he smokes 20 cigarettes a day which he has done since age 15. He says he does not use drugs other than 'a few bongs' when out on the fishing trawler. He thinks he has been vaccinated against hepatitis B.

Physical examination confirms large cauliflower-like growths of warts completely surrounding his anal opening, but is otherwise unremarkable. He agrees readily to an STI screen. The clinician finds that Andrew has a positive PCR test for chlamydia and a positive NAAT test for trichomoniasis on an FCU. He has good levels of HBsAb, a negative syphilis EIA, a negative HIV antibody test but his hepatitis C serology is positive. The clinician treats his chlamydia and trichomoniasis but is unsure how best to manage Andrew's extensive perianal warts and hepatitis C, so he consults the regional Sexual Health Clinic in Cairns.

If there is a clear view of the cervix during examination, the clinician can take:
- Direct swab for microscopy
- Direct swabs for gonorrhoea (culture and sensitivity) and chlamydia (NAAT)

Recommended blood tests are:
- A baseline full blood examination especially for the white cell count
- HCG if urine test is negative or equivocal and within three weeks of the last unprotected sexual intercourse

At the same time the clinician should arrange serological tests as appropriate after discussion with the patient (HIV, HBV, HCV, syphilis), a Papanicolaou smear if due, and should take throat and rectal swabs if necessary (see Table 12.3).

Other test:
- Pelvic ultrasound examination, if any question remains of possible ectopic pregnancy

Initial treatment of STI-related pelvic pain syndrome in women

All health practitioners encountering patients with possible STI-related PID should have a low threshold for treatment. Once the clinician is satisfied that she or he has excluded life-endangering causes of acute pelvic pain and that arrangements for follow-up are in place (see below), initiating treatment for PID will not have adverse consequences even if PID is not the cause of the pain. Trial of treatment is a reasonable course of action, as non-STI causes for pelvic pain will fail to respond, while STI-related PID will respond quickly and well to the following suggested regimen:

- Azithromycin 1g orally as a single dose immediately (B1)
- Doxycycline 100mg orally twice daily until review (not to be used in pregnancy D)
- Metronidazole 400mg orally twice daily until review (B2)

If gonorrhoea is even a small possibility, add to the above:

- Ceftriaxone 500mg intramuscularly as a single dose (safe in pregnancy B1). This dose can be repeated daily for three days if the patient has moderate to severe systemic symptoms, fever, rigors, malaise, headache or myalgia etc.

Treat or arrange treatment for male sexual partner(s) with azithromycin with or without ceftriaxone.

Review in three days to observe effect of treatment and to ensure male sexual partner(s) has (have) been seen and treated. If treatment is proving ineffective and tests fail to confirm an STI, antibiotic therapy can be stopped and the clinician should initiate further tests to establish the diagnosis (e.g. ultra-sound scan, CT scan, laparoscopy).

Ongoing treatment for specific STIs causing pelvic pain syndrome in women

On the third day if the patient has improved, continue doxycycline and metronidazole (as above) to a total of 14 days.

Review test results:

If tests show gonorrhoea and there are systemic symptoms, give ceftriaxone 500–1000mg intramuscularly daily until systemic symptoms settle. If tests confirm chlamydia, continue doxycycline. When the patient is having difficulty adhering to the treatment, or if patient is pregnant (a rare event as PID is uncommon in pregnancy) a suggested alternative (with a limited evidence base) is: repeat 1g azithromycin at review visit on day 3, then on day 7 and day 14 preferably by directly observed therapy. If tests confirm the presence of anaerobic micro-organisms, continue metronidazole. When the patient is having difficulty adhering to the treatment, two single-dose treatments with metronidazole might be preferable, e.g. 2g on review visit day 3, then on day 7 and day 14, although this suggested alternative is without an evidence base.

If other possible causative STI micro-organisms are isolated on laboratory tests (e.g. Ureaplasma urealyticum, Mycoplasma hominis or genitalium) and the patient is failing to respond to the standard regimen, clinicians should consult a sexual health physician for further advice (see Table 12.4).

Follow-up (see Table 12.5)

Clinicians should ask patients to return for follow-up in three days. The clinician should see the patient again on day 7 and day 14 for further review.

7. Scrotal swelling

Description and causes

There are many abnormal swellings boys and men discover in the scrotum over the course of a lifetime. They are a source of much anxiety but most are totally benign (varicocoeles, epididymal cysts). Generally, worried patients can be reassured about their scrotal swellings. There are three main situations where this is not the case:

- Torsion of the testis (sudden onset, acutely painful)
- Testicular cancer (gradual onset, usually not painful; rock hard on palpation)
- Epididymo-orchitis (gradual onset, slowly increasing pain)

Epididymo-orchitis is an STI-related scrotal swelling in young men.[13] In older men who have varying degrees of prostatomegaly, epididymo-orchitis may occur secondary to a low grade bladder infection. However, STI-related epididymo-orchitis can occur in men of all ages. STI-related epididymo-orchitis follows urethritis whether symptomatic, or more commonly asymptomatic, and in theory any of the STI causes of urethritis can also cause epididymo-orchitis (see Table 12.2). In practice, gonorrhoea and chlamydia (serovars D–K) are the most common aetiologies. Epididymo-orchitis is an infection in the epididymis which spreads, if untreated, to involve the testis itself. The epididymis is tender, enlarged and firm or hard on palpation. In later disease, the epididymis and testis may become difficult to define from each other, the whole becoming a knobbly tender mass.

Differential diagnosis

Scrotal swellings may be:

- Infective
  - STI-related (*Neisseria gonorrhoeae*, *Chlamydia trachomatis* D–K, other STIs)
  - secondary to bladder neck infections (Pseudomonas sp, coliforms)
  - secondary to a sexually acquired coliform urinary tract infection due to unprotected insertive anal intercourse
  - tuberculosis (relatively common in countries where TB is endemic)
  - brucellosis
  - syphilitic gumma (very rare nowadays)
- Neoplastic
- Developmental (cysts, hydrocoeles, varicocoeles),
- Traumatic
- Due to torsion (itself really due to a developmental abnormality)

Diagnostic tests

In any patient under 35 years old with a significant scrotal swelling, clinicians must first exclude torsion (unlikely past 25 years of age), and testicular cancer. If the swelling is of sudden onset, is very painful and very tender on palpation, the clinician must arrange, as a matter of urgency, a Doppler ultrasound scan and/or a surgical opinion. If the swelling is firm and hard on the surface or in the body of the testis and is clearly differentiated from the epididymis, which feels normal on palpation, a cancer is likely and again an ultrasound scan should be done as soon as possible.

In all other situations and with a suggestive sexual history, look for the presence of urethral discharge. If a urethral discharge is present the clinician should collect swabs of the discharge. If not, as is the more common scenario in epididymo-orchitis, FCU can be used instead. The recommended tests are for gonorrhoea, trichomoniasis (if NAAT available), chlamydia, MSSU, serological tests as appropriate after discussion with the patient (HIV, HAV, HBV, HCV, syphilis) and rectal swabs (culture and sensitivity for gonorrhoea and NAAT for chlamydia) if appropriate, as well as throat swab for culture and sensitivity for gonorrhoea if relevant (see Table 12.5 for details of recommended tests).

In men who have engaged in unprotected insertive anal intercourse, a sexually acquired coliform urinary tract infection (UTI) can lead to epididymo-orchitis, so MSSU for microscopy, culture and sensitivity is an essential investigation to ensure this possibility is not overlooked.

Initial treatment of STI-related scrotal swelling

All health practitioners encountering patients with possible STI-related scrotal swelling should have a low threshold for treatment. Once the clinician is satisfied that she or he has excluded other significant causes of scrotal swelling (torsion and tumour) and is satisfied arrangements for follow-up are in place (see below), initiating treatment for epididymo-orchitis will not have adverse consequences even if STI-related epididymo-orchitis eventually proves not the cause of the painful swelling. STI-related epididymo-orchitis will respond quickly and well to the following suggested regimen:

- Azithromycin 1g orally as a single dose immediately
- Doxycycline 100mg orally twice daily until review.

Remember, strains of gonorrhoea which have a predilection for the epididymis rarely cause symptomatic urethritis. Gonococcal epididymo-orchitis is still possible in the absence of a profuse purulent urethral discharge. If gonorrhoea is even a small possibility, add to the above:

- Ceftriaxone 500mg intramuscularly as a single dose. This dose can be repeated daily for three days if the patient has moderate to severe systemic symptoms, fever, rigors, malaise, headache, myalgia etc.

If a clinician suspects an underlying sexually acquired urinary tract infection because of a history of unprotected insertive anal intercourse, the initial treatment regimen should be:

- Ciprofloxacin 500mg orally twice daily for 10 days.

Treat male and female sexual partners with azithromycin with or without ceftriaxone. Clinicians should first check female sexual partners for the possible presence of PID.

Review in three days to observe the effect of treatment and to ensure sexual partner(s) has (have) been seen and treated. If treatment is proving ineffective and tests fail to confirm an STI, antibiotic therapy can be changed in the light of MSSU results and/or the clinician can initiate further tests to establish the diagnosis (e.g. blood cultures, MSSU for mycobacteria).

Ongoing treatment for specific STIs causing scrotal swelling

On the third day if the patient has improved, continue doxycycline to a total of 14 days.

Review test results:
If tests show gonorrhoea and there are still systemic symptoms, give ceftriaxone 500–1000mg intramuscularly daily until systemic symptoms settle.
If tests confirm chlamydia, continue doxycycline.
When the patient is having difficulty adhering to the treatment, a suggested alternative (with a limited evidence base) is: repeat 1g azithromycin at review visit on day 3, then on day 7 and day 14 preferably by directly observed therapy.

If tests show trichomoniasis, a very uncommon contributor to epididymo-orchitis, add metronidazole 400mg orally twice daily for 14 days (see Table 12.4).
If other possible causative STI micro-organisms are isolated on laboratory tests (e.g. Ureaplasma urealyticum, Mycoplasma hominis or M. genitalium) and the patient is failing to respond to the above regimen, clinicians should consult a sexual health physician for further advice.

Follow-up: (see Table 12.5)

Clinicians should ask patients to return for follow-up in three days as outlined above. The clinician should also see the patient again on day 7 and day 14 to review progress.

8. STI-related skin rashes: genital

Description and causes

Most skin rashes affecting the genitals are not STI-related. Readers should consult dermatology or sexual health texts. There is a discussion of HIV-related skin rashes in Chapter 6. Specific STIs may cause the following genital skin rashes:

- Candidiasis – vulvitis with erythema and oedema accompanied by itch. Usually associated with vaginitis and cottage-cheese like discharge; and balanoposthitis – inflammation of the glans penis and undersurface of foreskin (if present)
- Trichomoniasis – vulvitis due to the irritation caused by a profuse frothy offensive discharge
- Recurrent outbreak of genital herpes – recurrent attacks of herpes are often very atypical and may masquerade as a non specific genital rash or fissuring
- Scabies – burrows and nodules on the soft genital skin of penile shaft, glans penis, and vulva. Buttocks and natal cleft are often involved. Rash is intensely itchy, so often accompanied by excoriation. There is accompanying generalised skin irritation and itching with further burrows around wrist area and between fingers
- Pubic lice – itchy rash and excoriation in pubic region accompanied by obvious pubic lice clinging to coarse body and pubic hair. There are frequently tell-tale small dots of blood seen on underclothing when many lice are present.
- Fixed drug eruption – included because often indirectly STI-related. This is a sharply demarcated erythematous circular lesion, sometimes weeping, classically on the glans penis due to a localised hypersensitivity reaction to a drug such as doxycycline.

Differential diagnosis

There is a wide differential diagnosis of genital rashes but all the above STI-related skin rashes are fairly easily recognised clinically or can easily be confirmed by performing appropriate tests. Common non-STI causes for genital skin rashes are:

- Psoriasis
- Lichen planus
- Lichen sclerosus (including balanitis xerotica obliterans on the penis)
- Eczema
- Contact dermatitis

Diagnostic tests

Patients who present with STI-related genital skin rashes may have been at risk for other more significant STIs. Clinicians should consider doing screening for other STIs as appropriate. To make the diagnosis of the specific rash, take swabs from affected areas for tests for candidiasis and herpes. To check for trichomoniasis, an HVS is best. To confirm scabies, look for a clear burrow, lay it open and extract mite on the tip of a fine needle and examine under low power microscopy. To confirm pubic lice, remove one from a hair with a pair of forceps and examine under a magnifying lens or low power microscopy. A fixed drug eruption has a characteristic appearance and history of drug exposure, but if uncertain do a punch biopsy and send for histology.

Initial and specific treatment for STI-related skin rashes: genital

Specific treatment can be prescribed immediately on recognition of the aetiology of the rash. See Table 12.4 for treatments for specific STIs. For genital skin rashes these are treatments for:

- Vulvo-vaginal candidiasis
- Trichomoniasis
- Recurrent herpes
- Scabies
- Pubic lice

For fixed drug eruption, stop the offending drug (e.g. doxycycline) and the rash will subside over three or four days.

Treat or arrange treatment for male or female sexual partner(s) as appropriate.

Follow-up: (see Table 12.5)

STI-related skin rashes: generalised

Description and causes

Generalised skin rashes have too many causes to discuss in this monograph. The decline in immune function associated with HIV infection leads to well characterised skin conditions and infections (see Chapter 6). In primary care practice, there are three significant generalised skin rashes of relevance to STIs which an astute clinician should try to exclude. These are:

- The rash of secondary syphilis: a generalised mainly macular erythematous rash, seen well on the trunk, but may also involve the palms and the soles. It too is non-itchy. It is usually accompanied by fever, malaise, headache and lymphadenopathy or may have little or no systemic symptoms.
- The rash of primary HIV infection (Chapter 4): a generalised mainly macular erythematous rash, seen well on the trunk, but may also involve the palms and the soles. It too is non-itchy. It is usually accompanied by fever, malaise, headache and lymphadenopathy. Primary HIV infection is very frequently mistaken for infectious mononucleosis.[14]
- The rash of disseminated gonococcal infection: seen on distal portions of the extremities as macules, papules, pustules, petechiae or ecchymoses, usually less than 30 in number. They are usually accompanied by joint involvement with arthralgias, tenosynovitis and sometimes frank arthritis. There is often accompanying fever and malaise, although this may be quite mild.[14]

Differential diagnosis
The differential diagnoses are many and require a thorough knowledge of dermatology.

Diagnostic tests
Testing for secondary syphilis requires an RPR and a specific treponemal test (TPPA, EIA or FTA ABS). In almost all cases the RPR will be 1/16 or greater.

In primary HIV infection, current tests in Australia will almost always be positive. There remains a short window period in very early infection where HIV tests may be negative and the diagnosis may be missed. A negative HIV antibody test does NOT exclude the diagnosis (for further discussion of this issue, see Chapter 4).

Accurate diagnosis of disseminated gonococcal infection (DGI) is not so easy. The mainstay of testing is to send swabs for culture and sensitivity from all possible sites of exposure (as judged by the sexual history)—a FCU for NAAT is quite adequate for urethral gonorrhoea if there is no urethral discharge. Gonococcal strains causing disseminated gonococcal infection are often asymptomatic at mucosal sites of infection. In addition, sending blood cultures for *Neisseria gonorrhoeae*, although they are only positive in about 40% of cases, and an aspirate for microscopy, and culture and sensitivity, from any joint effusion (if possible) will assist in confirming the diagnosis.

In addition to tests outlined above, in all three situations, clinicians should screen for other STIs in accordance with the sexual history. (See Table 12.3).

Initial treatment of STI-related skin rashes: generalised
In these three conditions, thinking of the diagnosis and initiating the appropriate tests is a major contribution to patient management and public health. In the case of syphilis and disseminated gonococcal infection, once tests have been taken, no harm is done in initiating treatment immediately on suspicion to render the patient asymptomatic and non-infectious as rapidly as possible.

In all three situations, clinicians must initiate discussions with patients about contact tracing in order to ensure that their sexual partner(s) are also seen, checked and treated as well.

Specific treatment for STI-related skin rashes
Secondary syphilis
(See Table 12.4)

Treat or arrange treatment for male or female sexual partner(s) as soon as possible.

Disseminated gonococcal infection
- Ceftriaxone 1g intramuscularly or intravenously (B1) daily for 7 days

Alternatively, if sensitivity tests show that the gonococcus is sensitive to ciprofloxacin and clinical response is good after 24–48 hours, regimen can be switched to:
- Ciprofloxacin 500mg orally twice daily (B3) until the end of day 7 of treatment AND
- Azithromycin 1g po (B1) as a single dose for possible accompanying chlamydial infection

If the patient is allergic to cephalosporins and the gonococcus is resistant to ciprofloxacin, the clinician should seek the advice of a sexual health or infectious diseases physician.

Test and treat, or arrange treatment, for male or female sexual partner(s) with single dose ceftriaxone. and azithromycin.

