HIV / Viral hepatitis

a guide for primary care

ashm
Australasian Society for HIV Medicine Inc

REVISED EDITION

About ASHM

The Australasian Society for HIV Medicine is the peak representative professional body for medical practitioners and other health care workers in Australasia who work in HIV 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.

The Society is a key partner in the Australian response to HIV, hepatitis and related diseases. It works closely with government, advisory bodies, community agencies and other professional organisations. It conducts a broad Education Program in HIV and viral hepatitis for medical practitioners, health care providers and allied health workers and manages programs of continuing medical education in HIV and viral hepatitis.

ASHM is governed by an elected voluntary board and managed by a small secretariat. It receives support from the Commonwealth Department of Health and Ageing, State and Territory Departments of Health and the pharmaceutical industry. ASHM convenes standing committees on a range of issues affecting its members including education, HIV treatment, viral hepatitis, international/development issues and professional affairs.

Benefits of ASHM membership:

- *Journal Club*, a bi-monthly publication reviewing relevant international journal articles, is mailed to members and is available on the website: www.ashm.org.au
- *ASHMNews*, the members' newsletter, is mailed to members every second month and is also available on the website.
- *The ASHM Directory of HIV, hepatitis and related services* is designed as a desktop compendium of useful contacts. It is released in print form in June/July each year. The Directory is on the website and updated regularly.
- The ASHM annual conference provides a timely forum for information exchange from the medical, scientific and community sectors.
- ASHM members receive a discount on conference registration, educational resources and registration in the continuing medical education activities. Some educational resources are free.
- Members involved in education or teaching activities can access resources from the Society.
- ASHM holds report-back sessions from major conferences around the world for members and makes these available through the website and/or on CD or printed format.
- Members can also enjoy a reduced subscription to *HIV Medicine*, ASHM's refereed journal, published by the British HIV Association and the European AIDS Clinical Society.
- By maintaining a comprehensive database of its members' interests, ASHM can alert its members to specific issues and promote various activities to them.

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HIV / Viral hepatitis

a guide for primary care

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Preface

HIV/Viral hepatitis: a guide for primary care was conceived 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 has been to produce a practical manual for risk assessment, testing, diagnosis and basic principles of management of HIV and viral hepatitis, by reviewing epidemiology, transmission, virology, history-taking, signs and symptoms, assessment and primary care management of these chronic viral conditions.

The primary audience for this monograph is intended to be clinicians who test for HIV and viral hepatitis and those who provide non-specialist care for infected patients. Physicians, medical students, nurses, allied health professionals, as well as individuals with a specific interest in these conditions, may also find *HIV/Viral hepatitis* useful.

HIV/Viral hepatitis elucidates key differences and similarities in the assessment, diagnosis and management of infections due to HIV, hepatitis B virus (HBV) and hepatitis C virus (HCV). The second edition of the monograph builds on the first, by utilising its strengths, and updating information in many of the chapters. Risk assessment and testing for HIV, HBV and HCV are often conducted together, because their patterns of transmission overlap. There also may be overlapping clinical management issues, for example in relation to sexually transmissible infections, management of fatigue or of other symptoms associated with chronic viral infections or patients with drug and alcohol dependence. In addition, the stigma associated with infection with one or more of these viruses has a bearing on psychosocial and legal issues.

The incorporation of viral hepatitis into an ASHM publication was a substantial change of direction. It reflects the trend in public policy and medical practice towards locating HIV/AIDS within the broader public and sexual health context. Also it 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*, in line with the priorities delineated in the National Hepatitis C Strategy and the National HIV/AIDS 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 diagnosis, management and referral of patients. It is hoped that *HIV/Viral hepatitis* will facilitate closer working relationships between general practitioners, specialists 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 the first and this revised, second edition 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 Australian College of Rural and Remote Medicine, the Australian Federation of AIDS Organisations, the National Association of People Living with AIDS and the Australian Hepatitis Council.

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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 (page 5) who contributed ideas and information to the project.

We would also like to acknowledge the contribution of Jenny Hoy's co-editors Greg Dore, Andrew Grulich, Michael Kidd, Ron McCoy, Anne Mijch and Simone Strasser, and ASHM project staff Julie Letts, Megan Nicholson, Vanessa Sparrow, and Vicky Fisher who has overseen the second edition of this monograph.

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HIV, HBV, HCV: similarities and differences

1

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Introduction

The three major blood-borne viruses (BBV), human immunodeficiency virus (HIV), hepatitis B virus (HBV) and hepatitis C virus (HCV), are members of different virus families but share one thing in common: their major mode of transmission is via blood or bodily fluids. This chapter compares the three agents, specifically focusing on their virology, 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.

Virology

HIV

The manifestations of HIV were first apparent in the early 1980s when an epidemic of unexplained cases of immunodeficiency was recognised 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 gp120 attaches to the CD4 receptor and the chemokine co-receptor CCR5. (These receptors are expressed on the surface of the CD4 lymphocyte, the cell HIV predominantly infects.) Attachment precipitates the fusion of the

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.
- 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.
- 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.
- 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.

membranes of virus and cell via the HIV envelope glycoprotein gp41, allowing the virus to enter the cell. The RNA then undergoes reverse transcription, a process whereby RNA is converted to deoxyribonucleic acid, or 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.[1]

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 surface antigen (HBsAg) and a core containing core antigen (HBcAg). Excess HBsAg is produced as sub-viral particles which circulate in the blood and permit convenient 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 '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-positive (anti-HBe+) and anti-HBs-positive (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 lifecycle 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.[2]

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 not yet 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.

Quasispecies and hypermutability

The replicase enzymes of all three viruses, the HIV reverse transcriptase, the HBV DNA polymerase and the HCV RNA polymerase, are hypermutatable. Mutation, particularly under immunological and/or 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.[3]

Transmission

While each 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.

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 United States. 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 in 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 can be reduced to less than 5% with the administration of antiretroviral therapy during pregnancy, labour and after delivery, and other interventions, such as caesarean section and avoidance of breast-feeding.[4] In Australia there have been 19,674 new diagnoses of HIV infection, with 9,083 cases of AIDS by the end of 2002 and 6,272 cases of AIDS-related deaths.[5]

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 HBsAg+ 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 the HBV carrier state has been estimated to be 160,000 to 200,000. The risk of transmission by percutaneous exposure such as a needle-stick injury is approximately 30% if the carrier has replicative disease (HBV DNA+ by hybridization assay or HBsAg+), compared with 3% for carriers with non-replicative disease (that is, people without HBeAg or HBV DNA).[2]

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 reported as the predominant risk factor in over 90% of the estimated 16,000 annual incident cases.[6] Among particular immigrant populations, poor infection-control practices during procedures such as vaccination (European- and Asian-acquired) and chemoprophylaxis programs for schistosomiasis (Egyptian-acquired) may have been responsible for many cases. The role of sexual transmission, if any, 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 coinfection and high HCV viral load. 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 coinfection or high levels of viraemia. Elective caesarean section in women with HIV/HCV coinfection is usually advocated, although its role in reducing perinatal transmission in women with HCV monoinfection is unclear. [7,8]

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% to 92%) suffer a mononucleosis-like seroconversion illness characterised by fever, pharyngitis,