Primary HIV infection
- See Chapter 4

Contact tracing of all sexual contacts over the past six months.

Follow-up: (see Table 12.5)

Summary
STIs have a wide variety of clinical manifestations, as well as none at all, and thinking about them in terms of the eight most commonly encountered syndromes may help clinicians achieve better management. Management of STIs in primary care is highly appropriate. It is vital that it be done well.

When the STI is unusual or complicated, fails to respond to recommended treatment, when there are difficult sexuality or other sexual health issues involved or where contact tracing is beyond the capacity of the primary care clinician, she or he should refer the patient to a specialist sexual health physician or clinic. In addition to specific therapy, psychosocial management, safe sex education, provision of information and referral when necessary are key features of the primary care of STIs, and are well within the capability of any competent clinician.

References:

1. Wasserheit JN. Epidemiological synergy: interrelationships between human immunodeficiency virus infection and other sexually transmitted diseases. Sex Transm Dis 1992; 19: 61–77.
2. Australasian Chapter of Sexual Health Medicine RACP 2004. Clinical guidelines for the management of sexually transmissible infections among priority populations. [Online] [access April 2007]. Available from http://www.racp.edu.au/public/SH_clinical_guidelines.pdf
3 Sexually transmitted infections in gay men action group (STIGMA) 2005. Sexually transmitted infection testing guidelines for men who have sex with men. [Online] [access April 2007]. Available from http://www.racp.edu.au/public/SH_MSMguidelines.pdf
4 Pao D, Fisher M, Hué S, Dean G, Murphy G, Cane P, et al. Transmission of HIV-1 during primary infection: relationship to sexual risk and sexually transmitted infections. AIDS 2005; 19: 85–90.
5 Trelle S, Shang A, Nartey L, Cassell JA, Low N. Improved effectiveness of partner notification for patients with sexually transmitted infections: systematic review. Br Med J 2007; 334: 54.
6 Australasian Society for HIV Medicine (ASHM). Australasian Contact Tracing Manual 2006. [Online] [access April 2007]. Available from http://www.ashm.org.au/contact-tracing/
7 Holmes KK, Levine R, Weaver M. Effectiveness of condoms in preventing sexually transmitted infections. Bull WHO 2004;82:454–61.
8 Auvert B, Taljaard D, Lagarde E, Sobngwi-Tambekou J, Sitta R, Puren A. Randomized, controlled intervention trial of male circumcision for reduction of HIV infection risk: The ANRS 1265 trial. PLoS Med 2005; 2 (11): e298.
9. Australian Government. Department of Health and Ageing. Therapeutic Goods Administration. Prescribing medicines in pregnancy, 4th edition 2006. Australian categorisation of drugs. http://www.tga.gov.au/docs/html/mip/medicine.htm (last accessed September 2007).
10 Russell D, Bradford D, Fairley C, editors. Sexual Health Medicine. Melbourne: IP Communications, 2005.
11 Maw R. Critical appraisal of commonly used treatments for genital warts. Int J STD AIDS 2004;15: 357–64.
12 Banikarim C, Chacko MR. Pelvic inflammatory disease in adolescents. Adolesent Med Clinics 2004; 15:273–85.
13 Horner PJ. European Branch of the International Union against Sexually Transmitted Infection and the European Office of the World Health Organization. European guideline for the management of epididymo-orchitis and syndromic management of acute scrotal swelling. Int J STD AIDS 2001; 12 (Suppl 3):S88–S93.
14 Rosenberg ES, Caliendo AM, Walker BD. Acute HIV infection among patients tested for mononucleosis [letter]. N Engl J Med 1999;340:969.
15 Guinto-ocampo H, Friedland LR. Disseminated gonococcal infection in three adolescents. Pediatr Emerg Care 2001;17:441–3.
16 Centres for Disease Control (USA) Sexually transmitted diseases treatment guidelines 2006. [Online] [access April 2007]. Available from http://www.cdc.gov/mmwr/PDF/rr/rr5511.pdf

Standard precautions and infection control

13

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The aim of this chapter is to provide:

- Detail about standard precautions and infection control guidelines for health care settings
- Guidance on the management of blood and body substance exposures and incidents

Introduction

The potentially infectious nature of all blood and body substances necessitates the implementation of infection control practices and policies. In Australia, infection control guidelines have been developed based on the United States Centers for Disease Control and Prevention model, in terms of 'standard precautions' and transmission based precautions. Standard precautions ensure a high level of protection against transmission of blood-borne viruses in the health care setting and the universal application reduces the potential for stigma and discrimination. Standard precautions are the minimum level of infection control required in the treatment and care of all patients to prevent transmission of blood-borne infections including HIV, HBV and HCV. Standard precautions should be implemented universally, regardless of information or assumptions about a patient's infection status. Additional precautions are further measures required to protect against transmission of infections such as tuberculosis.

This chapter provides a summary of the most recent Australian infection control guidelines endorsed by the Communicable Diseases Network of Australia (CDNA), National Public Health Partnership (NPHP) and Australian Health Ministers' Advisory Council (AHMAC): *Infection control guidelines for the prevention of transmission of infectious diseases in the health care setting*[1]. The CDNA guidelines describe in detail the practices and procedures necessary to prevent transmission of blood-borne infections, including HIV, HBV and HCV. Review of these guidelines is strongly recommended for clinicians and other health care workers implementing infection control procedures.

Implementation of standard precautions minimises the risk of transmission of blood-borne and other infections from health care worker to patient, from patient to health care worker and from patient to patient. Infection control guidelines are relevant in social and domestic contexts as well as occupational settings. The clinician should be ready to answer patients' questions about their clinic's infection control policies and provide advice for patients in relation to infection control in their daily environment.

Transmission of blood-borne viruses

The modes of transmission for blood-borne viruses are outlined in Table 13.1 and risk of transmission is discussed in more detail in Chapters 2 and 3.

Key points

- The potentially infectious nature of all blood and body substances necessitates the implementation of infection control practices and policies in the health care setting.
- The universal application of standard precautions is the minimum level of infection control required in the treatment and care of all patients to prevent transmission of HIV, HBV and HCV. These include personal hygiene practices particularly hand-washing, use of personal protective equipment such as gloves, gowns and protective eye wear, aseptic technique, safe disposal systems for sharps and contaminated matter, adequate sterilisation of reusable equipment and environmental controls.
- Vaccination is an important infection control strategy for HBV and HAV; all health care workers should be aware of their immune status and be vaccinated if appropriate.
- Clinicians and other health care workers who regularly perform exposure-prone procedures have a responsibility to be regularly tested for HIV, HCV and HBV if not immune. Health care workers who are aware that they are infected with HIV, HBV or HCV should not perform exposure-prone procedures.
- The current best practice guidelines for infection control procedures in Australian health care settings are outlined in *Infection Control Guidelines for the Prevention of Transmission of Infectious Diseases in the Health Care Setting* (2004).

TABLE 13.1 Precautions for preventing transmission of blood-borne viruses[1]

Disease	Mode of transmission	Recommended precautions	Immunisation
HAV	Contact (oral-faecal route)	Standard precautions Additional precautions for incontinent patients	Immunise health care workers at high risk
HBV	Blood-borne (direct contact with blood or body substances)	Standard precautions	Immunise all health care workers. Test for seroconversion 4–8 weeks after 3rd dose of vaccine
HCV	Blood-borne (direct contact with blood)	Standard precautions	No vaccine available
HIV	Blood-borne (direct contact with blood or body substances)	Standard precautions. Additional precautions may be required in the presence of complicating condition (e.g. Tuberculosis)	No vaccine available

Transmission of HBV is approximately 100 times more efficient than transmission of HIV and approximately 10 times more efficient than HCV.

The risk of blood-borne virus transmission is dependent on a number of factors. Incidents involving blood-to-blood contact with infectious blood are associated with a high risk of infection when:

- There is a large quantity of blood, indicated by visible contamination
- There is insertion of a needle directly into a vein or artery or deep cavity
- The patient has advanced HIV disease and/or high HIV viral load; high levels of HBV DNA and detectable HBeAg; HCV RNA detected by PCR

Transmission of blood-borne viruses in the health care setting is generally associated with failure to comply with recommended infection control guidelines and/or cleaning and disinfection protocols. In the case of HCV, patient-to-patient transmission has been associated with endoscopic procedures, The risk of transmission of HIV is estimated to be approximately 0.3% after a percutaneous needlestick injury with HIV-infected blood and 0.09% after a mucous membrane exposure. Transmission of HBV in the health care setting can be prevented through health care worker, patient and community hepatitis B vaccination programs.

Standard precautions

Standard precautions ensure a high level of protection against transmission of infection including blood-borne viruses in the health care setting and are recommended for the care and treatment of all patients and in the handling of:

- Blood including dried blood
- All other body substances, secretions and excretions (excluding sweat) regardless of whether they contain visible blood
- Non-intact skin
- Mucous membranes.

The universal application of standard precautions is the minimum level of infection control required in the treatment and care of all patients to prevent transmission of blood-borne viruses. These include personal hygiene practices, particularly hand-washing; use of personal protective equipment such as gloves, gowns and protective eyewear; aseptic technique; safe disposal systems for sharps and contaminated matter; adequate sterilisation of reusable equipment and environmental controls.

Standard precautions should be implemented universally, regardless of information or assumptions about a patient's blood-borne virus status, and therefore assist to reduce potential stigma and discrimination in the health care setting.

Hand hygiene

Hand-washing is generally considered the most important hygiene measure in preventing the spread of infection. Clinicians should wash their hands before and after significant contact with any patient and after activities that may cause contamination.

Hand-washing should occur:

- Before and after each clinical contact with a patient
- Before and after eating
- After using the toilet
- Before and after using gloves
- After contact with used equipment
- Immediately following contact with body substances

It is important to note that gloves are not a substitute for effective hand-washing. A routine hand-wash should include removal of jewellery and use of a cleaning solution (detergent with or without disinfectant) and water for 15 to 20 seconds, followed by drying with a single-use towel.

Skin care is important because healthy, unbroken skin provides a valuable, natural barrier to infection. Skin breaks should be covered with a water-resistant occlusive dressing. Alcohol-based hand rubs can be used in the absence of appropriate washing facilities.

Gloves

Gloves are a form of personal protective equipment. Clinicians and other health care workers should wear gloves whenever there is a risk of exposure to blood or body substances, and should change their gloves and wash their hands after contact with each patient and during procedures with the same patient if there is a chance of cross contamination. Gloves must be used when:

- Handling blood and/or body substances
- Performing venepuncture
- Touching mucous membranes
- Touching non-intact skin
- Handling contaminated sharps
- Performing invasive procedures
- Cleaning body substances spills or any equipment (instruments) or materials (linen) or surface that may have been contaminated by body substances

For further information about the appropriate use of sterile, non-sterile and general purpose gloves refer to *Infection control guidelines for the prevention of transmission of infectious diseases in the health care setting*.

Other personal protective equipment

Personal protective equipment should be readily available and accessible in all health care settings. The type of protective equipment required depends on the nature of the procedure, the equipment used and the skill of the operator. For example, the use of protective equipment is recommended in the following circumstances:

- Protective eyewear and face shields must be worn during procedures where there is potential for splashing, splattering or spraying of blood or other body substances
- Impermeable gowns and plastic aprons should be worn to protect clothing and skin from contamination with blood and body substances
- Footwear should be enclosed to protect against injury or contact with sharp objects

Needlestick or sharps injury prevention

Inappropriate handling of sharps is a major cause of accidental exposure to blood-borne viruses in health care settings. To minimise the risk of a needlestick or sharps injury, needles, sharps and clinical waste should be handled carefully at all times. Specifically, clinicians and other health care workers should:

- Minimise their handling of needles, sharps and clinical waste
- Not bend or recap needles or remove needles from disposable syringes
- Use safe needle-handling systems including rigid containers for disposal, which should be kept out of the reach of toddlers and small children
- Ensure 'sharps' containers are available at the point of use or in close proximity to work sites to aid easy and immediate disposal

Importantly, the person who has used a sharp instrument or needle must be responsible for the immediate and safe disposal of the sharp following its use.

Health care workers

Vaccination

Vaccination is an important infection control strategy to prevent the transmission of HBV and HAV. The *Australian Immunisation Handbook*[2] provides guidelines on the vaccination of health care workers. All clinicians and other health care workers who may come into contact with blood or body substances should be aware of their HBV vaccination status and be vaccinated if appropriate. Post-vaccination serological testing is recommended four to eight weeks after completion of the primary course , for people in the following categories:

- People at significant occupational risk (e.g. Clinicians and other health care workers whose work involves frequent exposure to blood and body substances)
- People at risk of severe or complicated disease (e.g. people with impaired immunity and people with pre-existing liver disease not related to HBV)
- People in whom a poor response to HBV vaccination is expected (e.g. patients undergoing haemodialysis)
- Sexual partners and household contacts of people with hepatitis B

If an individual's anti-HBs level is <10 IU/mL following the third dose of vaccine, the presence of HBsAg should be investigated. Individuals who are HBsAg negative are classified as a non-responder and should be offered further doses of HBV vaccine. These can be given as either a fourth dose or a further three doses administered monthly. Further testing should occur at least four weeks after the last dose. Health care workers who are non-responders after supplementary doses of HBV vaccine should be advised about the need for administration of Hepatitis B Immunoglobulin (HBIG) within 72 hours of a potential exposure to HBV.

Booster doses are no longer recommended in immunocompetent individuals after a primary course of HBV vaccine, as evidence suggests that a completed course of HBV vaccination provides long-lasting protection. This applies to children and adults, including health care workers.

Individuals at significant occupational risk who have a documented history of a primary course of hepatitis B vaccine, but unknown seroconversion status, and now have an anti-HBs level <10 mIU/mL, should be given a single booster dose of vaccine and have their anti-HBs level checked four weeks later. If the anti-HBs level is <10 mIU/mL, regard the individual as a non-responder, give two further doses of hepatitis B vaccine at monthly intervals, and re-test for anti-HBs levels at least four weeks after the last dose.

HAV vaccination is recommended for health care workers at increased risk of exposure to faecal contamination, including nursing and medical staff working with children, people with an intellectual disability and remote Aboriginal and Torres Strait Islander populations. Serology screening can be used to assist in the assessment of the need for HAV vaccination.

No vaccination is available to protect against transmission of HIV or HCV.

Testing

The mandatory testing of clinicians and other health care workers for HIV, HBV and HCV is not warranted due to the low risk of transmission if standard precautions are followed. Testing for blood-borne viruses should only be undertaken on the basis of clinical assessment or where testing is in the interest of patients and health care workers. Clinicians and other health care workers who regularly perform exposure prone procedures (refer to Table 13.2) have a responsibility to be regularly tested for HIV and HCV, and for HBV if they are not immune. The provision of confidentiality, privacy and consent for testing should be applied.

Occupational exposures

All clinicians and health care workers should have access to infection control guidelines that advise about the management of an occupational injury, including clear written instructions on the appropriate action to take in the event of a needlestick injury and other blood or body substance exposures involving either patients or health care workers. Clinicians and health care workers are encouraged to report occupational exposures immediately and all testing procedures and follow-up treatment should be fully documented. Confidentiality should be maintained.

In general, if an injury or incident occurs where blood or body substances come into contact with non-intact skin or membranes, the following action should be taken:

- Wash exposed membrane or injury with soap and water (an antiseptic could also be used on the skin)
- If eyes have been exposed, thoroughly rinse the eyes with tap water or saline while open
- If mouth has been exposed, thoroughly rinse the mouth with water and spit out
- Seek medical advice immediately for assessment of nature of the exposure, the risk of transmission of blood-borne viruses and the need for HIV or HBV post-exposure prophylaxis (PEP)
- If the exposure is significant and the source patient is known, their consent for HIV antibody, HCV antibody and HBsAg testing should be sought

For more information, contact the National Needlestick Injury Hotline (1800 804 823). The Hotline is a free 24-hour service for health care and emergency services workers who require assistance following a needlestick injury or other occupational exposure.

Post-exposure prophylaxis (PEP) in the health care setting

Depending on the nature of the exposure, PEP is available to health care workers to prevent infection with HIV and HBV. The sooner PEP is administered, the more likely it is to be effective in preventing infection. Clinicians should always refer to the most recent protocols and seek appropriate advice about administration of PEP because the area is constantly changing. Blood should be taken prior to or shortly after administration of PEP to check for prior exposure or infection.

TABLE 13.2 Exposure-prone procedures

High-risk or exposure-prone procedures

- Any submucosal invasion with sharp, hand-held instruments or procedures dealing with sharp pathology and bone spicules, usually in confined spaces or where visibility is poor (e.g. orthopaedic surgery, trauma, internal cavity surgery)

Variable-risk procedures

- Minor dental procedures (excluding examination) and routine dental extractions
- Internal and instrument examination and biopsy (e.g. endoscopy, vaginal examination, laparoscopy)
- Minor skin surgery

Low-risk procedures

- Interview consultation and dental examination
- Non-invasive examinations or procedures (aural testing, electrocardiograph, abdominal ultrasound)
- Intact skin palpation (gloves not required)
- Injections and venipuncture (gloves required)

Post-exposure prophylaxis for HIV in the health care setting

Post-exposure prophylaxis for HIV is a complex area. Currently HIV PEP consists of a combination of two to three drugs depending on the level of risk associated with the exposure and it is recommended that HIV PEP should be started between one and two hours after an exposure. Post-exposure prophylaxis for HIV is:

- Recommended for significant percutaneous exposure to blood or body substances involving a high risk of HIV transmission
- Offered (but not actively recommended) for ocular mucous membrane or non-intact skin exposure to blood or body substances
- Not offered for exposure to any non-bloody urine, saliva or faeces

Post-exposure prophylaxis for HBV in the health care setting

If the exposed person is not immune to HBV, or is unaware of their immune status, then HBIG should be given within 48–72 hours of exposure. For example:

- If the exposed person is not immune to HBV, or is of unknown immune status, HBIG should be administered within 72 hours of exposure
- If the exposed person is a non-responder to the HBV vaccine, HBIG should be given within 72 hours

There is currently no PEP available to prevent HCV infection.

Infected health care workers

Clinicians and other health care workers have a legal obligation to care for the safety of others in the workplace, which includes colleagues and patients. Clinicians and other health care workers infected with a blood-borne virus should consult State or Territory regulations to determine what restrictions are placed on their clinical practice. In general, it is recommended they do not perform procedures that carry a high risk of transmission of the virus from health care worker to patient, such as exposure-prone procedures (refer to Table 13.2).

Health care workers must not perform exposure-prone procedures if they are:

- Anti-HIV positive
- HBeAg positive and/or HBV DNA positive with high titres
- Anti-HCV positive and HCV RNA positive (by polymerase chain reaction).

Infection control in the primary care setting

Infection control guidelines for the prevention of transmission of infectious diseases in the health care setting[1] provides detailed information relating to the application of infection control in an office or primary health care setting including: routine cleaning; disinfectants and antiseptics; design and maintenance of health care premises; management of clinical waste and linen; and reprocessing of instruments and equipment. Specific procedures relating to the office practice and home and community care are included in the guidelines.

The general principles of infection control that apply to large health care settings also apply to office practices. Issues that relate to preventing transmission of blood-borne viruses include:

- All clinical waste such as dressings containing expressible blood, human matter (excluding hair, nails, urine and faeces) and blood sharps must be appropriately packed for transport and disposal according to local regulations
- Sharps are to be disposed of in yellow, rigid-walled containers containing the 'Biological Hazard' label and symbol
- Injecting equipment (including hypodermic syringes, needles, vials of local anaesthetic agent, dental local anaesthetic cartridges, dental needles, intravenous lines and giving sets) must be discarded after single use. Syringes used to hold single-use anaesthetic cartridges must be sterilised between patients
- Dressings, suture material, suture needles, scalpels, intracranial electrodes, pins or needles used for neurosensory testing, spatulas, electric clips and razor blades must also be discarded after single use
- Linen must be managed using standard precautions. Contaminated linen should have body substances removed with paper towels and cold running water, before being washed in cold or hot water. Drying at high temperature aids disinfection. Linen which is to be treated off-site must be packed in labelled, water-resistant, regulation bags
- Re-usable equipment and instruments should be re-processed and sterilisation/disinfection procedures followed in accordance with manufacturers' and national guidelines
- Sterile equipment must be used on critical sites (sterile tissue)
- Sterile equipment is generally recommended for semi critical sites (intact mucous membrane), except in the case of single-use clean tongue depressors and vaginal specula, which are used in procedures unlikely to penetrate the mucosa
- When steam or dry heat sterilisation is not suitable, other sterilisation systems such as ethylene oxide or automated, low-temperature chemical sterilisation may be used if acceptable to the instrument manufacturer

Management of blood and body substance spills in the health care setting

Management of blood and body substance spills depends on the nature of the spill, likely pathogens, type of surface and the area involved. The basic principles of spills management are:

- Standard precautions including use of personal protective equipment apply where there is a risk of contact with blood or body substances
- Spills should be cleaned up before the area is disinfected
- Generation of aerosols from spilled material should be avoided

All spills must be dealt with as soon as possible. In general cleaning blood and body substance spills should take into account the following factors:

- The nature of the spill (e.g. sputum, vomit, faeces, urine, blood or laboratory culture)
- The pathogens most likely to be involved in the spill
- The size of the spill (spot, small or large spill)
- The type of surface (e.g. carpet or impervious flooring)
- The area involved (i.e. whether the spill occurs in a contained area such as a microbiology laboratory or in a public area such as a hospital ward or outpatient area)
- The likelihood of bare skin contact with the soiled surface.

In the case of a small spill, wipe the area clean using a paper towel and then clean with detergent and warm water. A disposable alcohol wipe also may be used. Quarantine areas where soft furnishings are involved (carpet, curtains or seating) until dry. In the case of larger spills mop up with paper towel or use 'kitty litter' or granular chlorine, picking up the larger amount with cardboard.

In general, it is unnecessary to use sodium hypochlorite for managing spills because there is no evidence of any benefit from an infection control perspective. However, it is recognised that some health care workers may feel more reassured that the risk of infection is reduced through the use of sodium hypochlorite.

Legal and ethical issues

Legal liability may occur if inadequate care has been taken to prevent the transmission of infection in the health care setting. Regulatory authorities, including environmental protection services and Commonwealth, State/Territory and local governments, enforce laws and regulations relating to infection control and waste disposal. These regulations can vary considerably throughout Australia and such regulations should take precedence over the general information presented in this chapter. For further information contact State and Territory health departments and medical and other professional boards (refer to *ASHM Directory* available at www.ashm.org.au/ashm-directory). Legal issues are considered in greater detail in Chapter 14.

Summary

Standard precautions and infection control procedures protect against transmission of blood-borne viruses including HIV, HBV and HCV in the health care setting. Regardless of the perceived risk or assumptions about a patient's infection status, infection control procedures must be followed in all clinical settings to minimise the risk of transmission of blood-borne viruses.

References

1 Communicable Diseases Network of Australia (CDNA), National Public Health Partnership (NPHP), and Australian Health Ministers' Advisory Council (AHMAC). Infection control guidelines for the prevention of transmission of infectious diseases in the health care setting. Canberra: Commonwealth Department of Health and Ageing; 2004. Available from http://www.health.gov.au/internet/wcms/Publishing.nsf/Content/icg-guidelines-index.htm

2 Australian Government Department of Health and Ageing. Australian Immunisation Handbook, 9th Ed. Canberra; Commonwealth Department of Health and Ageing; 2008.

Further reading

The Royal Australian College of General Practice, *Infection Control Standards for Office-based Practices* (4th Edition) can be obtained from the RACGP Publications Department on (03) 8699 0495, or by downloading the order form at www.racgp.org.au/publications/orders and faxing back to (03) 8699 0400. The cost is $88 for RACGP members and $132 for non-members. For further information contact RACGP Publications on publications@racgp.org.au or standards@racgp.org.au

Legal responsibilities in relation to HIV and viral hepatitis

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Note: This chapter refers to a number of key Australian laws and policies relating to privacy, confidentiality and duty of care including a summary of leading legal cases. Although addressing some important questions, this information does not constitute legal advice. Practitioners who are uncertain about their statutory or common law obligations to patients or to the local Health Department, including privacy and reporting obligations, are strongly advised to contact their local health department, applicable privacy office or seek independent legal advice.

Introduction

While special issues arise concerning the treatment of people who may have the human immunodeficiency virus (HIV) or hepatitis infection, or are suspected of having the infection, for the most part those laws that pertain to the treatment of any patient also apply to these patients. This chapter will, where relevant, pass very briefly over those areas of law that deal with the treatment of patients generally and focus particularly on what is required of health care practitioners regarding HIV, hepatitis B virus (HBV) and hepatitis C virus (HCV), diseases that are of greater social sensitivity.

Each State and Territory's body of law deals with this area differently. In most cases the differences are a matter of degree. Occasionally the differences are significant. Table 14.1 summarises these laws as they apply in each State and Territory. It is useful in guiding health care practitioners as to their responsibilities to patients and in informing the content of counselling.

Provision of information to the patient

Normally given the misnomer of 'informed consent', the provision of information, and the exchange of information between a health care provider and a patient, is a key element in any treatment or procedure. When this is done well it allows the health care practitioner to discuss the risks and benefits of any treatment or procedure and the patient to consider these risks and benefits in the light of his or her circumstances. These discussions may be concluded in the course of a single consultation or may need to take place over the course of several consultations. The aim of such discussion is to enable the patient to consider the information that is provided in order to facilitate his or her decision-making. The result may be patient consent to the treatment or procedure, refusal or some other negotiated outcome. It is no longer possible to assert that the view of the health care provider should take precedence.

In many jurisdictions testing for HIV is subject to additional laws. These laws were drafted for a number of reasons. During the early 1980s, many health care practitioners in Australia were ill informed about HIV and responsible for poor treatment of those suspected of being HIV positive. A proliferation of horror stories from those people who had suffered at the hands of their practitioners in both surgery and hospital settings emerged. There was no treatment. Testing was often undertaken solely to prevent transmission to others. Testing was not necessarily in the interests of the patient, who would in all likelihood suffer from discriminatory behaviour. These circumstances indicated that legislative intervention was required. This testing regimen was called 'voluntary counselling and testing' (VCT).

The 2006 National HIV Testing Policy and 2007 National Hepatitis C Testing Policy highlight pre-test and post-test discussions as integral components of the testing process. Once a result is known, the patient is to be informed in person and a discussion must take place which includes, amongst other matters, how to prevent placing others at risk or (in the case of a negative result) how to maintain a negative status (Chapter 9).

It is incumbent on a health care practitioner to advise a person who is found to be infected of what the law may demand of him or her. For example, in some jurisdictions the law requires that a person disclose his or her status to a potential sexual partner. There are prohibitions on giving blood. In Western Australia if a person is found to have an infectious disease they commit an offence if they are engaged or employed in the handling, or packaging of food. In addition a person commits an offence if they allow a person

with an infectious disease to make clothing items on their premises. The table at the end of this chapter describes such obligations as they apply in each State and Territory.

Confidentiality

Health practitioners will be well aware of their duty to maintain the confidentiality of their patients. The reasons for this are clearly understood and relate, at the individual level, to the creation of a climate of trust between the health care practitioner and the patient, and at the population level to the protection of public health. If people believe that their trust will be betrayed they will be less likely to seek attention, and this may have an impact on the general health of the community. This duty is now reinforced by Commonwealth and State privacy laws.

There are also health specific laws requiring that medical practitioners not disclose any information regarding a person who has tested positive to an infectious disease.

In the ACT, NSW and Tasmania, disclosure of private information regarding infectious diseases is an offence, and in South Australia such disclosure attracts civil liability. Victorian legislation does not make disclosure a crime, but instead requires that medical practitioners and other people involved in the testing of HIV have appropriate systems in place for protecting the privacy of persons tested for HIV.

The duty to preserve privacy and confidentiality is complicated by a different, and at times contradictory, legislation. The first is ordinary notification to government of instances of HBV, HCV and HIV. The second is that further follow-up may be required where it is feared a patient is actively placing others at risk. Ordinary notification of infectious disease is necessary for the purposes of identifying risk factors, monitoring outbreaks, service planning, implementation and evaluation, and in some cases enabling contact tracing. Such information may also be used in research.

Notification of Third Parties

Health care practitioners may become aware a patient has placed one or more people at risk of contracting HIV, HBV or HCV. In such instances the health care practitioner may wish to encourage the patient to discuss the matter with those who may be at risk of infection. Alternatively, the health care practitioner may advise that the patient bring his or her partner/s or contact/s in so they may be counselled. This will raise particular difficulties where, for example, a woman has been diagnosed with HIV infection and lives in a situation where she is exposed to violence from her partner.

There will be the occasional patient whom the health care practitioner sincerely believes may have transmitted the infection to others and who refuses to cooperate. In such cases, depending on the jurisdiction, there may not be an immediate legal obligation to notify, however, the practitioner will need to weigh the relative moral issues. In the very rare instance where the practitioner believes his or her patient is intentionally placing others at risk, the obligation to notify becomes more compelling.

The case of BT v Oei [1999] NSWSC 1082 examined whether a medical practitioner owes a duty of care to the spouse of his or her patient. Dr Oei had not ordered an HIV test for AT, his patient. BT argued that Dr Oei, by virtue of his specialist training and knowledge, should have known that given AT's history and symptoms, AT was at risk of having HIV infection. This being so, it was reasonably foreseeable that AT, if HIV positive, would transmit the virus to sexual partners. After an extensive consideration of Australian and international law, the judge found that, had AT been appropriately counselled, he would have had a test for HIV which would have shown he had contracted HIV. Had AT been counselled properly, he would have understood the need to protect his partner from risk of infection. The couple would not then have engaged in unprotected sexual relations. The judge concluded that the doctor's negligent failure to properly advise AT with respect to a possible diagnosis of HIV and the need for an antibody test materially contributed to BT's infection with the virus.

Another recent judgement, PD v Dr Nicholas Harvey & 1 Ors [2003] NSWSC 487, reinforces this point. A couple attended a general practitioner together for pre-marital counselling and sexually transmitted infection (STI) screening. The man was found to be HIV positive. When he was given the result, he was referred to a specialist HIV clinic. When the woman rang, having ascertained that she was HIV negative, she asked about the man's result. She was told she could not be given the man's result without his consent. He told her his result was negative; they had unprotected intercourse, and she became HIV positive. She sued the doctors involved. The judge supported the doctors' observance of their duty not to disclose the man's result to the woman without his consent. However, having ascertained that the man had not told the woman his result, and that he did not attend the specialist clinic, the judge found the doctors were in breach of their statutory duty under the Public Health Act 1991 (NSW) to notify the Director-General of Health that an HIV-positive patient was placing another individual at risk. Under that Act the Health Department had power to intervene. Further, the judge found the pre-test counselling at the original joint consultation was negligently provided in that it did not meet the standard required under guidelines issued by the NSW Department of Health.

Many patients are reluctant for the doctor to ring their home or workplace; some patients instruct

their doctors not to ring under any circumstances, and other patients attend giving a false name and false contact details. In some cases the person with the infection will purposefully maintain ignorance concerning any identifying details of sexual or needle-sharing contacts. In some situations, the doctor is unable to initiate passing the result to the patient but relevant public health authorities must, of course, be informed of positive test results regarding notifiable diseases. At the same time, the clinician can report that the patient had not sought the result and could not be contacted. It would then be a matter for the public health authority to find the patient. Though extremely difficult, this may still be possible.

Contact tracing

Contact tracing is the practice whereby a medical professional or the relevant governmental agency traces all the contacts of a person who has, or is suspected of having, an infectious disease. Faced with an outbreak of an infectious disease which spreads rapidly through person-to-person contact, public health officials can use contact tracing to identify people at risk of infection and people or places contributing to the spread of the disease.

The nature of HIV, HBV and HCV, along with society's reaction to them, makes contact tracing a delicate exercise. Firstly, the stigma associated with HIV and the other blood-borne viruses means many people who have the infection do not want every person they are in contact with to know of the infection. Secondly, the nature of transmission, requiring transfer of bodily fluids, makes it unnecessary to identify any of a person's non-sexual contacts. Public health legislation in Australia is not cognisant of this difference in the nature of contact tracing between HIV, HBV and HCV and other infectious diseases, however. In every State or Territory which has contact tracing provisions (ACT, NSW, NT, Queensland and Tasmania), the powers of the relevant person to require and disclose information are identical no matter the type of condition.

Contact tracing powers vary between the various States and Territories. In the ACT, NT and Queensland authorised people can require that a person with HIV, HBV or HCV provide their name and address, the name and address of anyone they may have been in contact with, and information about how and in what circumstances the person acquired the infection. In Tasmania the Director of Public Health can require only that a person with a notifiable disease provide the name and address of any person he or she might have transmitted the disease to. NSW limits the extent of contact tracing to advising a contact of the possibility that they may have been exposed to an STI or a blood-borne virus, counselling and precautions to be taken to minimise the chance of infection or of passing it to others. Finally Victoria has the most circumscribed powers, only having power to require the name and address of contacts in the case of an infectious disease outbreak.

Additional powers exist in the ACT and Queensland for an authorised officer or contact tracing officer to advise contacts they may have been in contact with an infectious disease even where the person with the disease has told the doctor he or she does not wish the contact to be told. These provisions are understandable in the context of an infectious disease like tuberculosis, which can spread rapidly and is difficult to contain, but are less appropriate in the context of HIV, HBV and HCV unless there is evidence to suggest the person with the infection is likely to endanger the health of others.