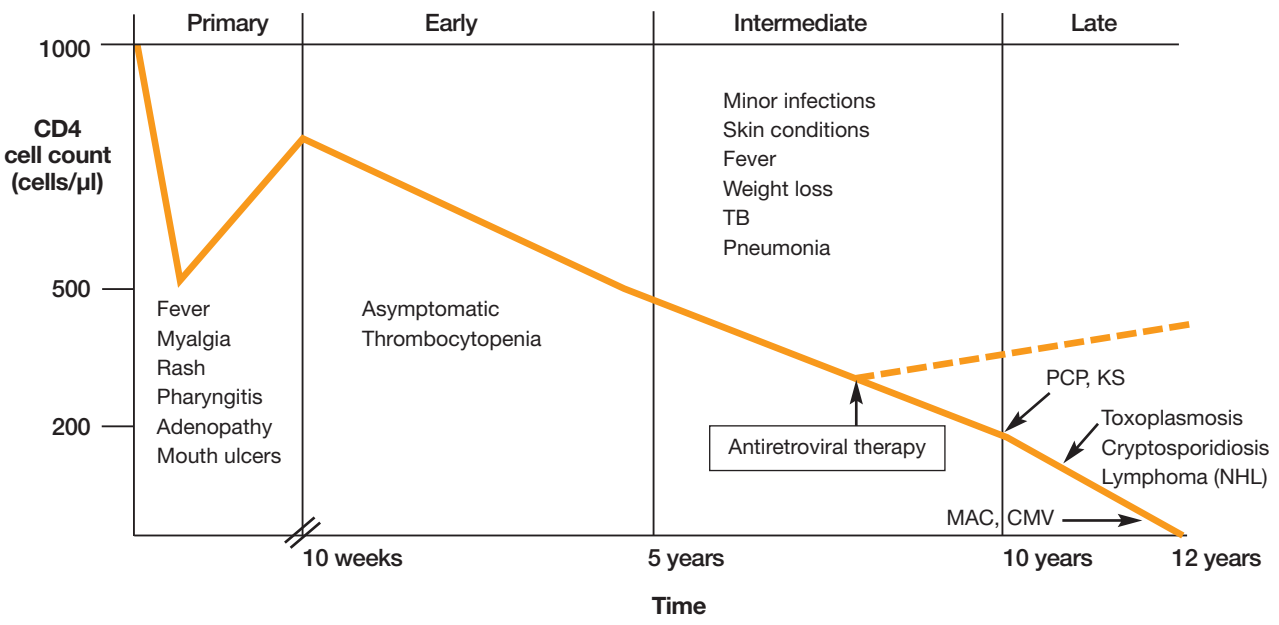

FIGURE 1.1 The various stages of HIV infection depicting the development of different opportunistic infections with advanced immunodeficiency and the impact of antiretroviral therapy on CD4 cell count recovery.

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. The level of this set point is the best available predictor of progression to AIDS. If left untreated, the patient experiences a gradual decline in CD4 cell count and, after a mean of ten years, develops AIDS with the onset of opportunistic infections or malignancies. At this time the CD4 cell count has usually fallen below 200 cells/µl and the patient is severely immunocompromised (Figure 1.1).[1,9]

HBV

HBV, by contrast, is almost exclusively an immune-mediated disease. The outcome of infection is largely determined by the age at infection, 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), although clinical acute hepatitis rarely occurs. If, however, an individual is infected as an adult, chronic infection will occur in less than 5% of individuals, 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 decade, 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 long-term carriers will die of cirrhosis or hepatocellular carcinoma (HCC) (Figure 1.2). However, if these

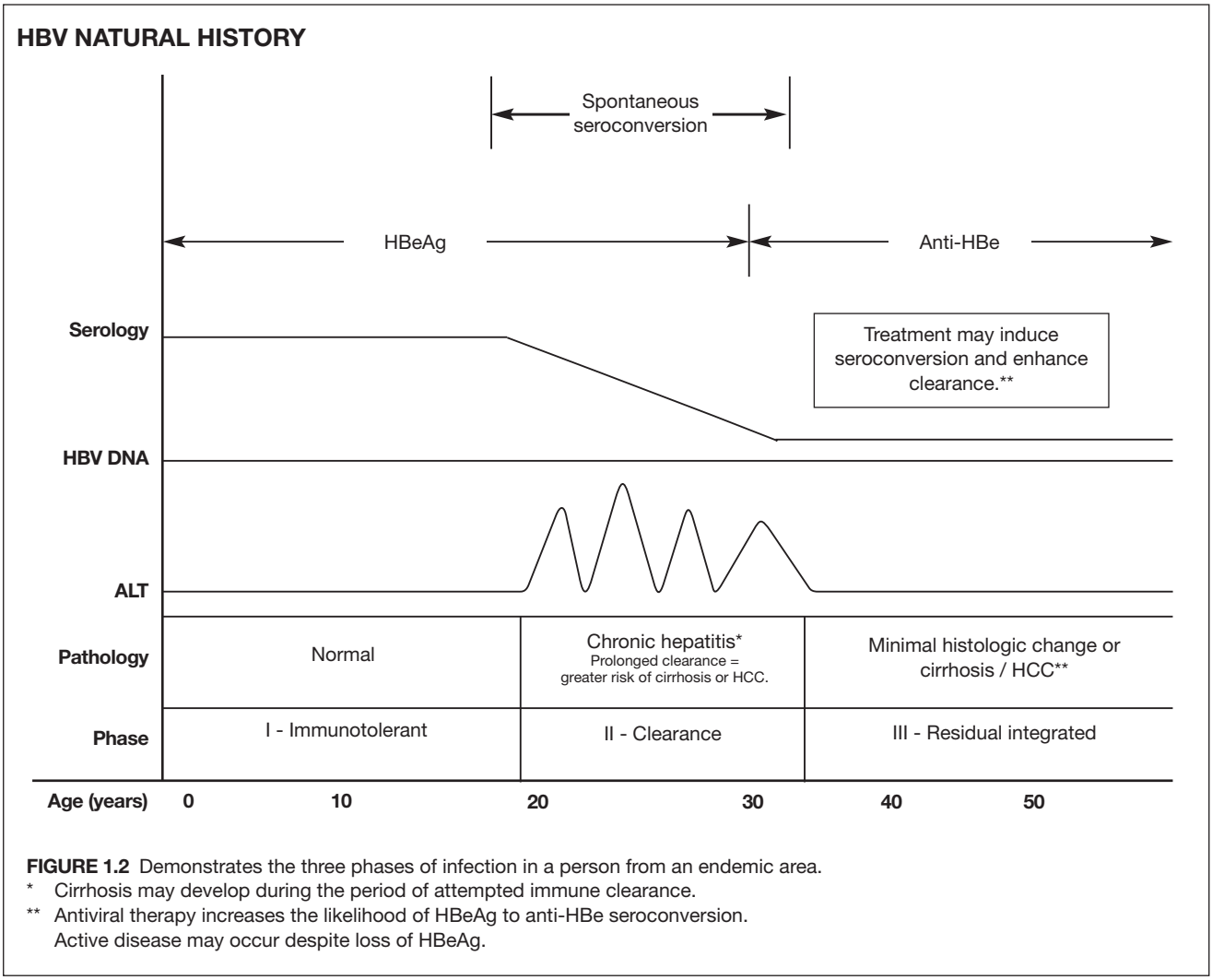

FIGURE 1.2 Demonstrates the three phases of infection in a person from an endemic area.
* Cirrhosis may develop during the period of attempted immune clearance.
** Antiviral therapy increases the likelihood of HBeAg to anti-HBe seroconversion. Active disease may occur despite loss of HBeAg.

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 HBV carrier then enters into the latent phase with an improved long-term prognosis (Figure 1.2).