It is unclear from the legislation what role medical practitioners play in the collecting of contact-tracing information. In each jurisdiction the powers of the relevant person to demand information appear unfettered (except in the case of Victoria which requires an outbreak) and therefore, as a matter of practicality it is likely that medical practitioners will be used as the major sources of such information. Many of the States have provisions which protect the medical practitioner from liability for any information given pursuant to an order under the relevant Act.

A list of relevant resources and professional guidelines relating to contact tracing can be found on the Australian Models of Care database available on the ASHM website (www.ashm.org.au).

Testing in health care or custodial settings

Health care and custodial settings are environments where the possibility of transmission of disease may be increased. In health care settings, transmission may occur where proper infection control procedures are not observed. In custodial contexts, particularly for people detained in correctional facilities, blood-borne viruses can be spread between inmates through intravenous drug use, the use of unsterilised tattoo equipment or unprotected sex. There is some anecdotal evidence that the practice of drug testing prison inmates has resulted in a shift from cannabis use (which remains detectable for up to six months) to injecting drug use (which can be flushed out in under 48 hours).[1] If this is true, the lack of clean needles in prison is likely to increase the prevalence of HIV, HBV and HCV and equally increase the risk to correctional workers.

If a person has, or may have contracted their infection in either of these settings, for the most part the standard laws regarding notification and testing will apply. Victoria does, however, have specific provisions aimed at infectious diseases contracted in these settings. The provisions give the Secretary of the Department of Human Services greater powers to order testing if an infection occurs in a health care or custodial context. In other circumstances the Secretary in Victoria can only order that a person be tested for an infectious disease if he or she believes the person to constitute a public health risk. In

health care and custodial settings, however, the Secretary can order tests even when the person does not represent a public health risk. This section covers situations where, for example, a health care practitioner may be at risk of contracting an infection from a patient, for example through a needlestick injury. Testing supports the appropriate provision of post exposure prophylaxis.

Otherwise, under corrections legislation, prisoners must submit to medical testing when ordered to do so and must comply with the instructions of a medical practitioner.

Criminal law

There are two types of criminal offences associated with HIV, HBV and HCV. The first has been discussed above and relates to the disclosure of information regarding a person with, or who is suspected of having, HIV, HBV or HCV infection. There are also laws in every jurisdiction making it an offence to transmit the infection to another person. The majority of these laws do not specify HIV, HBV or HCV, but instead refer to infectious diseases generally. As with the other areas of legislation, the scope and requirements of these offences differ between jurisdictions.

Offences regarding the spread of HIV, HBV and HCV exist both in public health law and criminal law. Typically the offences contained in the public health law have much lighter penalties than do the criminal provisions and they also allow for defences that the criminal law does not.

The ACT, NSW, Queensland, South Australia, Tasmania and Victoria have public health provisions which make it an offence for a person to transmit an infectious disease to another person. Penalties vary greatly between the jurisdictions. The least punitive requirements exist in the ACT which requires that a person with an infectious disease take 'reasonable precautions' not to pass it on. Failing to do so risks a $1000 fine. Stricter standards exist elsewhere; Queensland law, for example, prohibits the reckless spread of an infectious disease and prescribes up to a $30,000 penalty. In most jurisdictions it is a defence if the person who contracted the disease knew of, and voluntarily accepted, the risk.

The ACT is the only jurisdiction not to have any specific criminal provisions relating to the spread of HIV, HBV or HCV infection. The other States and the Northern Territory criminalise the spread of the infections in one of two ways. Either specific offences addressing HIV, HBV and HCV have been created or spreading a disease is incorporated within existing provisions which prohibit causing harm to another person.

Tasmania has specific provisions under the HIV/AIDS Preventative Measures Act. South Australia, Western Australia and the Northern Territory have adopted the latter approach and included 'disease' within the definition of 'harm' for the purposes of the criminal law. As a result, all of the provisions prohibiting harm also prohibit infecting someone else with a disease. For example, the prohibition on intentionally causing serious harm also prohibits intentionally causing a serious disease; similarly the prohibition on negligently causing harm also prohibits negligently causing a disease. This approach makes use of an extensive existing body of law and is thus more likely to address sensitive issues of HIV, HBV and HCV infection more effectively.

NSW, Queensland and Victoria have separate criminal offences addressing the deliberate (or recklessly in Queensland and Victoria) infecting of another with an infectious or grievous bodily disease. Victoria also has an HIV-specific crime of 'intentionally causing a very serious disease' (HIV is the only defined very serious disease) which carries a maximum penalty of 25 years imprisonment. This approach runs the risk of treating people accused of spreading HIV, HBV and HCV differently to someone accused of causing any other type of bodily harm. Although the consequences of infection with these diseases are long-term, these are issues which can be considered when assessing the gravity of the harm caused.

Thus, although it has been regarded as politically populist to create HIV specific offences, doing so is arguably unnecessary and indeed runs counter to the position adopted by agencies such as the World Health Organization, the Joint United Nations Programme on AIDS and the Office of the High Commissioner on Human Rights.

Anti-discrimination

Anti-discrimination provisions exist in every Australian jurisdiction which make it illegal to discriminate against someone on the basis of their having HIV, HBV or HCV. In each jurisdiction, discrimination is prohibited either on the basis of disability or impairment and, whichever word is used, it includes organisms in the blood which cause, or are capable of causing, a disease. Table 4.1 summarises each of these provisions. (NSW differs from the other States and Territories, as it is the only state that outlaws vilification on the grounds of HIV, of homosexuality and of being a transgender person. Vilification is defined as doing anything publicly that could encourage or incite hatred, contempt or severe ridicule).

The only aberrant jurisdiction is South Australia which prohibits discrimination on the basis of 'impairment' which is defined as a condition which impairs a person's functioning. As a result, the South Australian law will cover acquired immune deficiency syndrome (AIDS) and symptomatic HIV but may not include HIV before a person begins to display symptoms.

More pertinent questions for medical practitioners are, however, what constitutes discrimination on the

basis of disability or impairment and what behaviour health care practitioners must avoid when testing and treating people with HIV, HBV and HCV.

Discrimination on the basis of disability or impairment is, at its simplest, treating a person less favourably as a result of his or her (perceived) disability or impairment. Such treatment in a health care setting could include refusing to see a patient or offering different or inappropriate treatment to the patient.

Most complaints about discrimination on the basis of HIV status are related to the perceived link between homosexuality and HIV status. Health care workers must not treat someone as if they are HIV positive merely because they are homosexual and, similarly, they must not treat someone as homosexual merely because they are HIV positive. Treating homosexuality and HIV status as inextricably linked increases the stigma associated with each and makes both groups less likely to seek medical care.

Health complaints commissioners have, in the past, received complaints concerning doctors, dentists and other health service workers placing persons with HIV infection last on their consultation lists. However, better training on effective infection control procedures appears to have been successful.
In situations where a person's HIV, HBV or HCV status does pose a health risk, employers, sporting clubs and other relevant groups are encouraged to take an accommodating rather than exclusionary approach. Thus, rather than forcing a person to leave work or refusing to allow them to play sport, the various pieces of anti-discrimination legislation require that all possible accommodation of the disability or impairment occur and that any limitations on their behaviour be only those necessary to protect the health of others.

Infected health care workers

Health care workers who perform exposure-prone procedures have a responsibility to know their infectious status with regard to HIV, HBV and HCV and are encouraged to undertake voluntary testing[2] (Chapter 13). Health care workers have an obligation to care for the safety of others in the workplace (including patients) under both common law and the Occupational Health and Safety and Welfare Act 1986.

Conclusion

It has often been noted that unlike many other infectious diseases, HIV, HBV and HCV are not easily transmitted to others. Laws in Western Australia, for example, which make it an offence for a person with an infectious disease to work in food preparation, are wholly inappropriate in relation to HIV, HBV and HCV. Similarly obsolete is a Northern Territory law that gives a bus conductor the power to stop a person with contagious diseases from riding on a bus. Hopefully a legal and social milieu, cognisant of the impact of discriminatory and stigmatising behaviour, will facilitate an environment in which good health care is possible and the incidence of new infections is reduced.

References

1 Crofts N, Thompson S, Wale E, Hernberger F. Risk-behaviours for blood-borne viruses in Victorian prisons. Aust NZ J Criminol 1996;29(1):6.

2 Communicable Diseases Network of Australia (CDNA), National Public Health Partnership (NPHP), and Australian Health Ministers' Advisory Council (AHMAC). Infection control guidelines for the prevention of transmission of infectious diseases in the health care setting. Canberra: Commonwealth Department of Health and Ageing; 2004. Available from http://www.health.gov.au/internet/wcms/Publishing.nsf/Content/icg-guidelines-index.htm

TABLE 14.1 Laws as they apply in each State and Territory

Commonwealth

Subject	Section	Act	Notes / Summary
Privacy		Privacy Act 1988 Sets out the National Privacy Principles (NPP)	The NPP govern how all health workers, hospitals etc. must collect, handle, retain and disclose personal information. The general rule is that information should only be collected when necessary and the information should not be disclosed to any third party.
		Privacy Amendment (Private Sector) Act 2000	Extends the operation of the NPP to all private sector workers, including health workers.

Australian Capital Territory

Subject	Section	Act	Notes / Summary
Notifiable condition	Schedule 1	Public Health Notifiable Condition Determination 2005	HIV, AIDS and viral hepatitis are notifiable conditions.
Notification to patient	s 102	Public Health Act 1997	If a doctor or nurse believes a person has or may have a notifiable condition, he or she must give the patient information about transmission and prevention of transmission of that condition. Failure to do so may have implications under other legislation.
Notification to Department	s 102A	Public Health Act 1997	Doctor or nurse commits an offence if he or she believes a person has a notifiable condition and he or she fails to notify the Chief Health Officer (CHO). Doctor must also notify the CHO if a patient of the doctor dies of what the doctor believes is a notifiable condition.
Notification by pathologist	s 103	Public Health Act 1997	If a pathologist tests a person and the test indicates the person has or may have a notifiable condition, the pathologist, or the person in charge of the laboratory, must notify the CHO.
Notification by hospital	s 104	Public Health Act 1997	Hospital must notify CHO of any in-patient with a notifiable condition.
Contact tracing	s 106	Public Health Act 1997	Where an authorised officer believes on reasonable grounds a person has a notifiable condition, he or she may request that the person provide: • The person's name and address • Information about how the person acquired the condition • Information about the circumstances under which the person may have transmitted the condition • The name and address of any contact of the person The person must not refuse this request without a reasonable excuse.

Informing contacts	s 108	Public Health Act 1997	If a person with a notifiable condition advises a responsible person that he or she refuses to tell a contact about the condition and refuses to give the responsible person permission to do so, the responsible person may contact the CHO who may then inform the contact. A responsible person is a doctor, nurse practitioner, counsellor or person responsible for the care, support and education of the person.
Privacy	s 110	Public Health Act 1997	A person shall not without good reason or consent of that person disclose any information regarding a person having a notifiable condition, unless for the purposes of the Act, or another law of Commonwealth, State or Territory, or authorised under a code of practice.
Privacy of doctors, pathologists	s 111	Public Health Act 1997	It is an offence for a person to disclose without reasonable excuse or consent any information regarding a person with a notifiable condition in which the doctor, pathologist etc. is identifiable.
Prostitution			
Sexually transmitted infection (STI)	Dictionary	Prostitution Act 1992	HIV is an STI. Hepatitis is not.
Operator responsibility	s 24	Prostitution Act 1992	Operator of a brothel must take reasonable steps to ensure that a prostitute does not provide commercial sexual service if the prostitute has an STI.
Prostitute responsibility	s 25	Prostitution Act 1992	A person shall not provide or receive commercial sexual services if he or she knows or can reasonably be expected to know he or she has an STI.
Medical testing	s 26	Prostitution Act 1992	It is an offence for an operator or owner of a brothel to fail to take reasonable steps to ensure that prostitutes receive regular medical testing for STIs. It is also an offence for a prostitute to mislead a person about the results of a test.
Condoms	s 27	Prostitution Act 1992	Operator or owner of a brothel must take all reasonable steps to ensure that condoms are used. Penalties are provided for failure to comply.
Offences			
Unauthorised assertions	s 107	Public Health Act 1997	It is an offence to assert to a person who has been exposed to or may be a source of infection that a third person has a transmissible notifiable condition without the consent of the third person.
Transmission	r 21	Public Health Regulation 2000	A person with a transmissible notifiable condition must take reasonable precautions not to pass that condition on to another person. Penalty is 10 penalty units.
The ACT does not have a separate offence for transmitting a serious disease and the Crimes Act 1900 does not define harm to include inflicting a disease.			

Non-discrimination	s 7 (j)	Discrimination Act 1991	Must not discriminate on the basis of disability which includes 'the presence in the body of organisms that cause or are capable of causing disease' (s 5AA(e))

New South Wales

Subject	Section	Act	Notes / Summary
Scheduled medical condition	Schedule 1	Public Health Act 1991	NSW legislation divides medical conditions into 5 categories. HIV and hepatitis B and C are Category 3 conditions. HIV and AIDS are Category 5 conditions. AIDS is also a Schedule 3 notifiable disease.
Notification	s 16	Public Health Act 1991	A positive test result for a Category 3 medical condition must be notified to the Director General in an approved form. Where the positive test result is for a medical condition that is also a Category 5 medical condition, such notification must not disclose the person's name and address. The obligation falls on the person who certifies the result of the test, not the treating doctor.
Confidentiality	s 17	Public Health Act 1991	Notification to the Director General of a Category 5 medical condition must not include the person's name or address. A person who acquires information about Category 5 testing must take reasonable steps to prevent disclosure unless disclosure is with consent, in the course of administration of the Act, by court order or to a person involved in the care, treatment or counselling of the person affected.
Advice	r 12	Public Health (General) Regulation 2002	The Director General or an authorised medical practitioner may notify a person with a Category 2 or 3 condition of measures to be taken and activities to be avoided in order to minimise the danger of passing the condition to another person.
Contact tracing	r 13	Public Health (General) Regulation 2002	The Director General may notify a person whom they reasonably believe may have been in contact with a person suffering from a Category 2, 3 or 4 medical condition of measures to be taken, and activities to be avoided, in order to minimise the danger of the first person contracting the condition or passing it to a third person.

Public Health Orders			
Examination	s 22	Public Health Act 1991	The Director General may make an order requiring that a person be tested for a Category 4 or Category 5 medical condition if the Director General believes on reasonable grounds that the person is suffering from a Category 4 or Category 5 medical condition.
Behaviour	s 23	Public Health Act 1991	The Chief Health Officer or a medical practitioner authorised by the Director General may make a public health order (PHO) if a person is believed on reasonable grounds to be suffering from a Category 4 or Category 5 medical condition and is behaving in a way that is endangering or is likely to endanger the public health. A PHO may require that the person refrain from specified conduct, undergo counselling or specified treatment, or if the Order is based on a Category 5 medical condition, be detained at a specified place.
Confirmation by Tribunal	s 25	Public Health Act 1991	A PHO based on a Category 5 medical condition ceases to have effect if an application to the Administrative Decisions Tribunal is not served on the person to whom the PHO applies within 3 business days of the PHO, or if the Tribunal does not confirm the PHO, or vary the PHO and confirm it as varied.
Offence to contravene	s 28	Public Health Act 1991	It is an offence for a person to whom a PHO applies to contravene a PHO.
Apprehension	s 29	Public Health Act 1991	An authorised medical practitioner can give a certificate which is the grounds for apprehension by a police officer of a person who has contravened a PHO.
Revocation	s 31	Public Health Act 1991	If an authorised medical practitioner considers that the person is no longer a risk to public health, the practitioner must revoke the order immediately.
Unlawful release	s 34	Public Health Act 1991	It is an offence to release, or to attempt to release, a person detained under a PHO without lawful authority to do so.
Transfer of human tissue			
Prescribed contaminant	r 14	Human Tissue Regulation 2005	HIV and viral hepatitis are 'prescribed contaminants'.
False statements	s 20E	Human Tissue Act 1983	A donor must not sign a certificate that is false or misleading in a material particular.
Restrictions on liability	s 20F	Human Tissue Act 1983	No action lies against the donor of blood unless the donor has signed a false certificate. No action lies against a supplier of blood products if the supplier was an exempt supplier, and the donor signed a certificate, and tests indicated that no prescribed contaminant was present in the blood.

Correctional setting	s 73	Crimes (Administration of Sentences) Act 1999	Any prisoner can be forced to undergo any medical procedure deemed necessary by Justice Health for the preservation of the prisoner's life or to prevent serious damage to the prisoner. This includes testing for HIV, HBV and HCV.
Offences			
Sexually transmissible medical condition	s 13	Public Health Act 1991	It is an offence for a person who knows they have a sexually transmissible medical condition to have intercourse with another person unless that person has been informed of the risk of contracting the disease and voluntarily accepts that risk. It is also an offence for an owner or occupier of premises who knowingly permits a person with a sexually transmissible medical condition to have intercourse with another person on their premises. Maximum penalty of 50 penalty units ($5500).
Causing a grievous bodily disease	s 36	Crimes Act 1900	A person who maliciously and with intent causes, or attempts to cause, another person to contract a grievous bodily disease is committing an offence.
Non-discrimination	Part 4A	Anti-Discrimination Act 1977	It is an offence to discriminate on the basis of disability which includes 'the presence in a person's body of organisms that cause or are capable of causing disease or illness' (s.4).

Northern Territory

Subject	Section	Act	Notes / Summary
Notifiable disease	s 6	Notifiable Diseases Act 1999	Minister may by notification in the Gazette declare a disease to be a notifiable disease.
Notification			
Medical practitioner	s 8	Notifiable Diseases Act 1999	If a medical practitioner diagnoses that a person is an infected person or considers that a person is a suspect person in relation to notifiable disease, the medical person must give specified information about the notifiable disease to a medical officer.
Pathology laboratory	s 16	Notifiable Diseases Act 1999	If a pathology laboratory diagnoses a person with a notifiable disease, the person in charge must give specified information about the notifiable disease to the Chief Health Officer.
Proprietor of hotel, hostel, boarding house	r 48	Public Health (Shops, Boarding Houses, Hostels and Hotels) Regulations	Proprietor who becomes aware that any person is suffering from or suspected to be suffering from an infectious disease on a premises must immediately notify the Medical Officer of Health of the circumstances, and must isolate the person.

Advice	s 10	Notifiable Diseases Act 1999	When a doctor diagnoses a notifiable disease, he or she must explain the nature of the disease and the measures necessary to prevent the spread of the disease. That advice may be provided to the parents of a person under 18 years of age.
Disclosure protected	s 30	Notifiable Diseases Act 1999	No action lies against a person including doctor or pathology laboratory for notifying the Minister or other person as required.
Testing			
Person	s 7	Notifiable Diseases Act 1999	A person who has reasonable grounds to believe he or she may be an infected person or suspected infected person shall consult a medical practitioner at the first reasonable opportunity.
Contact tracing	s 9	Notifiable Diseases Act 1999	A person who is infected shall provide to a doctor or authorised person either the name and address of person he or she may have contracted the disease from or the name and address of all persons he or she has been in contact with during a specified period.
Behavioural order	s 11	Notifiable Diseases Act 1999	A medical officer may serve an infected person with a notice in writing directing the person to carry out measures the officer believes necessary for the treatment or to prevent transmission of the disease.
Appeal	s 12	Notifiable Diseases Act 1999	A person can appeal to the Local Court against a notice given under s 11.
Enforcement	s 13	Notifiable Diseases Act 1999	The Chief Health Officer may order compliance with a s 11 notice. CHO may also order orally or in writing the infected or suspect person be detained in hospital, that premises be disinfected and bedding destroyed and take all steps necessary to give effect to the order made by the CHO.
Notice to attend	s 14	Notifiable Diseases Act 1999	CHO may by notice in the Gazette require a person or class of persons to attend at specified times for medical examination.
Blood Donation			
Liability of Red Cross	s 26B	Notifiable Diseases Act 1999	In an action against the Red Cross for transmitting a notifiable disease through blood transfusion, it is a defence if the Red Cross complied with the specified requirements in taking, testing, processing and handling the blood.
Employment			
Barbers	r 18	Public Health (Barbers' Shops) Regulations	A barber suffering from a contagious disease shall not attend to a customer.
Taxi	r 12	Taxis Regulations	A taxi driver may refuse to pick up a person who is apparently suffering from an infectious disease.

Bus	r 45	Motor Omnibus Regulations	A conductor of an omnibus shall not allow a person suffering from an infectious or contagious disease to be carried in the omnibus.
Correctional setting	s 75	Prisons (Correctional Services) Act	If in the opinion of a visiting medical officer a prisoner is deemed a threat to him- or herself or others, the Director can order medical examination and/or treatment, including the provision of blood or bodily secretions.
Offences			
Bribes	s 35	Notifiable Diseases Act 1999	A medical practitioner or authorised person commits an offence if he or she accepts a reward on account of a failure to perform his or her duty.
Recklessly endangering life	s 174C	Criminal Code Act	Creates offence if reckless conduct gives rise to danger of death.
Recklessly endangering serious harm	s 174D	Criminal Code Act	Creates offence if reckless conduct gives rise to danger of serious harm.
Negligently causing serious harm	s 174E	Criminal Code Act	Creates offence if conduct negligently causes serious harm.

Queensland

Subject	Section	Act	Notes / Summary
Notifiable condition	s 64(1)	Public Health Act 2005	Notifiable condition is defined in the regulations.
	Schedule 1	Public Health Regulation 2005	HIV, AIDS and all hepatitis are notifiable conditions.
Notifiable diseases	Schedule 6	Stock Regulation 1988	The term 'notifiable disease' applies to animals and does not include HIV or AIDS.
Notifiable Conditions Register	s 67	Public Health Act 2005	Chief Executive (CE) must create and maintain a register of persons about whom notification has been received.
Notification by doctor	s 70	Public Health Act 2005	Doctor must notify CE when a person is diagnosed or provisionally diagnosed with a notifiable condition.
Anonymity	s 74	Public Health Act 2005	Notification may occur with an anonymity code.
Confidentiality	s 77	Public Health Act 2005	Confidential information must not be disclosed.
	s 81	Public Health Act 2005	Confidential information can be disclosed where the disclosure is in the public interest (as judged by the CE and where the CE has, in writing, authorised the disclosure).
Contact Tracing			
Disclosure	s 80	Public Health Act 2005	The prohibitions against disclosure of information in s 77 do not apply where the information is disclosed with authorisation by CE for the purpose of monitoring the patterns of notifiable conditions; identifying the sources of outbreaks; identifying persons who may transmit a notifiable condition to others; identifying persons who may have contracted, or may be at risk of contracting a notifiable condition to prevent or minimise transmission of the condition; or contact tracing by a contact tracing officer.

Functions	s 89	Public Health Act 2005	A contact tracing officer has the following functions: a. identifying persons who may have contracted a notifiable condition b. identifying persons who may transmit a notifiable condition to others c. informing persons who may have contracted a notifiable condition so that they may seek medical examination and treatment d. providing information to persons who may have contracted a notifiable condition to prevent or minimise transmission of the notifiable condition e. obtaining information about the following to prevent or minimise transmission of a notifiable condition— (i) how a person has, or may have, been exposed to the notifiable condition (ii)how a person has, or may have, exposed other persons to the notifiable condition.
Power to require information	s 99	Public Health Act 2005	Where a contact tracing officer reasonably believes that a person has a notifiable condition or has been in contact with someone who has a notifiable condition, the officer can, after explaining to the person that information is needed to attempt to prevent or minimise the spread of the condition, require that person to provide his or her name, address and the name and address of any person who may have transmitted the condition to the person or who the person may have transmitted the condition to.
An offence not to provide information under s 99	s 100	Public Health Act 2005	Person must comply with request under s 99 unless the person has a 'reasonable excuse'
Detention	s 113	Public Health Act 2005	CE may order that a person be detained if the CE believes 'the person's condition and likely behaviour constitutes an immediate risk to public health; and is satisfied the person has been counselled, or reasonable attempts have been made to counsel the person about the condition and its possible effect on the person's health and on public health.'
Orders by magistrate Detention	s 116 s 117	Public Health Act 2005	Following a sworn application, CE may obtain order for detention from magistrate. Orders including a detention order may be made in the person's absence if magistrate believes the person represents an immediate risk to public health.
Initial examination	s 118	Public Health Act 2005	If satisfied that a person has a controlled notifiable condition and that a medical examination is necessary, Magistrate may make an 'Initial Examination Order' requiring that a person submit to examination for a notifiable condition.
Behavioural	s 125	Public Health Act 2005	If satisfied that a person has a controlled notifiable condition and the condition constitutes an immediate risk to public health, a Magistrate may make a 'Behavioural Order'.

Detention	s 129 s 130	Public Health Act 2005	If satisfied that a person has a controlled notifiable condition and the condition constitutes an immediate risk to public health a Magistrate may issue a 'Detention Order' which requires that the person remain in detention for not more than 28 days.
Warrant	s 136	Public Health Act 2005	Warrant for apprehension of a person may be issued to enforce Initial Examination Order or Detention Order.
Correctional settings	s 21	Corrective Services Act 2006	A prisoner must submit to any medical examination or treatment deemed necessary by a doctor.
Offences			
Recklessly spreading disease	s 143	Public Health Act 2005	Person must not recklessly spread a controlled notifiable condition. It is a defence if the person placed at risk knew of the condition and voluntarily accepted the risk. Maximum penalty of 400 penalty units ($30 000) or 2 years imprisonment.
Grievous bodily harm	s 317	Criminal Code 1899	Offence to intentionally transmit a serious disease to another person. Liable to life imprisonment. A 'serious disease' is defined in s 1 as one that is likely to endanger life and would include HIV, AIDS, and hepatitis.
Risk minimisation	s 151	Public Health Act 2005	Every person involved in the provision of a declared health service must take reasonable precautions to minimise risk of infection to other people. This includes dentists, nurses, employers with a first aid room, etc.
Employment			
Therapeutic goods	s 176	Health Regulation 1996	Person suffering from any contagious or infectious disease cannot be employed for the purpose of making therapeutic goods.
Prostitution	s 77A	Prostitution Act 1999	It is an offence for a prostitute to provide or offer to provide prostitution services unless a prophylactic is used. A licensee or approved manager must take reasonable steps to ensure a prophylactic is used.
Sexually transmissible infections	Schedule 4	Prostitution Act 1999	HIV is a STI for the purposes of the Act.
	s 90	Prostitution Act 1999	Prostitute with an STI is not allowed to work as a prostitute at a licensed brothel.
Non-discrimination	s 7(h)	Anti-Discrimination Act 1991	Must not discriminate on the ground of 'impairment' which includes 'the presence in the body of organisms capable of causing illness or disease' (Schedule Dictionary).

South Australia

Subject	Section	Act	Notes / Summary
Notifiable disease	Schedule 1	Public and Environmental Health Act 1987	HIV, AIDS and viral hepatitis are notifiable diseases.
Controlled notifiable disease (CND)	Schedule 2	Public and Environmental Health Act 1987	HIV, AIDS and viral hepatitis are CNDs.
Notification	s 30	Public and Environmental Health Act 1987	Where a doctor or person prescribed by regulation believes a person is suffering from a notifiable disease, he or she must inform the Department within 3 days. If after receipt of the report the Department believes the person poses an immediate threat to public health it must notify the council for the Local Government area in which the person resides.
Order testing	s 31	Public and Environmental Health Act 1987	Where the South Australian Health Commission believes a person has a CND, it can require by written notice that the person be examined for that disease. If the person refuses to be tested, a magistrate may issue a warrant requiring apprehension and examination.
Quarantine	s 32	Public and Environmental Health Act 1987	Where a medical practitioner has certified that a person has a CND and the Commission believes that person poses a risk to public health, a magistrate may issue a warrant for detention at a place of quarantine. The order is only to be for 3 days and after that time must be renewed by a magistrate up to a maximum of 6 months. The Supreme Court can extend an order beyond 6 months.
Behaviour	s 33	Public and Environmental Health Act 1987	The Commission may give appropriate directions to a person suffering from a CND to reside at a specified place, refrain from performing specified work, submit to an examination or other directions in order to limit the spread of that disease.
Report to Councils	s 35	Public and Environmental Health Act 1987	The Department shall on a monthly basis provide reports to Local Councils as to the occurrence of notifiable diseases in its area and the threat, if any, they pose.
Actions to prevent spread of disease	s 36	Public and Environmental Health Act 1987	The Commission may take any action necessary to prevent the spread of a notifiable disease.
Prostitution	s 13 s 21 s 25A	Summary Offences Act 1953	It is an offence to consort with prostitutes, occupy premises frequented by prostitutes or engage in procurement for prostitution.

Offences			
Preventing transmission	s 37	Public and Environmental Health Act 1987	A person with a CND will take all reasonable steps to prevent transmission of the disease to others.
Causing harm	s 23 s 24	Criminal Law Consolidation Act 1935	It is an offence to cause harm or serious harm to another person with intent to cause harm or serious harm. Physical harm includes infection with a disease (s 21).
Non-discrimination	Part 5	Equal Opportunity Act 1984	Part 5 prohibits discrimination on the basis of 'mental or physical impairment'.

Tasmania

Subject	Section	Act	Notes / Summary
Notifiable disease	Table 1	Notifiable Diseases Guidelines	HIV, AIDS and viral hepatitis are notifiable diseases.
Notification	s 48	Public Health Act 1997	The Director may require any person or class of person, agency or public authority to notify the Director of the presence of any notifiable disease in a sample of tissue, substance or secretion.
Information from doctor	s 50	Public Health Act 1997	If a doctor believes that a person he or she is attending has a notifiable disease, he or she must provide that person with any information about the transmission and prevention of the disease.
Order for examination	s 41	Public Health Act 1997	The Director may require that a person he or she believes to have a notifiable disease undergo a medical examination.
Directions	s 42	Public Health Act 1997	Director may make the following directions to someone who has or is suspected to have a notifiable disease: • That the person be placed in isolation • That the person be placed in quarantine • That the person be placed under supervision • Further medical examination be conducted • That the person provide the name and address of any person she or he might have transmitted the disease to • Preventing the person from performing specified work • That the person do or not do anything as the Director determines
Warrant	s 43	Public Health Act 1997	Director may apply to a magistrate for a warrant to enforce any order made under s 42.
Order by magistrate	s 46	Public Health Act 1997	A person arrested under a s 43 warrant must be brought in front of a magistrate as soon as practicable. The magistrate may order the person to comply with the Director's order and may also vary, add to or make any other order.
Appeal to Supreme Court	s 47	Public Health Act 1997	Any person subject to an order under s 45 may appeal that order to the Supreme Court.
Period of detention	s 44	Public Health Act 1997	Detention is not to exceed 48 hours without magistrate approval or 6 months without Supreme Court approval.

Report to Council	s 49	Public Health Act 1997	Director must provide a report to a council on the occurrence of any notifiable disease in its area.
Transmission	s 51	Public Health Act 1997	A person who is aware of having a notifiable disease must take all reasonable measures and precautions not to transmit it to any other person and must not knowingly or recklessly place another person at risk. A penalty exists for breach of this section.
Investigation	s 52	Public Health Act 1997	The Director may carry out any investigation or inquiry into any occurrence of any notifiable disease.
Preventing spread	s 53	Public Health Act 1997	The Director may require any person to take any action to stop the spread of any notifiable disease.
Correctional settings	s 30	Corrections Act 1997	Prison director may require a prisoner to undergo a test for HIV or other blood-borne disease.
Offences			
Intentionally or recklessly placing another at risk of becoming infected with HIV	s 20	HIV/AIDS Preventive Measures Act 1993	A person must take all reasonable measures to prevent the transmission of HIV. It is an offence for a person who is aware of being infected with HIV to knowingly or recklessly place another person at risk of becoming infected with HIV unless that person knew and voluntarily accepted the risk of being infected.
Non-discrimination	s 16	Anti-discrimination Act 1998	Must not discriminate on the basis of disability which includes 'the presence in the body of organisms causing or capable of causing disease or illness' (s 3).

Victoria

Subject	Section	Act	Notes / Summary
Infectious disease	Schedule 2	Health (Infectious Diseases) Regulations 2001	HIV, AIDS and viral hepatitis are infectious diseases.
Notifiable disease	Schedule 3	Health (Infectious Diseases) Regulations 2001	HIV and AIDS are notifiable diseases.
Order for test when spread by or to a care giver	s 120A	Health Act 1958	If the Secretary reasonably believes that an incident has occurred in which an infectious disease could have been transmitted while a care-giver or custodian is acting in that capacity and any of those people to whom the disease could have been transmitted have been counselled about the risk of transmission of the disease, the Secretary may make an Order requiring the person named in the Order to be tested for the disease.
	s 120AB	Health Act 1958	These powers can also be exercised by a senior medical officer at a hospital.
	s 120B	Health Act 1958	If the circumstances in s 120A apply and a specimen of the person's blood is available, that may be tested rather than making an order to have the person tested.
	s 120D	Health Act 1958	When advising a person that he or she needs to be tested, the Secretary or authorised officer must not divulge the name of the person from whom the disease originated.