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.[2]

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 from between 25 to 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. 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.[10] Estimates of

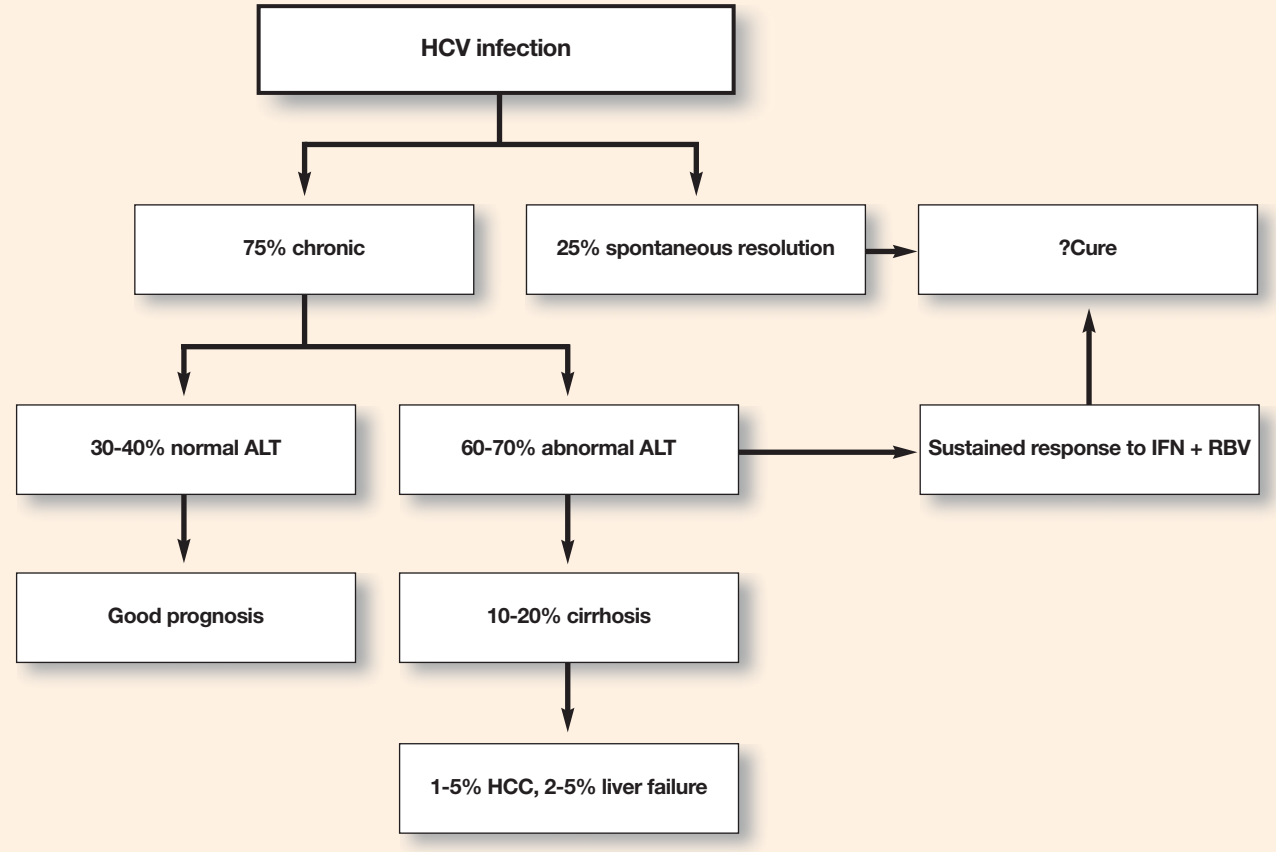

FIGURE 1.3 The natural history of hepatitis C infection and the impact of successful therapy on infection.

hepatitis–C related mortality are 1 and 4 % at 20 and 40 years respectively.[10] Despite this, an increasing burden of advanced liver disease is anticipated within Australia over the 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 sex, heavy alcohol intake, coinfection 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.

Coinfection

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. Individuals with HIV and HCV coinfection 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/HCV coinfection.[11]

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 antiretrovirals: 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 threshhold.

Although the optimal time to commence therapy has not been established, Australian and international guidelines recommend that treatment should be considered when the CD4 count is between 200–350 cells/mm^3 or 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 HIV-infected individuals. The life expectancy of people with a CD4 cell count over 200 cells/µl is projected to be in excess of 30 years. This success has meant that HIV infection may become a chronic manageable disease. 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 restitution. Immunological benefit may be modest (CD4 cell counts frequently remain below normal levels) but often occur in individuals who fail to achieve full virological suppression.

At present we do not know the long-term durability of the response in those who achieve viral control or whether drug resistance and loss of efficacy will ultimately emerge. Most of these drugs do have significant side-effects and require complex dosing schedules, making adherence (a major determinant of resistance) an issue for concern. Long-term survival of these patients also has unmasked chronic drug toxicities, particularly metabolic problems such as lipodystrophy and lipoatrophy, hyperlipidaemia, insulin resistance and hepatic mitochondrial toxicity.[12]

HBV

Current therapy for chronic HBV infection involves either alpha interferon (IFN) or lamivudine and is only considered when a patient enters the immune clearance phase, as the mechanism of therapy is to augment the existing endogenous immune response. The aim of therapy in an HBeAg+ patient is to facilitate a durable seroconversion to anti-HBe with resolution of liver inflammation (Figure 1.2). Interferon therapy for 4–6 months results in HBeAg seroconversion in approximately 30–40% of individuals but is associated with significant side-effects. Lamivudine for 12 months results in about 20% seroconversion in patients who have greater than twice the upper limit of normal serum alanine aminotransferase (ALT) level, with even higher rates (around 50%) if the serum ALT level exceeds five times the upper limit of normal. Seroconversion increases linearly for up to three years, although at a cost of viral resistance, which reaches at least 50% at this time. The overall resistance rate appears to be 20% per year treated. The treatment of HBeAg-negative infection is problematic and should probably be undertaken only if there is aggressive liver disease. Therapy probably needs to be lifelong, as withdrawal of therapy is associated with rebound viraemia and significant hepatitis flares. Ultimately, chronic HBV, like HIV, may be best treated with combination therapy.[11,12,13]

Progression to end-stage liver disease may mandate liver transplantation, although aggressive reinfection of the graft is problematic and necessitates the use of preventative strategies including antiviral therapy and HBV immunoglobulin.

HCV

Assessment of the need for therapy usually requires liver biopsy unless patients have a contraindication such as coagulopathy. This is due to the inability of non-invasive investigations to accurately assess disease activity. Therapy is usually given to patients with fibrosis and/or moderate inflammation on biopsy, as per S100 treatment guidelines.

Treatment for HCV has markedly improved in recent years. The combination of ribavirin with the newer form of interferon known as pegylated-interferon or PEG-interferon has greatly improved response rates compared to interferon-alfa monotherapy, and this combination is now considered standard of care. 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 dosing. 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/ribavirin combination are in the region of 35% for genotype 1 and 80% for genotype 2/3 . With pegylated interferon there is a significant improvement in genotype 1 response rates by approximately 10% to between 42 and 52%.[16,17,18] The anticipated SVR rate for genotype 2/3 patients remains very high at around 80%. The duration of therapy required is also genotype dependent with genotype 2/3 patients requiring only 6 months of therapy compared to 12 months of therapy 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 (>95%) of patients remaining clear of 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.[3,19]

Prevention

There is an effective and safe vaccine for HBV which is currently being introduced into Australia as a component of the universal vaccine program. While this program takes effect, it is important to offer vaccination to high-risk patients. Unfortunately, technical difficulties associated with vaccine development suggest that effective vaccines for HIV and HCV are at least 5–10 years away.

Prevention strategies 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.

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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 blood-borne viral infections in particular can facilitate both treatment and prevention. Therapy for HIV infection can postpone immune damage and prevent development of opportunistic infections and malignancies, while improved therapies for HBV and HCV can clear 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 HIV, HBV and HCV.