General orders	s 121	Health Act 1958	Secretary can order in writing a person to be tested if he or she reasonably believes a person is infected or has been exposed to infection, the person is likely to transmit the disease and there is a serious risk to public health. If test is positive, Secretary can order counselling if appropriate. If counselling is unsuccessful, Secretary can impose restrictions on the person's behaviour or movements. If restriction is insufficient, Secretary can order detention.
Appeals	s 122	Health Act 1958	Person subject to an order under s 121 may appeal to the Supreme Court.
Emergency powers	s 123	Health Act 1958	Governor in Council can declare a state of public health emergency for the purpose of stopping, limiting or preventing the spread of an infectious disease.
	s 124	Health Act 1958	If the Governor so declares, the Secretary can make orders requiring that persons of a specified class be prevented from leaving or entering a prescribed area, or that they be arrested without warrant and detained in the proclaimed area. Can also order any building or land to be seized, disinfected or destroyed if it is contributing to the spread of infection.
Testing for HIV	s 127	Health Act 1958	Doctor must not test for HIV unless he or she is satisfied that the person has received sufficient information on the medical and social consequences of a positive diagnosis. The person must not be advised of a positive test except in person by a doctor.
Privacy	s 128	Health Act 1958	Any person who discovers that another has been tested for or has tested positive for HIV must take all steps to develop and implement systems to protect the privacy of that person. A penalty exists for breach of this section.
Records	s 130	Health Act 1958	Pathology laboratories must keep records of the number of HIV tests, the number of people tested who fall into each prescribed category and any other information required by the regulations. Prescribed categories are: (i) homosexual male contact; (ii) coagulation factor recipient; (iii) injecting drug user; (iv) transfusion recipient; (v) heterosexual contact; (vi) occupational contact; (vii) screening recipient.
Blood and tissue donation	s 136	Health Act 1958	A donor must not make a false statement regarding HIV/AIDS infection when donating blood or tissue. A penalty exists for breach of this section.

Powers in the event of an infectious disease outbreak	r 15	Health (Infectious Diseases) Regulations 2001	If the Secretary believes that an outbreak of infectious disease has occurred or may occur, the Secretary may: • enter any premises without a warrant and search for and seize any goods • in writing require any person who may have been in contact with an infected person to provide information about the contact • in the case of a premises where the disease may be spread: - inspect the premises - direct the proprietor to disinfect the premises and dispose of anything • close a school • give reasonable directions to a person to take any action that she considers necessary to prevent or limit the spread of the infectious disease.
Correctional settings	s 29	Corrections Act 1986	Principal medical officer of a prison can direct a prisoner to submit to medical tests. In making decision medical officer is to consider the safety of everyone in the prison.
Offences	s 120	Health Act 1958	It is an offence to knowingly or recklessly infect another person with an infectious disease. It is a defence if the person placed at risk knew of the condition and voluntarily accepted the risk.
Prostitution	r 28	Health (Infectious Diseases) Regulations 2001	A proprietor must ensure that condoms are used in a brothel.
	r 29	Health (Infectious Diseases) Regulations 2001	Proprietor must not force a prostitute to provide service if he or she has refused on the basis that he or she suspects the client has an infectious disease or because the client has refused to wear a condom.
Prostitutes infected with an STI	s 19	Prostitution Control Act 1994	The manager of a brothel must not allow a prostitute to provide services when the prostitute has an STI.
	s 20	Prostitution Control Act 1994	A prostitute must not provide services if he or she is infected with an STI.
Non-discrimination	s 6	Equal Opportunity Act 1995	Prohibits discrimination on the basis of 'impairment' which includes 'the presence in the body of organisms that may cause disease'.

Western Australia

Subject	Section	Act	Notes / Summary
Notification by doctor	s 276	Health Act 1911	Obligation of notification to the Executive Director, Public Health rests with clinician, nurse practitioner and responsible pathologist or pathology laboratory.
	s 289	Health Act 1911	Doctor, nurse practitioner and responsible pathologist of pathology laboratory who notify of an infectious disease incur no civil liability and are taken not to have breached duty of confidentiality.
Notification by employer	r 2.5	Occupational Health and Safety Regulations 1996	Employer must notify the Commissioner if a person contracts HIV or viral hepatitis in the course of work which involves 'exposure to human blood products, body secretions, excretions or other material which may be a source of infection.'

Employment			
Employment - food handling	s 246X	Health Act 1911	A person with an infectious disease commits an offence if he or she is engaged or employed in the handling, packaging etc of food. A medical officer can require a person engaged in food handling to submit to a test for an infectious disease.
Employment - apparel	s 279	Health Act 1911	An owner or occupier of a factory, workshop or place from which work is given commits an offence if he or she allows a person with an infectious disease to make wearing apparel on the premises unless he or she could not reasonably be aware that the person had an infectious disease.
Infectious Diseases (ID)			
HIV/AIDS is a dangerous ID	Schedule 1	Health (Dangerous Infectious Diseases) Notice 2000	HIV and AIDS are each declared to be dangerous infectious diseases.
ID – removal to hospital	s 263	Health Act 1911	Medical Officer of Health may order any person suffering an infectious disease removed to hospital for treatment in any case where it is considered in the interest of public health to do so.
ID - exposure	s 264	Health Act 1911	A person suffering an ID commits an offence if she exposes herself in a public place (or public vehicle) without precaution as to infecting others
Non-discrimination	s 66A	Equal Opportunity Act 1984	Prohibits discrimination on the basis of 'impairment' which includes 'any defect or disturbance in the normal structure or functioning of a person's body' (s 4)
Venereal disease	s 248	Health Act 1911	The Governor may declare any infectious disease to be a dangerous infectious disease for the purposes of the Act. Venereal disease is not an infectious disease for the purposes of the Act.
Giving blood	Schedule 1	Blood and Tissue (Transmissible Diseases) Regulations	Person giving blood must provide declaration that blood is free from HBV, HCV and HIV. All blood taken for transfusion is tested for HBV, HCV and HIV and if it tests positive, the person will be notified.
Prostitution	s 8	Prostitution Act 2000	Condom must be used to prevent the transmission of bodily fluid from one person to another.
Correctional settings	s 95D	Prisons Act 1981	Medical officer can force a prisoner to undergo any medical treatment or testing deemed necessary.
Offences	s 294(8) or 297 as read with s 1(4)	Criminal Code	Sections 294 (8) and 297 make it an offence to do any act that is likely to result in a person having a serious disease or to cause grievous bodily harm to another. S.1(4) provides that any reference to causing or doing bodily harm to a person includes a reference to causing a person to have a disease which interferes with health or comfort or to have a serious disease.
Non-discrimination	s 66A	Equal Opportunity Act 1984	Prohibits discrimination on the basis of 'impairment' which includes 'any defect or disturbance in the normal structure or functioning of a person's body' (s 4).

Guardianship and enduring powers of attorney

If there is a possibility that a patient may become incompetent, health care practitioners should advise their patients to consider options that might include 'enduring powers of attorney' or 'enduring powers of guardianship'. The laws that apply to substituted decision-making can be quite complex and vary between States. Patients should be referred to the relevant authorities in their jurisdiction for assistance.

Name	State	Street Address	Postal Address	Phone numbers	Emails
Public Advocate of the ACT	ACT	Level 3 12 Moore St Canberra City 2601	PO Box 1001 Civic Square ACT 2608	Tel: (02) 6207 0707 Fax: (02) 6207 0688	pa@act.gov.au
Guardianship & Management of Property Tribunal	ACT	Magistrates Court, 4 Knowles Place, Canberra ACT 2601.	GPO Box 370 CANBERRA CITY ACT 2601	Ph: (02) 6217 4281 Ph: (02) 6217 4282 Fax: (02) 6217 4505	tribunals@act.gov.au
Office of the Public Guardian	NT	2nd Floor, Casuarina Plaza Darwin Darwin Public Guardian Alice Springs Public Guardian		Ph: (08) 8922 7343 Ph: (08) 8922 7304 Ph: (08) 8922 7116 Ph: (08) 8951 6739	
Guardianship Tribunal	NSW	Level 3 2a Rowntree Street Balmain NSW 2041	Guardianship Tribunal Locked Bag 9 Balmain NSW 2041	Ph: Toll free1800 463928 Main switch: (02) 9555 8500 Telephone typewriter: (02) 9552 8534 Fax: (02) 9555-9049	gt@gt.nsw.gov.au
Office of the Public Guardian	NSW	Sydney office: Level 15, 133 Castlereagh St Sydney NSW 2000 Blacktown office: Level 2D, 15-17 Kildare Rd Blacktown NSW 2148 Gosford office: Suite 3, 40 Mann St Gosford NSW 2350	Sydney office: PO Box A231 Sydney South NSW 1235 DX 1335 Sydney Blacktown office: PO Box 168 Blacktown NSW 2148 DX 8132 Blacktown Gosford office: PO Box 487 Gosford NSW 2350 DX 7229 Gosford	Sydney office: Ph: (02) 9265 3184 Fax: (02) 9283 2645 Blacktown office: Ph: (02) 9671 9800 Fax: (02) 9671 9804 Gosford office: Ph: (02) 4320 4888 Fax: (02) 4320 4818	
The Office of the Adult Guardian	QLD	Level 3 Brisbane Magistrates Courts Complex 363 George Street Brisbane Qld 4000	PO Box 13554 George Street Brisbane Qld 4003	Ph: (07) 3234 0870 Outside Brisbane 1300 653 187 Fax: (07) 3239 6367	adult.guardian@justice.qld.gov.au

Guardianship and enduring powers of attorney *continued*

Guardianship and Administration Tribunal	QLD	Level 9 259 Queen Street Brisbane Qld 4000	GPO Box 1639 Brisbane Qld 4001	Ph: (07) 3234 0666 Outside Brisbane: 1300 780 666 Fax: (07) 3221 9156	guardianship@justice.qld.gov.au
Office of the Public Advocate	SA	Level 7, ABC Building 85 North East Road Collinswood 5082	Level 7, ABC Building 85 North East Road Collinswood SA 5081	Ph: (08) 8269 7575 Toll Free Number (for country South Australia only) 1800 066 969 Fax: (08) 8269 7490	OPA@agd.sa.gov.au
Guardianship Board	SA	Level 8, ABC Building 85 North East Road Collinswood 5082	Guardianship Board PO Box 138 Prospect SA 5082	Toll Free Number (for country South Australia Only) 1800 800 501 Ph: (08) 8368 5600 Fax: (08) 8368 5699	guardianshipboard@agd.sa.gov.au
Office of the Public Guardian	TAS	Level 3, 15 Murray Street Hobart Tas 7000	GPO Box 825 Hobart Tas 7001	Ph: (03) 6233 7608 Fax: (03) 6233 4882	public.guardian@info.tas.gov.au
Guardianship and Administration Board	TAS	First Floor 54 Victoria Street Hobart 7000	The Registrar Guardianship and Administration Board GPO Box 1307 Hobart Tas 7001	Ph: (03) 6233 3085 Fax: (03) 6233 4509 After hours emergency service: (03) 6233 3085	guardianship@justice.tas.gov.au
Victorian Civil and Administrative Tribunal	VIC	55 King Street, Melbourne, Victoria 3000, Australia DX 210576		Guardianship List: Tel- (03) 9628 9911 or 1800 133 055 Fax- (03) 9628 9932	vcat@vcat.vic.gov.au

Guardianship and enduring powers of attorney *continued*

Office of the Public Advocate	VIC	5th Floor 436 Lonsdale Street Melbourne Victoria 3000		Tel 1300 309 337 Fax (03) 9603 9501 TTY (03) 9603 9529 ACE 133677 (03) 9603 9500	publicadvocate@justice.vic.gov.au
Office of the Public Advocate	WA	Level 1 30 Terrace Road EAST PERTH WA 6004		Tel: (08) 9278 7300 Country Freecall: 1800 807 437 Fax: (08) 9278 7333	
State Administrative Tribunal.	WA	Level 4 12 St Georges Terrace PERTH WA 6000		Tel: (08) 9219 3111 or 1300 306 017 (for regional STD callers) Fax: (08) 9325 5099	

Contact and referral information

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The following list provides websites and phone numbers for a range of state, national and international organisations that will be useful to both clinicians and patients. For further details of HIV, sexual health and hepatitis C specialists and services, please consult the ***ASHM Directory***, available from the ASHM office and online at http://www.ashm.org.au/ashm-directory/

	WEBSITE	PHONE NUMBER
GENERAL CONTACTS		
Australasian Society for HIV Medicine (ASHM)	www.ashm.org.au	02 8204 0700
Australian Department of Health and Ageing (DoHA) (Population Health Division)	www.health.gov.au www.health.gov.au/pubhlth/	02 6289 1555
Ministry of Health – New Zealand	www.moh.govt.nz/moah.nsf	0011 64 496 2000
National Serology Reference Laboratory (NRL)	www.nrl.gov.au	03 9418 1111
PROFESSIONAL BODIES		
Australian College of Rural and Remote Medicine	www.acrrm.org.au	07 3105 8200
Australasian Society for HIV Medicine (ASHM)	www.ashm.org.au	02 8204 0700
Australasian Chapter of Sexual Health Medicine (AChSHM)	www.racp.edu.au	02 9256 9643
Gastroenterological Society of Australia (GESA)	www.gesa.org.au	02 9256 5454
Royal Australian College of General Practitioners (RACGP)	www.racgp.org.au	03 8699 0414 or 1800 331 626
Royal Australian College of Physicians (RACP)	www.racp.edu.au	02 9256 5444
Royal College of Nursing Australia	www.rcna.org.au	02 6283 3400 or 1800 061 660
Royal College of Pathologists of Australasia	www.rcpa.edu.au	02 8356 5858

INTERNET RESOURCES

Below is a selection of useful and interesting websites on HIV, hepatitis and sexually transmitted infections (STIs). This list is not intended to be exhaustive.

HIV: AUSTRALIAN

- **Australasian Society for HIV Medicine – www.ashm.org.au**
- **Australian Research Centre in Sex, Health and Society – www.latrobe.edu.au/arcshs/**
- **Macfarlane Burnet Institute for Medical Research and Public Health – www.burnet.edu.au**
- **National Association of People Living with HIV/AIDS, Australia (NAPWA) - www.napwa.org.au**
- **National Centre in HIV Epidemiology and Clinical Research – www.med.unsw.edu.au/nchecr/**
- **National Centre in HIV Social Research – www.arts.unsw.edu.au/nchsr**
- **Australian Centre for HIV and Hepatitis Virology Research – www.hiv.edu.au (formerly the National Centre for HIV Virology Research)**
- **The National Drug and Alcohol Research Centre (NDARC) – www.med.unsw.edu.au/ndarc/**
- **Australian Federation of AIDS Organisations (AFAO) – www.afao.org.au**
- **AIDS Council of NSW (ACON) – www.acon.org.au**
- **HIV/AIDS Legal Centre – www.halc.org.au**

HIV: AUSTRALIAN *CONTINUED*

- Queensland Association for Healthy Communities (QAHC) – www.qahc.org.au
- Victorian AIDS Council/Gay Men's Health Centre (VAC/GMHC) – www.vicaids.asn.au/content/default.asp
- Tasmanian Council on AIDS, Hepatitis and Related Diseases (tasCAHRD) – www.tascahrd.org.au
- The AIDS Council of South Australia (ACSA) – www.acsa.org.au
- Northern Territory AIDS and Hepatitis Council (NTAHC) – www.ntahc.org.au
- The Western Australian AIDS Council (WAAC) – www.waaids.com
- The AIDS Action Council of the ACT (AIDS Action Council) – http://aidsaction.org.au

HIV: INTERNATIONAL

- AEGiS (AIDS Education Global Information System) – www.aegis.com
- AIDSmap – www.aidsmap.com
- AIDS.ORG – www.aids.org
- The Body – ww.thebody.com/index.shtml
- HIVdent – www.hivdent.org
- HIVInSite – http://hivinsite.ucsf.edu/
- The Johns Hopkins AIDS Service – www.hopkins-aids.edu
- Liverpool HIV Pharmacology Group (LHPG) – www.hiv-druginteractions.org
- Medscape HIV/AIDS – www.medscape.com
- New Zealand AIDS Foundation – ww.nzaf.org.nz
- UNAIDS: The Joint United Nations Program on HIV/AIDS – www.unaids.org

HEPATITIS: AUSTRALIAN

- Australasian Society for HIV Medicine – www.ashm.org.au
- ACT Hepatitis C Council – www.acthepc.org
- Australia Liver Association – www.gesa.org.au/associations.cfm#Anchor-Australian-47857
- Digestive Health Foundation (DHF) – www.gesa.org.au/dhf-about.cfm
- Hepatitis Australia – www.hepatitisaustralia.com
- Hepatitis C Council of NSW – www.hepatitisc.org.au
- Hepatitis C Council of Queensland – www.hepatitisc.asn.au
- Northern Territory AIDS and Hepatitis Council – www.ntahc.org.au
- Hepatitis C Council of South Australia – www.hepccouncilsa.asn.au
- Tasmanian Council of AIDS, Hepatitis and Related Diseases (TasCAHRD) – www.tascahrd.org.au
- Hepatitis C Council of Victoria – www.hepcvic.org.au
- Hepatitis C Council of Western Australia – www.hepatitiswa.com.au
- Alcohol and Drug Information Service (ADIS) – www.dao.health.wa.gov.au/tabid/69/Default.aspx
- Reach Out – www.reachout.com.au
- Australian Injecting and Illicit Drug Users League (AIVL) – www.aivl.org.au
- Australian Drug Foundation – www.adf.org.au
- Multicultural HIV/AIDS and Hepatitis C Service – www.multiculturalhivhepc.net.au
- Gastroenterological Society of Australia (GESA) – www.gesa.org.au
- National Hepatitis B Alliance – www.alliance.hepatitis.org.au