Diagnosis of each of these infections requires a simple blood test. 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. It should always be borne in mind that individuals may prefer to conceal a history of risk behaviour. 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.

Clinical assessment: might the patient be positive?

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

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.
- 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.
- The decision to test should be based on an assessment of risk as well as physical examination. Individuals may prefer not to reveal a history of risk behaviour, and 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 late and to suffer resultant poor clinical outcomes.

Patients with acute HIV, HCV or HBV infection may present with symptoms (Chapters 4 and 5), and diagnosis of HIV or viral hepatitis should be considered in any febrile illness, particularly if there is a possibility of recent exposure. When symptoms of chronic infection do 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. 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),

CASE STUDY 1

Clinical assessment: cough and fever may indicate an 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 carinii* 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 attends 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 time of presentation, he has been with his current girlfriend for over a year and they 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 sexually transmissible infections, 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.

while decompensated cirrhosis (liver failure) is associated with development of ascites, splenomegaly and abdominal venous distension (Chapters 6 and 7).

Risk assessment: might this patient be positive?

Risk assessment is based on a thorough history of the patient's sexual practices, drug use, tattoos and piercings and 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 (Chapter 3). Whilst taking a complete history may not be an option at every general practice contact, it may be possible to accrue this information over a period of time. Alternatively, the patient may be offered a follow-up appointment to allow risk assessment to be completed.

When faced with an individual who is an identifiable member of a 'high-risk group' (e.g. an openly gay man or an opiate-dependent drug user), the possibility of infection with a blood-borne virus is likely to suggest itself. However, as transmission is actually linked to certain risk behaviours, rather than group membership, it is likely that considering the possibility of infection with HIV, HBV or HCV only in persons from so-called 'high-risk groups' will lead to undetected infections. Many individuals who are from such 'high-risk groups' remain at very low risk because of the nature of their sexual or drug-use practices, while individuals 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/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/or language barriers to disclosure;
- fear that confidentiality will be breached.

A minority of individuals 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.

Sexual health context

A person diagnosed with a sexually transmissible infection (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. Full evaluation of a person with an STI includes HIV, HBV and often HCV antibody testing.

Consideration of HIV risk should be made with regard to all patients who present with an STI. Although statistically 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 investigate fully any patient diagnosed with an STI or blood-borne viral infection (Chapter 13). Failure to diagnose can lead to ongoing transmission as well as clinical progression.

More than 20 years into the HIV epidemic, there is some evidence that 100% use of condoms is becoming less common among gay men in Australia.[1] Surveys in Melbourne and Sydney have shown increasing levels of reported unprotected anal intercourse with casual partners, and surveillance data reveal increasing rates of gonorrhoea in these populations.[2] Regular testing for gonorrhoea and other STIs in men who have sex with men 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.

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 safe sex practices (Chapter 3).

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

CASE STUDY 3

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

Sexually transmissible infections

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 a sexually transmissible infection (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 slightly raised 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 years 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 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 is much relieved to hear that the risk of transmission to her baby is quite low and that transmission to her partner very unlikely.

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 positive person carries a high risk of transmission for both HIV and HBV but a very low risk of transmission for HCV (Table 2.1).[3] 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.[4]

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. However, proven interventions can reduce the risk of perinatal transmission of HIV and HBV to less than 5%.[5,17]

In contrast to the lower efficiency of HCV transmission in the sexual contact setting, HCV is probably 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 non-specific nature of symptoms and signs of both HIV and chronic viral hepatitis prior to advanced disease makes the assessment of risk behaviour a crucial component of the initial diagnosis of these conditions.

Prevalence and transmission

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

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

	HIV	HBV[1]	HCV[2]
Sexual contact			
Unprotected anal (receptive)	very high	very high	very low[3]
Unprotected anal (insertive)	high	very high	very low[3]
Unprotected vaginal	high[4]	very high	very low[3]
Unprotected oral (cunnilingus and fellatio, receptive and insertive)	very low	low-moderate	negligible
Mother to child (perinatal)			
No intervention	20-45%	30-90%	5%[5]
With intervention	<5%[6]	<5%[7]	NA[8]
Occupational exposure (needle-stick)	0.3%	20-40%	2-10%
Sharing injecting equipment among IDUs	very high	very high	extremely high[9]
Unsterile tattooing and piercing	high	very high	very high
Unsterile medical and other procedures	high	high	high

1 Refers to chronic hepatitis B (HBsAg+), with higher risk where source is HBeAg+ and/or HBV DNA+.
2 Refers to chronic hepatitis C (HCV RNA+).
3 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 coinfection).
4 Some evidence of higher risk for male-to-female than female-to-male transmission.
5 Higher risk (15-20%) in presence of HIV/HCV coinfection, related to higher HCV viral load.
6 Proven interventions include antiretroviral therapy, caesarean section and avoidance of breastfeeding.
7 Intervention includes HBV immunoglobulin and vaccination.
8 There is no currently proven intervention for perinatal HCV transmission.
9 Some evidence of HCV transmission when sharing injecting equipment other than needles (e.g. spoons, tourniquets).

TABLE 2.2 Prevalence estimates for HIV, HBV and HCV in Australia[1]

	HIV	HBV [2]	HCV
Injecting drug users	1-2%[3]	40-50%[4]	50-60%[3]
Sexual orientation			
Homosexual/bisexual men	5-10%[5]	40-50%[4]	5-7%[6]
Homosexual/bisexual women	<1%	2-5%[6]	2-5%[6]
Heterosexual men	<1%	1-2%	1-2%
Heterosexual women	<1%	1-2%	1%
Ethnicity			
Indigenous Australians	<1%[7]	20-30%[8]	2-5%[9]
Asian	<1%	20-30%[8]	2-5%[10]
Other	<1%	1-2%	1-2%
Health care workers[11]	<1%	1-2%	1-2%
Recipients of blood products[12]			
People with clotting disorders[13]	20-30%	50-60% [7]	0-80%
Other	1%	1-2%	2-5%

1 Some of these estimates are based on limited data, and should be considered as guides to levels of infection rather than true prevalence values.
2 Based on prevalence of anti-HBc, indicating previous exposure. Approximately 95% of people exposed to HBV as adolescents/adults clear HBV infection (HBsAg- and anti-HBs+) and are immune to re-infection.
3 Based on data from the National Needle and Syringe Program survey.[2]
4 Prevalence of chronic hepatitis B (HBsAg+) estimated to be 2-3%.[7,8]
5 Based on self-reported HIV status among gay men at gay community fair days in Australian capitals.[1]
6 Higher prevalence estimates than heterosexual groups due to higher prevalence of injecting drug use.[9,10]
7 Despite higher rates of other STIs, HIV prevalence is similar among indigenous and non-indigenous Australians.[11]
8 The majority of transmission occurs during the perinatal period or early childhood, therefore the estimate for chronic hepatitis B (5-10%)[12] is higher than for other high-risk groups (2-3% for IDU, homosexual men).
9 Higher estimate due to increased prevalence of injecting drug use and incarceration.[13]
10 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).
11 Although cases of occupational transmission of blood-borne viruses have been reported, including five cases of HIV,[14] prevalence of HIV, HBV and HCV is estimated to be similar to the general population.
12 In Australia, screening for HBV was introduced in the early 1970s, HIV in 1985, and HCV in 1990.
13 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).[15]

Australia: HIV in men who have sex with men; HBV and HCV among injecting drug users (IDUs); HBV in indigenous Australians and Asian-born populations; and all three viruses in people with haemophilia (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.

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.

TABLE 2.3 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 noninfectious 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.

CASE STUDY 5

HBV transmission: perinatally acquired infection

HBV prevalence and transmission

Aaron is an 18-year-old medical 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 subsequent HBV testing. Due to the possibility of perinatally acquired infection, his GP stresses the particular importance of HBV testing for his mother.

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 of over 1% and within these countries there are certain populations, particularly injecting drug users and sex workers, with much higher HIV prevalence.

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 amongst those newly diagnosed, as do visitors to high prevalence regions. During 1998–2002, over 50% of people who acquired HIV through heterosexual contact were from a high prevalence country or had reported heterosexual contact with a person from a high prevalence country.[2]

Proven prevention strategies

There are several proven means of reducing the efficiency of transmission of HIV, HBV, and HCV (Table 2.3). 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). Other interventions such as post-exposure prophylaxis may also have a role in prevention (Chapter 4). Antiretroviral therapy, caesarean section, and avoidance of breast-feeding have reduced the risk of perinatal transmission of HIV to less than 5%.[16]

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 a decade away.

Summary

HIV, HBV and HCV are different and distinct viral infections in terms of epidemiology and risk factors for transmission, although some points of similarity occur, particularly in regard to modes of transmission. The recommendation to test for HIV, HBV and HCV should be based on reported risk factors for transmission or 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.

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3 Talking with the patient: risk assessment and history-taking

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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 HIV and viral hepatitis. A thorough sexual and drug-use history is required to identify specific risk factors and behaviours of concern regarding HIV 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;
  - a willingness to discuss sexual and drug-use behaviour in detail;
  - careful listening 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 diseases and sexually transmissible infections (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/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 back 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/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/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/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 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/her with unusual or challenging language or concepts.

Although patients are often reluctant to report stigmatised behaviour, 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. However, 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/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/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 and referral to another clinician or service may be appropriate.

TABLE 3.1 What prevents effective communication?

• Poor 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 lack of interest or prejudice)
• Not listening to the patient
• Inappropriate use of open and closed questions
• Interrupting the patient excessively

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, HBV and HCV may be asked. These questions may address:

- a history of blood transfusions;
- tattoos (including where, when and whether done professionally);
- country of birth and residence;
- cultural practices (such as initiation ceremonies);
- family history;
- vaccination history;
- piercing.

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 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.

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

TABLE 3.3 Injecting drug use equipment and language

Common injecting equipment

The drug(s); water; spoon; filter; swab; tourniquet; syringes; needles; disposal containers.

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); whacked or hit (an injection of drugs); user (person who injects drugs); works (equipment); Harry (heroin); the gear (illicit drugs generally); goey, whiz or speed (amphetamines).

TABLE 3.4 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?

Injecting drug use history

Important information to obtain about injecting drug use includes:

- whether and when any needles or injecting equipment 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 3.5 has a summary of safer injecting practices. Chapter 14 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 yourself?[1] Other useful questions regarding drug history are outlined in Table 3.4.

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 3.5 and Chapter 14). It is appropriate to discuss whether the patient wishes to reduce or cease drug use, and whether he/she would like referral to an appropriate treatment service. Alternatively, non-injecting routes of administration, such as snorting and swallowing, may reduce risk.

Sexual history

The purpose of taking a sexual history is to assess and limit the risk of acquisition of infection with HIV or another STI. Sexual orientation or identity does not always equate with particular behaviour, therefore information about sexual practices, barrier/ condom use and the risk behaviours of sexual

partners is more specific and useful than the patient's stated sexual orientation and/or marital/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. Oral sex confers a lower risk of HIV transmission and 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 or hands is generally considered low risk. However, this type of penetration may result in trauma that can provide a portal of entry for infection. The clinician may need to establish the nature of non-penetrative practices. Some non-penetrative practices such as mutual or non-shared masturbation are low-risk activities. Other non-penetrative sexual practices, such as sado-masochism and piercing during sex (which may involve mucosal trauma or blood-to-blood contact), may have a moderate-to-high risk of transmission. Examples of questions to be asked during sexual risk assessment are listed in Table 3.7.

When asking about 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 3.6 provides a checklist of information to gather when taking a sexual history.

Where appropriate, condom use should be explored in detail. Questions relating to condom usage, as outlined in Table 3.7, 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

TABLE 3.5 Safe injecting procedures[5]

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 drugs into 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 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 – 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.

TABLE 3.6 Sexual history checklist

- Number of sexual partners and their gender
- 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
- Past STIs and their treatment

TABLE 3.7 Risk assessment – useful questions

Sexual practice

- 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 have any concerns about HIV or other STIs (e.g. chlamydia, herpes)?
- Are you sexually active?
- How many sexual partners have you had? Over the last three months? Since the last STI screen?
- When did you last have a sexual partner?
- Have you had any other sexual partners?
- Are your sexual partners male, female or both?
- What types of sexual activity do you engage in with your partner? Vaginal? Oral? Anal? (Clarification may be needed.)
- Have you ever had an STI (e.g. chlamydia, herpes, gonorrhoea)?
- Do you know whether your sexual partners have been at risk for HIV or STI? 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?

Condom usage

- Do you or your partner/s use condoms? Always or how often?
- When did you start using them?
- When don't you use them?
- What are your reasons for not using condoms?
- Do you have any problems using condoms?
- Do they fit well?
- Do you use a water-based lubricant?
- Have any condoms broken?
- When do you put the condom on? When the penis is erect?

Other transmission risks

- Did you have a blood transfusion or use blood products before 1990 in Australia?
- Have you had a medical procedure or blood transfusion overseas? Where and when?
- Do you have tattoos? (Ask for details.) Professionally done?
- Have you ever had a sexual partner or household member who had hepatitis C or B?
- Have you ever had a sexual partner or household member who was at risk of hepatitis C or B?
- Have you ever been in prison?

digital/sex toy penetration. Lubricants may reduce the risk of vaginal trauma and subsequent infection.

Prevention and harm reduction messages

Opportunities for harm reduction and safe sex education often arise during 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 individuals 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/she can discuss episodes of unsafe behaviour without being judged or lectured. Gaining an understanding of the patient's perspective and responding to his/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/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 'boys are in charge of condoms' or 'he looked young and healthy, so he couldn't have HIV'.

If a clinician chooses not to explore safe sex and harm-reduction strategies with a patient during a consultation, this 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/educator (Chapter 14). 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.

TABLE 3.8 Tips on safe sex and harm reduction messages

- 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 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.

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, 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 and consultation with colleagues. However, if impediments persist, referral to another clinician or service is recommended.

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4 Exposure and acute HIV infection

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Introduction

Early diagnosis, monitoring and treatment of patients with recently acquired HIV infection can significantly 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 and support.

Key points

- Early diagnosis of HIV disease has significant potential benefits. Monitoring and treatment can delay progression to clinical disease, 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, rapid referral to an antiretroviral prescriber, sexual health centre or hospital emergency department is necessary.
- 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.

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, central nervous system and skin cells also become infected. 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 other viral infections.

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 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 ten 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 for up to three weeks after onset of symptoms. The duration of the illness is most commonly 4–14 days but may be longer.[1,2] Approximately 50–90% of patients report signs or symptoms suggestive of primary HIV infection at the time of seroconversion.[3,4,5,6] Patients who experience symptomatic primary HIV infection appear to have more rapidly progressive HIV disease than those who do not.

TABLE 4.1 Symptoms and signs of primary HIV infection[7]

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	24%
	Transient reversible neurological signs (neuropathies, Guillain-Barré)	Rare
Skin	Rash	40-80%
	Genital ulcers	5-15%
Initial laboratory findings	Thrombocytopenia	45%
	Leukopenia	40%
	Raised liver enzymes	20%
Diseases caused by transient immunosuppression	Oral/oesophageal candidiasis Gut infections *Pneumocystis carinii* pneumonia (PCP)	Rare

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 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.