HEPATITIS: INTERNATIONAL

- Hepatitis Foundation of New Zealand – www.hepfoundation.org.nz
- Hepatitis Resources Network (HRN) – www.h-r-n.org
- National Health and Medical Research Council, Australian Immunisation Handbook, available at: www.immunise.health.gov.au
- World Health Organization – www.who.int

STIs: AUSTRALIAN

- Australian Herpes Management Forum – www.ahmf.com.au
- Australian Indigenous Health Infonet – www.healthinfonet.ecu.edu.au
- Sexual Health and Family Planning Australia – www.shfpa.org.au
- HIV, Hepatitis and STI Education and Resource Centre – www.hivhepsti.info
- Health Insite – www.healthinsite.gov.au/topics/Sexually_Transmitted_Infections
- Melbourne Sexual Health Centre – www.mshc.org.au
- Queensland Health Sexual Health Information – www.health.qld.gov.au/sexhealth/
- Sydney Sexual Health Centre – www.sesahs.nsw.gov.au/sydhosp/SSHC.asp
- The South Eastern Centre Against Sexual Assault, Victoria – www.secasa.com.au

STIs: INTERNATIONAL

- American Social Health Association – www.ashastd.org
- British Association for Sexual Health and HIV (BASHH) – www.bashh.org
- Centers for Disease Control and Prevention, USA, Sexually Transmitted Diseases – www.cdc.gov/std/default.htm
- Health Canada Sexually Transmitted Infections – www.hc-sc.gc.ca/dc-ma/sti-its/index_e.html
- The New Zealand Sexual Health Society – www.nzshs.org/content/nzshs/home/2-20.htm

APPENDIX 1

Patient information – Natural history and transmission of HIV

What is HIV?	Human immunodeficiency virus (HIV) is the virus that causes AIDS.
What is AIDS?	Acquired immune deficiency syndrome (AIDS).
How does HIV affect people?	When a person first contracts HIV, a flu-like illness may occur. In most cases, without treatment, HIV slowly causes damage to the immune system. The body becomes less able to fight infection and illness. As HIV disease advances, a person may develop AIDS. An AIDS diagnosis generally means that the immune system is severely weakened and that life-threatening illnesses may occur. These illnesses include infections (e.g. pneumonia) and cancers. Recently, more effective treatments have become available. However, it is unknown whether these treatments can indefinitely delay the decline of the immune system. Before these treatments became available it took an average of 8–12 years after initial HIV infection for AIDS to develop.
How is HIV monitored?	Regular check-ups and blood tests are conducted to monitor the progress of the disease: • viral load indicates viral activity • CD4 cell count indicates extent of damage to the immune system.
How many people have HIV?	In Australia in 2006, 998 new HIV infections were reported, bringing the total number of people living with HIV nationwide to 16,675.
How is HIV transmitted?	HIV is present in certain bodily fluids of people with the infection (i.e. blood, semen, vaginal fluids and breast milk). It may be passed on by sexual contact, any activity that allows a bodily fluid to enter the blood stream via a break in the skin, or from mother to child. It is not passed on through normal household contact or by kissing.
How is HIV transmission prevented?	HIV transmission is significantly reduced by: • safe sex, which is any sexual activity that does not allow the transfer of one person's body fluids (blood, semen, vaginal fluid) into another. This means using condoms and water-based lubricants for any vaginal or anal intercourse and avoiding oral sex if there are cuts or sores on the genitals or in the mouth. If sex toys are to shared, they should be covered by a condom (Chapter 3) • safe injecting using only sterile equipment (needles, syringes, swabs, spoons, filters, tourniquets and water) to inject each time or thoroughly cleaning equipment where this is not possible. Alternatively, drugs can be smoked, snorted or swallowed (Chapter 3 and Appendix 4) • interventions during pregnancy and labour, and avoidance of breast-feeding • standard precautions (Chapter 13).

APPENDIX 2

Patient information – Natural history and transmission of HBV

What is HBV?	Hepatitis B virus (HBV) is a blood-borne virus that can cause hepatitis. Hepatitis means inflammation of the liver.
What does the liver do?	The liver is the second largest organ and plays an important role in many vital functions of the body. Some of the liver's many functions include: • acting as a filter to remove alcohol and other toxic substances from the body • processing and clearing drugs and medications • manufacturing the many chemical substances needed by the body.
How does HBV affect people?	When someone has HBV infection, his or her body produces tiny proteins called antibodies in an attempt to eliminate the virus. During the first 45–180 days (six weeks to six months), the person may feel slightly ill or off-colour and develop joint pains. Sometimes people with HBV develop typical symptoms of hepatitis (fatigue, yellowed skin or eyes). A very small number of people die within the first few weeks or months of hepatitis B infection. Most adults completely recover from hepatitis B infections, while most babies with the infection (children under one year of age) will develop chronic HBV infection. The appearance of particular antibodies is thought to indicate that HBV is eliminated from the body. Around 2–4% of adults with HBV infection develop chronic infection which can last for several decades. Chronic hepatitis B infection causes no symptoms in many people, but some will develop long-term liver inflammation, liver scarring and liver cancer. This can take decades to develop. The symptoms are mild for many people. However, for a minority of people, hepatitis B may be quite debilitating.
How many people have HBV?	There are no exact records of how many people are infected with HBV in Australia. However, it has been estimated that 0.5% of the population (100,000) is chronically infected. It is estimated that 50% of these cases are migrants from endemic HBV regions such as Asia. This rate is also higher among men who have sex with men and injecting drug users. Around 1–2% of people from Mediterranean countries, parts of Eastern Europe, and the former USSR have chronic HBV infection. This is as high as 10% in some Indigenous Australian, central African and South East and East Asian populations. First generation immigrants usually have similar rates to those of their country of origin.
How do people know what is happening to their liver?	A liver function test monitors the level of liver enzymes in the blood. If there is damage to liver cells, these levels may be raised. Liver function tests are often a poor indicator of illness outcome. People who want a more detailed and reliable indication of liver damage should consider a liver biopsy. This is a procedure where a small amount of liver tissue is taken using a needle.
How is HBV transmitted?	Transmission of the virus may occur following exposure of non-intact skin or mucous membranes to infected blood or, less efficiently, after exposure to infected body fluids. Transmission can occur through sexual contact (semen or vaginal secretions), the use of contaminated objects that pierce the skin (e.g. injecting drug use, tattooing, razorblades or acupuncture equipment) or the sharing of toothbrushes. If saliva that contains HBV pierces the skin or mucous membrane (e.g. by biting), transmission may occur. Mother-to-child transmission commonly occurs if vaccination and immunoglobulin are not administered.
How is HBV transmission prevented?	HBV is prevented through vaccination. HBV immunoglobulin is recommended for newborn infants of mothers with the infection, and vaccine for health care workers and high risk groups such as injecting drug users and men who have sex with men. In addition, the risk of HBV transmission is reduced by: • practising safe sex (Chapter 3) • safe injecting practices (Chapter 3 and Appendix 4) • avoiding sharing and reusing contaminated objects that pierce the skin • standard infection control precautions (Chapter 13)

APPENDIX 3

Patient information – Natural history and transmission of HCV

What is HCV?	Hepatitis C virus (HCV) is a blood-borne virus that can cause hepatitis. Hepatitis means inflammation of the liver.
What does the liver do?	The liver is the second largest organ and plays an important role in many vital functions of the body. Some of the liver's many functions include: • acting as a filter to remove alcohol and other toxic substances from the body • processing and clearing drugs and medications • manufacturing the many chemical substances needed by the body
How does HCV affect people?	When someone gets the HCV infection, his or her body produces tiny proteins called antibodies in an attempt to eliminate the virus. During the first 2–8 weeks, the person may feel slightly ill or off-colour. Typical hepatitis symptoms (fatigue, yellowed skin or eyes) are uncommon with initial HCV infection. In approximately 75% of initial hepatitis C infections, antibodies do not eliminate the hepatitis C virus. When the virus is not eliminated, HCV infection is ongoing. This is called 'chronic hepatitis C'. Most people eventually develop some signs of hepatitis C illness—usually after ten years or so. The symptoms are mild for many people. However, for a minority of people, hepatitis C may be quite debilitating. The exact nature and timing of short-term and long-term consequences of HCV infection are not clear. The most commonly reported signs of hepatitis C illness are fatigue or pain in the upper right side of the abdomen. Only one person in five develops severe scarring of the liver or cirrhosis. If it occurs, cirrhosis usually takes 20–40 years to develop. Less than one in ten people develop liver failure or liver cancer. These conditions usually take 20–40 years to develop. In a small proportion of people, the virus can cause problems in parts of the body other than the liver, such as the joints, skin and kidneys.
How many people have HCV ?	It is estimated that: • approximately 1–2 in every 100 Australians are infected with HCV • 80% of Australians infected with HCV acquired the virus through injecting drug use • 5–10% of Australians living with HCV acquired the virus through transfusion of blood and blood products between the 1970s and 1980s • 10–15% of Australians infected with HCV are from culturally and linguistically diverse backgrounds
How do people know what is happening to their liver?	A liver function test monitors the level of liver enzymes in the blood. If there is damage to liver cells, these levels may be raised. Liver function tests are often a poor indicator of illness outcome. People who want a more detailed and reliable indication of liver damage should consider a liver biopsy. This is a procedure where a small amount of liver tissue is taken using a needle.
How is HCV transmitted?	HCV is spread through infected blood entering someone else's bloodstream (e.g. by sharing and reusing contaminated syringes and other injecting equipment, non-sterile tattooing or piercing, and non-sterile medical procedures). Mother-to-child transmission occurs in less than 5% of cases. Sexual transmission of HCV is regarded as very rare, although anal penetration or the presence of blood may increase the risk of sexual transmission.
How is HCV transmission prevented?	The risk of HCV transmission is reduced by: • safe injecting practices (Chapter 3 and Appendix 4) • avoiding sharing and reusing contaminated objects that pierce the skin • standard infection control precautions (Chapter 13) • practising safe sex.

Appendices 1–3 written by Katherine Fethers et al, authors of Chapter 9.

APPENDIX 4

Safer injecting and cleaning injecting equipment

The sharing of injecting equipment is the single greatest risk factor for contracting hepatitis C virus (HCV) among those who inject drugs. There are options other than injecting drugs, such as smoking, snorting or swallowing drugs, which will significantly reduce the risk of contracting HCV, human immunodeficiency virus (HIV) and other blood-borne viruses. If snorting is the alternative mode of administration, the sharing of straws is not recommended due to a low risk of HCV transmission.

Injecting with sterile equipment	For people who do choose to inject drugs, transmission can be prevented through the exclusive use of sterile fits (needle and syringe), water and swabs (one to swab the spoon and one to swab the arm), clean filters, a clean and detachable tourniquet, and clean hands. The injecting space should also be clean and all blood contact avoided. Sterile equipment is equipment that has undergone a process that destroys viruses, bacteria and germs. Sterile injecting equipment includes pre-packaged fits, water and swabs, that are marked as sterile. All other equipment needs to be cleaned with soap and water or with a swab. Table 3.4 describes safe injecting procedures in detail. There is no way of eliminating the risk of viral transmission from used syringes. If patients seek advice about re-using injecting equipment, the need for sterile equipment must be reiterated.
Using cleaned injecting equipment	People who decide to inject with a used fit must be advised that they risk becoming equipment infected with HIV, hepatitis B virus (HBV) and HCV. In addition, they should be advised that: • using your own fit will be safer than a fit used by another person • the more thoroughly a fit is cleaned, the less risk of infection • cleaning is important for people who are already infected with a blood-borne virus infection because they can be re-infected with another strain of HCV, HBV or HIV. Re-infection with another strain of HCV or another hepatitis virus may place added strain on the liver.
How to clean injecting equipment	The following are directions on how to clean used injecting equipment. A clean workspace equipment and a safe area for fluid disposal (sink, bin, drain etc) are required. Wash your hands before you begin.
1. Equipment	Three separate containers filled with: **a.** Clean water from the cold tap, for rinsing the blood out of your fit. Use water from the cold tap – preferably soapy water. This is best for rinsing out blood because water that is too hot or too cold can cause the blood to congeal and stick inside the fit, where it can shed microscopic particles into your mix. **b.** Full strength bleach for soaking and bleaching your fit (5.25% sodium hypochlorite). **c.** Clean water from the cold tap to rinse the bleach from your fit.
2. Cleaning process	**a. Rinsing:** • Rinse the fit in clean water from the cold tap from the first container. • Squirt the water out into your sink or safe fluid disposal area. • Repeat until you cannot see any traces of blood. **b. Bleaching:** • Use full strength bleach (at least 5.25% sodium hypochlorite and check the use-by date). • Take the fit apart. • Soak it completely, covering it with bleach for at least two minutes. **If you can't soak:** • Draw the bleach into the fit and shake it for at least thirty seconds (or while you count slowly to 30). • Squirt the bleach out into your sink or safe disposal area. • Repeat the process at least once, again counting slowly to thirty (as above). **c. Flushing:** • Draw up fresh water from the third container. • Do NOT use water from the FIRST container as this has been contaminated with blood. • Squirt, flushing the water into the safe fluid disposal area or sink. • Repeat flushing process until all the bleach has been removed. • FLUSH AT LEAST SIX TIMES.

APPENDIX 4 - CONTINUED

3. When you have cleaned your fit follow the guidelines for safer injecting (References 5 and 6 in Chapter 3)

4. Some handy hints for being 'blood aware'	• Stock up on equipment so you won't be caught short. • Make sure the surface where you prepare your hit is clean. • Wash your hands with warm soapy water before and after injecting. This will remove any traces of blood from your fingers, as well as any unhygienic dirt. • No matter how well-cleaned, never let your used equipment, or anyone else's used equipment, come into contact with a group mix. Unless sterile fits are used to mix and divide up, then each member of the group must have their own water, spoon and filter (as well as their own fit). • If someone is going to help you inject, make sure they wash their hands before and after. • It is best to have your own tourniquet that you don't share. Try not to get blood on your tourniquet. Detachable (medical) tourniquets will make this easier. • Rinse your fit in clean water from the cold tap immediately after your hit, even if you are disposing of it. This will remove most of the blood that is present, and therefore reduce the chance of a virus staying alive in your fit. It will also prevent it from blocking, and help reduce the likelihood of 'dirty hits' if you have to use the fit again. • If you are going to save your fit for personal re-use, keep track of it (mark it), and keep it safe. • Wash or swab your spoon after each hit, and wash your tourniquet with soapy water as soon as possible to remove blood spills. • Always dispose of fits safely, in an approved disposal bin, sharps container or childproof, puncture-proof container. Whenever possible, return sharps containers/used fits to your local needle and syringe program. • Do not reuse swabs, filters or opened sterile water: they become contaminated with bacteria and fungi when exposed to air. Dispose of them in the recommended sharps container you have used to dispose of your used fits, or place inside two plastic bags (double bagging). Return your sharps container to your local needle and syringe program. If it is not possible to return your used fits to a needle and syringe program, you can place the sealed container into the rubbish bin. • Also dispose of blood-contaminated materials as above. If you get blood on your clothes, etc. throw them straight into the wash with a good measure of washing powder.

Appendix 4 adapted from: Australian Injecting and Illicit Drug Users League. Cleaning Fits. Canberra: National Hepatitis C Education and Prevention Program, Australian National Council on HIV/AIDS and Related Diseases; 2001.