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. Provision of full pre-test counselling is required to prepare the patient for the possibility of a positive diagnosis and to provide him/her with the required information about HIV infection (Chapter 8).

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

Potential exposure to HIV often indicates a risk of HBV and/or HCV infection. Consequently, investigations for HBV and HCV should be considered in the context of acute HIV infection (Chapter 5).

Investigations

When risk assessment and/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 or proviral HIV DNA 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 the mandatory Therapeutic Goods Authority (TGA) approval needed for their use in the primary diagnosis of HIV infection.

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.
Qualitative PCR for HIV DNA	HIV DNA may become positive within a few days of symptoms and negative at one month.
Quantitative HIV RNA viral load by RT PCR b-DNA	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 or ELISA)	EIA may take up to three weeks to become positive after onset of clinical signs and symptoms.
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.

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.

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 14).

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 GP, with the support of either an HIV-experienced GP and/or a hospital-based specialist. Most of the physical symptoms are treatable with simple analgesics and antiemetics. Hospital admission may be required occasionally for rehydration or management of rare manifestations such as encephalitis or Guillain-Barré syndrome (Table 4.3).

Very early treatment with antiretrovirals – 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 9).

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. Clinicians inexperienced in the management of HIV infection need to contact an HIV-experienced GP or hospital centre to discuss further management. If the patient proceeds with treatment during primary infection, 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 individuals 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/or 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 13).

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
Qualitative HIV DNA polymerase tests – positive
Western Blot test result – not ready
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

PEP presentation and issues of safe sex and disclosure

PEP, safe sex and disclosure

David is a middle-aged, married man who presents to his general practitioner, Dr Betheras, for HIV post-exposure prophylaxis (PEP) 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.

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 13). She continues to monitor the situation in conjunction with the general practitioner providing PEP.

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.[8,9]

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.[10,11,12]

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.[13] For women of childbearing age, there may be fears and concerns about how HIV affects their future reproductive life.[14] Simple acceptance, in the face of perceptions of social stigma and discrimination, may be the most valuable support 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.[15]

Emotional support and acceptance can also assist the person to make beneficial alterations to his/her lifestyle, such as changes to diet and exercise, reduced drug and alcohol use and practising safe sex.[11]

Post-exposure prophylaxis: 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, can reduce the risk of HIV infection.[16] 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.

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. As detailed in Chapter 2, highest risk is defined as sexual exposure to an HIV-infected individual 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. For percutaneous, occupational exposures, the NSW Needlestick Injury Hotline (1800 804 823) can provide advice to health care workers regarding the level of risk (Chapters 12 and 14).

Assessment should address whether the source is known to have HIV infection and/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 counselling.

PEP

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 PEP. 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 Chapter 14 and the *ASHM Directory*.

PEP 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/her sexual and/or injecting drug use risk behaviours is a vital component of the PEP process. Patients may require referral to an experienced counsellor.

Testing for HIV antibody is required six months 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 and endorsed by the Australian National Council on AIDS, Hepatitis C and Related Diseases (ANCAHRD) and the Inter-governmental Committee on AIDS, HIV and Related Diseases (IGCAHRD). The guidelines are available at http://www.ancahrd.org/pubs/index.htm or by calling toll free (within Australia): 1800 022 863

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 14). Research has identified the importance of contact with HIV-positive communities in helping newly diagnosed patients come to terms with their new status and continue with their lives.[12]

However, whilst 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 patient's 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.

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. 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 and harm minimisation strategies. Provision of information and psychosocial support are key elements of management following a possible HIV exposure or diagnosis with primary HIV infection.

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Exposure and acute viral hepatitis

5

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Acute hepatitis

Epidemiology

In Australia, 400–500 cases of HAV infection and 400 cases of newly acquired HBV infection are reported annually.[1] An estimated 16,000 new cases of HCV infection occur annually but only 400–700 cases of newly acquired HCV are 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.

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.
- Preventative 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.

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 infected with HBV are more likely to develop chronic HBV infection than adults. Early studies of HCV infection have suggested that a significant proportion (85%) of people acutely infected develop chronic viraemia. However, more recent studies suggest that rates of chronic infection may be as low as 55%.[3] 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 extra-hepatic manifestations.

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 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 coinfection.
• 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 ALT is usually 10–100 times the upper limit of normal with the 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 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

counselling (Case Study 1 and Chapter 8). Specific serological investigations are indicated in Flowchart 5.1 and Table 5.5.

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 generally not used as a diagnostic tool in acute HBV infection. In patients with HBV infection, hepatitis D virus (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.

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 exhibit signs of encephalopathy, as well as for patients who are unable to maintain an adequate fluid intake and/or have prolongation of the INR or a rising bilirubin (greater than 300 mmol/l).

Most drugs should be avoided during acute hepatitis. Analgesics are generally not required and aspirin, narcotics and sedatives should be avoided. Small amounts of paracetemol may be used for 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.

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. Infected people 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.

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. However, in prolonged cholestasis after HAV infection, corticosteroids may reduce serum bilirubin and relieve itch. The role of interferon and nucleoside analogues in the treatment of acute HCV and HBV is not established. Although individual clinical trials have been unable to demonstrate a benefit of interferon therapy in acute HCV, meta-analysis has shown a benefit of interferon in terms of normalisation of ALT and clearance of viraemia. It is unclear whether a strategy of treating only those patients who develop chronic infection is any less effective than treatment during the acute phase.[4] Interferon therapy is not currently available under Section 100 of the Pharmaceutical Benefits Scheme for acute hepatitis C and referral to a specialist for advice is recommended for patients considering treatment.

In the case of acute HBV, infection will resolve spontaneously in the majority of adults and antiviral therapy is not indicated. It should be noted that 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 10).

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.

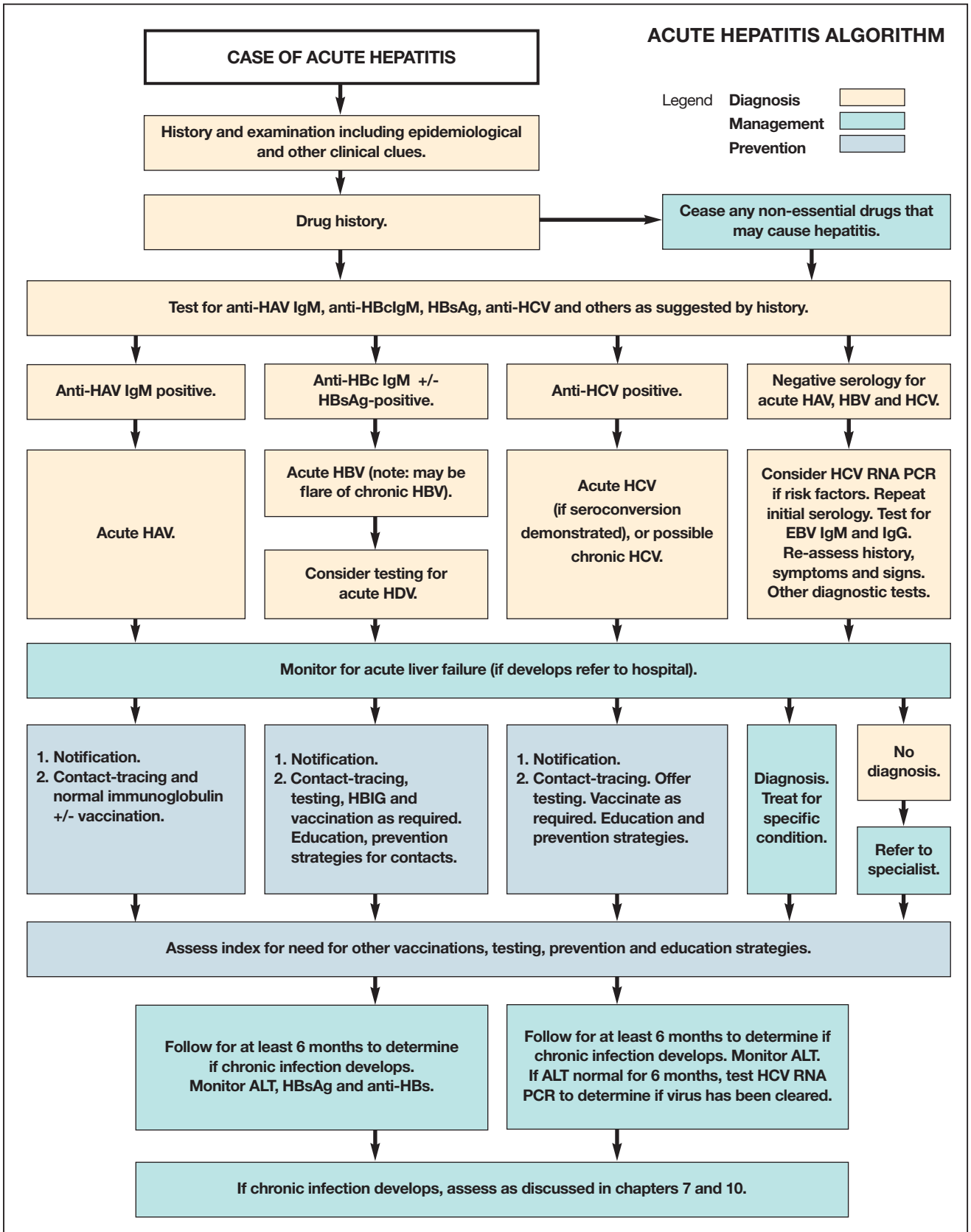
Altered mental status (hepatic encephalopathy) and coagulopathy in the setting of acute hepatitis defines acute liver failure. Typically, non-specific symptoms such as malaise, nausea, intractable vomiting and sleep disturbance develop in the previously healthy person, followed by jaundice, the rapid onset of altered mental 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 5.5 and Flowchart 5.1 provide details of HBV follow-up.



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

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. Review of appropriate State or Territory guidelines is recommended.

Public health notification

Cases of acute hepatitis are notifiable by doctors and diagnostic laboratories. Public health units coordinate the response to outbreaks of 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 preventative measures, such as vaccination, should also be taken.

Specialist and/or 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.

TABLE 5.3 Persons for whom hepatitis A vaccine is recommended[6]

• 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

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, should take extended leave. 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 12). Further information may be obtained from relevant State and Territory health departments or medical registration boards (Chapter 14).

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 preventative 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 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 individuals 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 counselling.

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 immediate management, as post-exposure prophylaxis is not currently available. However, the infectivity of a source that is repeatedly negative for HCV RNA in serum is probably negligible.[5]

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 is recommended and should be given within two weeks 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/her place of work should receive normal human immunoglobulin. If the patient is a childcare worker, then unvaccinated co-workers should receive normal human immunoglobulin. HAV vaccine can be commenced simultaneously with normal human immunoglobulin and should be considered for those at ongoing risk of HAV infection.[6]

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 48 hours. (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 14). The anxieties and concerns of the

TABLE 5.4 Persons for whom hepatitis B vaccination is recommended[6]

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

patients regarding transmission to sexual partners and family can be addressed by a discussion of modes of transmission and preventative strategies (Case study 1, Chapters 2 and 3). Describing potential health outcomes, as well as the process of determining infection status, also may 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. Breast-feeding is regarded as safe unless blood is present in the milk.

Immunisation[6]

HAV vaccination is recommended for some populations at high risk (Table 5.3). Screening for

TABLE 5.5 Serodiagnosis of acute and chronic viral hepatitis

Interpretation	anti-HAV IgM	anti-HAV total	HBsAg	anti-HBs	anti-HBc IgM	anti-HBc total	HBeAg	anti-HBe	HBV DNA	anti-HCV	HCV PCR
Acute hepatitis A	+	–	–	–	–	–	–	–	–	–	–
Past hepatitis A	–	+	–	–	–	–	–	–	–	–	–
Acute hepatitis B	–	–	+	–	+	+ or –	+	–	–	–	–
Acute liver failure - hepatitis B	–	–	+ or –	–	+	–	+ or –	–	+ or –	–	
HBsAg 'carrier' (non-replicating)	–	–	+	–	–	+	–	+	–	–	–
Chronic hepatitis B (replicating)	–	–	+	–	+ or –	+	+	–	+	–	–
Previous (resolved) hepatitis B	–	–	–	+ or –	–	+	–	+	–	–	–
Recent HBV vaccination	–	–	–	+	–	–	–	–	–	–	–
Acute hepatitis C	–	–	–	–	–	–	–	–	–	+ or –	+
Chronic hepatitis C (symptomatic or asymptomatic)	–	–	–	–	–	–	–	–	–	+	+
Resolved hepatitis C	–	–	–	–	–	–	–	–	–	+ or –	–

Note: coinfection or superinfection may make interpretation more complicated.

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.

Since 2000, the HBV vaccination has been available in Australia to all newborns and it is recommended for all children of 10–13 years who have not received a primary HBV vaccination. Once there is serological evidence of a response to immunisation, no further testing is required in immunocompetent persons and boosters are no longer recommended. HBV vaccination is also recommended for populations at high risk (Table 5.4). 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.

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.[6] 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 14).

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 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.

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6 Signs and symptoms of chronic HIV disease

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Introduction

Since the mid-1990s, the clinical manifestations of chronic 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 HIV-infected people 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 United States 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 (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 9).

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

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.

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 possibility to the astute clinician. Some of these clinical clues are tabulated in Table 6.2. Whenever HIV antibody testing is recommended, there should be an awareness of the psychosocial impact of testing and full pre-test counselling should be undertaken (Chapter 8).

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 management of pregnant women and as part of screening for sexually transmissible infections (STIs). HIV antibody screening is performed at 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 8.

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 HIV-infected individuals, these symptoms continue chronically, indicating high-level immune system activity.

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 HIV-infected people, 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 unmodified HIV infection when the CD4 cell count falls below 500 cells/µl (Tables 6.1–3). Most of these are other chronic viral infections and the appearance of clinical disease in HIV-infected people 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 HIV-infected people. 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 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 HIV was seen only in elderly men, is now known to be

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 or kansasii (disseminated)
- Mycobacterium tuberculosis disseminated or pulmonary*
- Pneumocystis carinii pneumonia
- Pneumonia (recurrent bacterial) *
- Progressive multifocal leukoencephalopathy
- Salmonella septicaemia (non-typhoidal, recurrent)*
- Toxoplasmosis (brain)

* Requires HIV diagnosis.