APPENDIX 5

State and Territory Departments of Health blood-borne virus and sexually transmitted infection notification requirements

Infection	QLD	NSW	ACT	VIC	WA	NT	TAS	SA
HIV and AIDS	HIV is notifiable by laboratories and doctors on positive result AIDS is notifiable by clinical diagnosis	HIV is notifiable by laboratories on positive result AIDS is notifiable by clinical diagnosis	HIV is notifiable by laboratories and doctors on positive result AIDS is notifiable by clinical diagnosis	HIV is notifiable by laboratories and doctors on positive result AIDS is notifiable by clinical diagnosis	HIV is notifiable by laboratories and doctors on positive result. AIDS is notifiable by clinical diagnosis	HIV is notifiable by laboratories only AIDS is notifiable by clinical diagnosis	HIV is notifiable by laboratories only AIDS is notifiable by clinical diagnosis	HIV is notifiable by laboratories and doctors on positive result AIDS is notifiable by clinical diagnosis
HCV	HCV is a controlled notifiable condition which is notifiable by laboratories/ doctors on positive result	Acute viral hepatitis is notifiable by medical practitioners. HCV notifiable by laboratories	Notifiable – 2 categories: newly acquired and unspecified by laboratories and doctors	Written notification within five days of the initial diagnosis, by laboratories and doctors	Notifiable – 2 categories: newly acquired and unspecified by laboratories and doctors	Notifiable – 2 categories: newly acquired and unspecified by laboratories and doctors	Notifiable – 2 categories: newly acquired and unspecified by laboratories	Notifiable by laboratories and doctors
HBV	Acute and chronic notifiable by laboratories/ doctors on positive result	Acute viral hepatitis is notifiable by laboratories and doctors	Notifiable – 2 categories: newly acquired and unspecified by laboratories and doctors	Written notification within five days of the initial diagnosis, by laboratories and doctors	Notifiable – 2 categories: newly acquired and unspecified by laboratories and doctors	Notifiable – 2 categories: newly acquired and unspecified by laboratories and doctors	Notifiable – 2 categories: newly acquired and unspecified by laboratories	Notifiable by laboratories and doctors
HPV	Not notifiable	Not notifiable	Not notifiable	Not notifiable	Not Notifiable	Not notifiable	Not notifiable	Not notifiable
HSV	Not notifiable	Not notifiable	Not notifiable	Not notifiable	Not Notifiable	Not notifiable	Not notifiable	Not notifiable
Syphilis	Including congenital. A controlled notifiable condition notifiable by laboratories/ doctors on positive result	Notifiable by laboratories and doctors	Notifiable – 2 categories; <2 year duration or > 2 year duration or unspecified duration by laboratories and doctors	Written notification within five days of the initial diagnosis, by laboratories and doctors	Notifiable – 2 categories: infectious and non-infectious by laboratories and doctors	Notifiable – 2 categories: infectious and non-infectious by laboratories and doctors	Notifiable – 2 categories: infectious and non-infectious by laboratories	Notifiable by laboratories and doctors
Gonorrhoea	Notifiable by laboratories/ doctors on positive result	Notifiable by laboratories	Notifiable by laboratories and doctors	Written notification within five days of the initial diagnosis, by laboratories and doctors	Notifiable by laboratories and doctors	Notifiable by laboratories only	Notifiable by laboratories only	Notifiable by laboratories and doctors
Chlamydia	Notifiable by laboratories/ doctors on positive result	Notifiable by laboratories	Notifiable by laboratories and doctors	Written notification within five days of the initial diagnosis, by laboratories and doctors	Notifiable by laboratories and doctors	Notifiable by laboratories only	Notifiable by laboratories only	Notifiable by laboratories and doctors
Trichomoniasis	Not notifiable	Not notifiable	Not Notifiable	Not notifiable	Not notifiable	Notifiable by laboratories only	Not notifiable	Not notifiable

Glossary of terms

Ab	antibody
AChSHM	Australasian Chapter of Sexual Health Medicine of the RACP
ACRRM	Australian College of Rural and Remote Medicine
AFAO	Australian Federation of AIDS Organisations
Ag	antigen
AHC	Australian Hepatitis Council
AIDS	Acquired Immune Deficiency Syndrome
AIVL	Australian Injecting and Illicit Drug Users League
ALA	Australian Liver Association
ALT	alanine aminotransferase or alanine transaminase
ANA	antinuclear antibody
ANCAHRD	Australian National Council on AIDS, Hepatitis C and Related Diseases (obsolete; now replaced by MACASHH)
Anilingus	oro-anal sex
Anoscopy	inspection of anal canal and rectal lining through a (usually) disposable instrument called an anoscope (also called proctoscopy)
Anti-HAV IgM	antibody to HAV IgM - signifies recent exposure to HAV
Anti-HAV IgG	antibody to HAV IgG - signifies past exposure to HAV or successful vaccination
Anti-HBc IgM	antibody to hepatitis B core antigen - signifies recent exposure to HBV
Anti-HBc IgG	antibody to hepatitis B core antigen - signifies past exposure to HBV
Anti-HBe	antibody to hepatitis Be antigen
Anti-HBs	antibody to hepatitis B surface antigen - associated with non-replicative phase or successful vaccination
Anti-HCV	antibody for HCV - indicates infection with HCV has occurred
Anti-HDV IgG and IgM	antibody to the hepatitis D virus
APTT	activated partial thromboplastin time
ARV	antiretroviral therapy
ASHM	Australasian Society for HIV Medicine
AST	aspartate aminotransferase
B-cell	a type of immune cell
Balinitis	inflammation of the glans penis
Balinoposthitis	inflammation of the glans penis and the prepuce (foreskin)
BBV	blood-borne virus
BCG	Bacille Calmette-Guerin (tuberculosis vaccine)
Bd, bid	twice daily
b-DNA	branched deoxyribonucleic acid
Beats	public toilets, parks and other outdoor venues where MSM 'beat a path' looking for sexual partners

BV	bacterial vaginosis, a common complex syndrome resulting in a change in the vaginal ecosystem with raised vaginal pH; often asymptomatic but sometimes associated with an abnormal vaginal discharge
CAH	chronic active hepatitis
CALD	culturally and linguistically diverse
C & S	culture and sensitivity
CCR5	chemokine co-receptor on the surface of cells which may be used in HIV-cell fusion
CD4 cell	a helper T-cell which carries the CD4 surface antigen. CD4 cells are the primary target of HIV and CD4 cell numbers decline during HIV disease
CD8 cell	a killer or cytotoxic T-cell which carries the CD8 surface antigen
Chancre	the painless ulcer of primary syphilis
Chancroid	a tropical STI caused by Haemophilus ducreyi, virtually never seen in Australia or New Zealand
CHAP smear	ano-rectal cytology for HPV in MSM
Chlamydia	a sexually transmitted infection caused by *Chlamydia trachomatis*
Circumcision	removal of the prepuce (foreskin)
Clue cells	vaginal epithelial cells with bacteria adhering to the surface and partially obscuring the borders, characteristic of bacterial vaginosis microscopically
CMV	cytomegalovirus
CNC	clinical nurse consultant
Condylomata acuminata	genital warts
Condylomata lata	moist warty growths occurring in perineum in secondary syphilis
Contact tracing	the following up, diagnosis and (where possible) treatment of all sexual partners of a patient infected with an STI. Also called 'partner notification'
Crabs	see pubic lice
Cunnilingus	oral sex - mouth to vulva
DG	disseminated gonococcal infection
Dipping	vaginal or anal sex without a condom for varying periods of time prior to ejaculation, i.e. the condom is only applied when the insertive partner is getting near ejaculation
DNA	deoxyribonucleic acid
DoHA	Commonwealth Department of Health and Ageing
Donovanosis	a rare STI of great chronicity causing considerable destruction of genital structures if untreated. Seen only in remote Indigenous communities in Australia
EBV	Epstein Barr virus
EIA	enzyme immunoassay; an immunoassay in which an enzyme, such as a peroxidase, is used as a marker to indicate the presence of specific antigens or antibodies, (as in treponemal EIA, a specific serological test for syphilis)
ELISA	enzyme linked immunosorbent assay
Epididymo-orchitis	inflammation of epididymis primarily, spreading secondarily to testis
FBC	full blood count
FCU	first catch specimen of urine
Fellatio	oral sex – mouth to penis
Fisting	sexual act where fist and forearm are inserted into vagina or ano-rectum
Fitz-Hugh Curtis syndrome	transcoelomic spread of pelvic infection with *Chlamydia trachomatis* or *Neisseria gonorrhoeae* to the liver surface causing a perihepatitis
Fomites	materials (e.g. towels, sheets etc) which, once contaminated with a microbiological or virological agent, allow transmission of that infection to another individual
FTA-ABS	fluorescent treponemal antibody absorbed serology test, a specific serological test for syphilis

Genital herpes	infection of ano-genital region with sexually transmitted HSV-1 or HSV-2
Genital warts	exophytic clinical manifestation of sexually transmitted ano-genital HPV infection
GESA	Gastroenterological Society of Australia
GGT	gamma glutamyltransferase
GI	gastrointestinal
GIT	gastrointestinal tract
Gonorrhoea	a sexually transmitted infection caused by *Neisseria gonorrhoeae*
GP	general practitioner
gp120	glycoprotein on the surface of HIV which binds to the CD4 receptor
gp41	glycoprotein on the surface of HIV involved in fusion between HIV and the CD4 cell
GUD	(ano)-genital ulcerative disease
HAART	highly active antiretroviral therapy
HASTI	HIV/AIDS and Sexually Transmissible Infections Subcommittee of the Ministerial Advisory Committee on AIDS, Sexual Health and Hepatitis
HAV	hepatitis A virus
HAVAb	hepatitis A antibody test (IgM or IgG)
HBcAb	see anti-HBc
HBcAg	hepatitis B core antigen
HBeAb	see anti-HBe
HBeAg	HBV 'e' antigen - a marker of viral replication and infectivity
HBIG	hepatitis B immunoglobulin
HBsAg	hepatitis B surface antigen - a marker of current infection which persists in individuals who become carriers
HBsAb	see anti-HBs
HBV	hepatitis B virus
HCC	hepatocellular carcinoma
HCV	hepatitis C virus
HDV	hepatitis D virus
HHV-8	human herpesvirus-8 - associated with Kaposi's sarcoma
HIV	human immunodeficiency virus
HPV	human papillomavirus
HSIL	high grade squamous intraepithelial lesion
HSV	herpes simplex virus
HVS	high vaginal swab
Hydrocoele	scrotal swelling caused by accumulation of fluid around the testis, between the serosal layers of the tunica vaginalis
IASHC	Indigenous Australians' Sexual Health Subcommittee of the Ministerial Advisory Committee on AIDS, Sexual Health and Hepatitis
IDU	injecting drug user
IFN	interferon
Ig	immunoglobulin
INR	international normalised ratio - a test of blood clotting
IV	intravenous
IU	international unit (measurement)

KS	Kaposi's sarcoma
Latency	the situation where an infection enters a quiescent asymptomatic phase and is only detectable by appropriate testing
LCR	ligase chain reaction - a NAAT
LFT	liver function test
LGV	lymphogranuloma venereum - a tropical STI caused by *Chlamydia trachomatis* serovars L1–L3, now becoming endemic amongst highly sexually active MSM
LKM	liver kidney microsomal
LSIL	low grade squamous intraepithelial lesion
MAC	Mycobacterium avium complex
MACASHH	Ministerial Advisory Committee on AIDS, Sexual Health and Hepatitis
MAI	Mycobacterium avium intracellulare
µl	microlitre
ml	millilitre
mmol	millimole
MSM	men who have sex with men - a rather unsatisfactory but widely used term to describe all men who ever have sex (of any type) with another man
MSSU	midstream specimen of urine
NAAT	nucleic acid amplification test
NAPWA	National Association of People Living with AIDS
NCHECR	National Centre in HIV Epidemiology and Clinical Research
NHMRC	National Health and Medical Research Council
NNRTI	non-nucleoside reverse transcriptase inhibitor
NPEP	non-occupational post-exposure prophylaxis
NRTI	nucleoside analogue reverse transcriptase inhibitor
NSU	non specific urethritis - urethritis where exhaustive laboratory testing fails to find a specific cause (a non gonococcal, non chlamydial, non herpetic, non trichomonal etc urethritis)
OCP	ova, cysts and parasites - looked for on microscopy of faecal specimens
OI	opportunistic infection
Oral sex	use of the mouth in sexual activity (i.e. anilingus, cunnilingus or fellatio)
p24	a core HIV protein, the primary protein detected by the HIV antigen test which is incorporated with the HIV antibody test in Australia
Partner notification	see contact tracing
Pathogenicity	the ability of a micro-organism to cause disease in its host
PBS	Pharmaceutical Benefits Scheme
PCP	Pneumocystis jiroveci pneumonia
PCR	polymerase chain reaction, a NAAT
PCT	porphyria cutanea tarda
PEP	post-exposure prophylaxis
pg/ml	picogram per millilitre
PHI	primary HIV infection
PI	protease inhibitor
PID	pelvic inflammatory disease
Pili	hair like appendages found on the surface of some bacteria (especially *Neisseria gonorrhoeae*)
PML	progressive multifocal leucoencephalopathy

Prepuce	foreskin
Proctitis	inflammation of rectal mucosa
Proctoscopy	inspection of the rectal mucosa through a (usually) disposable instrument called a proctoscope (also called anoscopy)
Pubic lice	an infestation of body and pubic hair caused by Pthirus pubis, usually sexually transmitted in adults
Qd	once daily
Qds, qid	four times daily
RACGP	Royal Australian College of General Practitioners
RACP	Royal Australasian College of Physicians
RF	rheumatoid factor
Rimming	anilingus, oro-anal sex
RNA	ribonucleic acid
RPR	rapid plasma reagin test - a non-specific quantitated serological test for syphilis
RT	reverse transcriptase
Salpingitis	inflammation of a Fallopian tube - a component of PID
SBP	spontaneous bacterial peritonitis
Scabies	skin infestation caused by Sarcoptes scabiei, often sexually transmitted in adults
Screening	testing for the presence of an asymptomatic condition in an apparently healthy individual
SDA	strand displacement amplification assay - a NAAT
Section 100	a section of the Pharmaceutical Benefits Scheme which provides access to highly specialised drugs
Seroconversion	process whereby a serological test for a given microbiological or virological agent changes from non-reactive to reactive, coinciding with recent infection
Serology	diagnostic identification of antibodies (usually), sometimes antigens, in serum
Serovar	group of closely related microorganisms distinguished by a characteristic set of antigens
Sexually transmitted infection (STI)	any infection which is mainly transmitted from one individual to another by sexual activity (e.g. all the usually accepted STIs such as syphilis, gonorrhoea and genital herpes)
Sexually transmissible infection (STI)	any infection which is capable of being transmitted from one individual to another by sexual activity given suitable circumstances (e.g. enteric infection during oro-anal sexual contact)
SI	squamous intraepithelial
SMA	smooth muscle antibody
SOPVs	sex on premises venues, such as saunas and sex clubs frequented by MSM
Spirochaete	family of motile, spiral shaped gram negative bacteria of which *Treponema pallidum* is the best known
SSRI	selective serotonin re-uptake inhibitors
STD	sexually transmitted disease - a term now largely replaced by the more accurate term STI
STI	sexually transmissible infection or sexually transmitted infection (see above)
SVR	sustained virological response (negative HCV RNA and normal ALT six months after completion of therapy for HCV)
Syndromic management	the approach of treating STI symptoms and signs based on the organisms most commonly responsible for each syndrome (WHO definition)
Syphilis	a sexually transmitted infection caused by *Treponema pallidum*
T-cell	white blood cell or lymphocyte
Td, tds, tid	three times daily
TMA	transcription mediated assay - a NAAT

TPHA	*Treponema pallidum* haemagglutination assay - a largely superseded specific serological test for syphilis
TPPA	*Treponema pallidum* particle agglutination - a specific serological test for syphilis
Transmission	
- horizontal	transmission of an infection from person to person in the community
- vertical	transmission of an infection from mother to foetus or infant
Trichomoniasis	a sexually transmitted infection causing vaginitis and urethritis
U & E	urea and electrolytes
VVC	vulvo-vaginal candidiasis
VZV	varicella zoster virus
WHO	World Health Organization
WSW	women who have sex with women - a rather unsatisfactory term used to describe all women who ever have sex (of any type) with another woman

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ASHM RESOURCES

ASHM produces a range of HIV and Viral hepatitis related resources, available in electronic and hard copy format for health care professionals. Resources may be downloaded directly from the ASHM website at www.ashm.org.au or ordered by contacting the ASHM office on +**61 2 8204 0700** or email **resources@ashm.org.au .**

PUBLICATIONS:

Monographs

- HIV Management in Australasia: a guide for clinical care
- HIV, Viral Hepatitis and STIs: a guide for primary care
- Coinfection HIV and Viral Hepatitis: a guide for clinical management
- Testing, trials and re-thinking human rights: reflections from the HIV pandemic
- HIV and hepatitis C: policy, discrimination, legal and ethical issues
- Australasian Contact Tracing Manual Ed 3

Patient Fact Sheet (including priority language translations)

- HIV patient fact sheet (available online only)
- Hep C in Brief

Journal Supplements

- General Practitioners and Hepatitis C
- Nurses and Hepatitis C
- Dental Health and Hepatitis C
- Prehospital Care Workers and Blood-borne Viruses

Distance-Learning Resources

- Clinical Science of HIV Medicine. ASHM Short Course in HIV Medicine: Module 1
- 'Talking Together': contemporary issues in Aboriginal and Torres Strait Islander health: HIV, hepatitis and sexual health

Online Resources:

- Australian HIV Models of Care database
- Australian commentary on the US DHHS Guidelines for the use of Antiretroviral Agents in HIV-1 infected adults and adolescents
- ASHM Directory: HIV, hepatitis and related services

To place an order for ashm resources, please visit:

www.ashm.org.au/resource-order-form

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