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

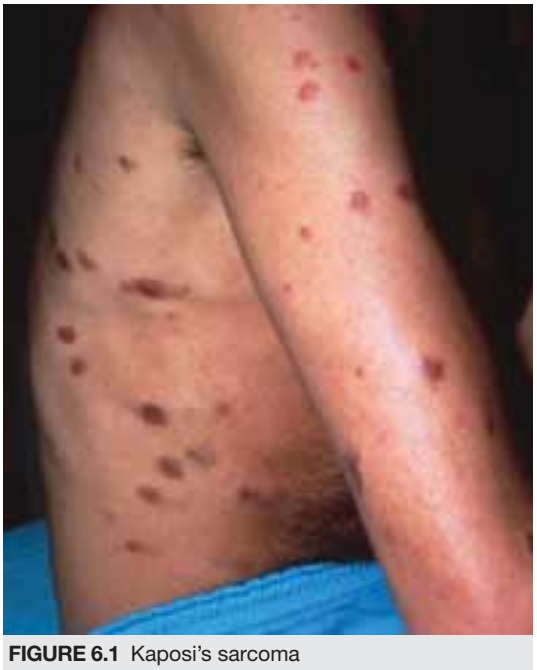

FIGURE 6.1 Kaposi's sarcoma

caused by human herpesvirus type 8 (HHV8). HHV8 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 (KS) 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 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 HIV-infected people 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 when immune function is restored.

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 Pap 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 non-HIV-infected

individuals, persistent appearance of molluscum contagiosum in adults should lead to consideration of HIV infection. Molluscum contagiosum is caused by a poxvirus and, in HIV-infected individuals, its incidence and severity relate to the degree of immunosuppression. The condition is diagnosed clinically. Differential diagnosis in the HIV-infected patient would include cutaneous cryptococcosis infection and, in individuals 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 HIV-infected people 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.

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, groins and feet. Standard treatment with steroid creams or topical ketoconazole is often effective at 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 where response to simple 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 also has been described. Immune recovery has been shown to improve these psoriatic lesions in HIV-infected individuals.

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 fluconazole capsules 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 (ANUG), is commonly seen in the months before

FIGURE 6.2 Seborrhoea

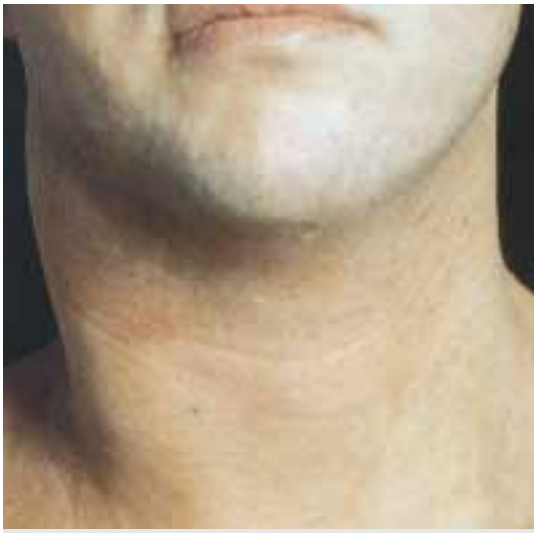

FIGURE 6.3 Immune reconstitution and *Mycobacterium avium* complex (MAC)

clinical progression of HIV. Skilled care from a dentist who is sensitive to the needs of HIV-infected people is required if loss of otherwise healthy teeth is to be avoided. 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 coinfection

As other HIV-related opportunistic infections are prevented or controlled, liver disease secondary to coinfection with HBV or HCV and liver toxicity from antiretroviral agents have become more prominent. Coinfection 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 coinfected people is currently being investigated. 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 9 and 10).

In the HIV-infected person, 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 coinfection 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*. 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 by an Australian team led by immunologist Dr Martyn French.[5] An immune reconstitution illness is usually temporary 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.

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

In the untreated person with HIV, *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 the chest X-ray and is con-

TABLE 6.3 Febrile syndromes in HIV-infected individuals

Differential diagnosis of undifferentiated fever in the HIV/AIDS patient

Current or nadir CD4 cell count < 200 cells/μl	Current or nadir CD4 cell count ≥ 200 cells/μl
• Disseminated *Mycobacterium avium*	• Bacterial infections, e.g. pneumonia, septicaemia
• *Pneumocystis carinii* 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*	

firmed 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 cotrimoxazole taken once daily by people with CD4 cell counts below 250 cells/μl has dramatically reduced the incidence of the 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 HIV-infected individuals (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 1,200 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 an HIV-infected person. 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 individuals with very severe immunosuppression.

Advanced HIV disease is associated with diarrhoea and, if no specific cause is found after a full diagnostic assessment, antidiarrhoeal 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

HIV-infected individuals have a 250- to 650-fold increased risk of AIDS-related lymphoma over the background population, with lymphoma

FIGURE 6.4 Body composition changes

occurring most frequently in people with CD4 counts below 100 cells/µl. Eighty-five percent of all AIDS-related lymphomas are systemic non-Hodgkin's lymphoma (SNHL), 15% are primary CNS 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 HHV8 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 HIV-infected people 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 (PML).

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

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 picture is still seen in people who are unable to tolerate antiretroviral medication, or where viral resistance limits its effectiveness, most bodily changes in HIV-infected people 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 HIV-infected people 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 an HIV diagnosis, consideration should be given to the management of psychosocial concerns as well as the clinical manifestations of the infection. Post-test counselling 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 (Chapters 8 and 9).

HIV-infected people now face a variety of serious challenges, including new manifestations of HIV-related illnesses and medication-related toxicities. While improved prognosis has led some HIV-infected patients 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 acknowledgement and management (Chapter 9).

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 HIV-infected people also visit general practitioners, who are ideally placed to detect adverse developments at an early stage and to facilitate optimal therapy. Chapter 9 addresses management of the HIV-infected patient, particularly in regard to antiretroviral therapy, psychosocial management, and support and referral.

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7 Signs and symptoms of chronic viral hepatitis

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Introduction

Acute infection with HBV or 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 year of infection in approximately a quarter of infected individuals, 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.

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.
- Liver biopsy remains the definitive investigation for staging of liver disease.

The natural history of HBV infection is primarily determined by the age of the individual at the onset of infection. When acquired at birth or during early childhood, the risk of development of chronic infection is high, with only 2% of infants spontaneously clearing the virus within three years of infection and 15% clearing 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. 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 and/or slowly progressive liver disease;
- progressive liver disease;
- advanced liver disease complications;
- extrahepatic manifestations.

In this classification, 'early and/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), portal hypertension (e.g. ascites, oesophageal varices) and/or 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 and/or slowly progressive disease' and 'progressive disease'. A long asymptomatic phase followed by signs associated with cirrhosis or decompensation is not uncommon.

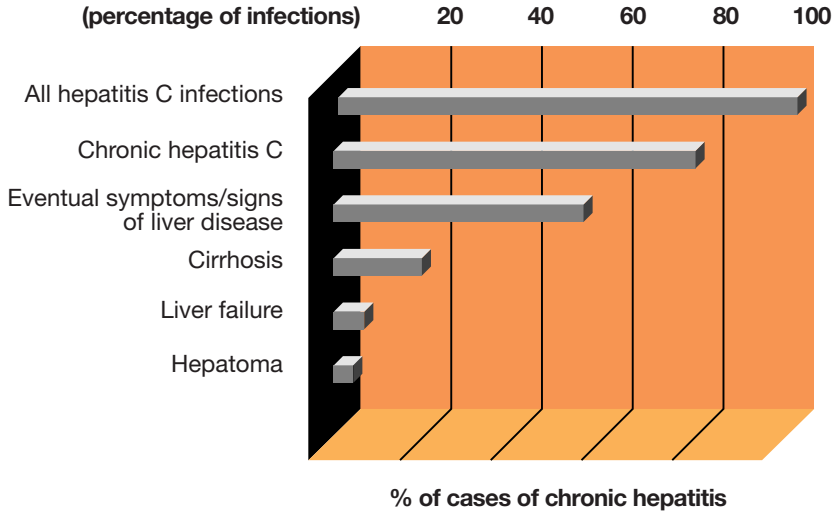

FIGURE 7.1 The proportion of HCV-infected persons who develop complications.

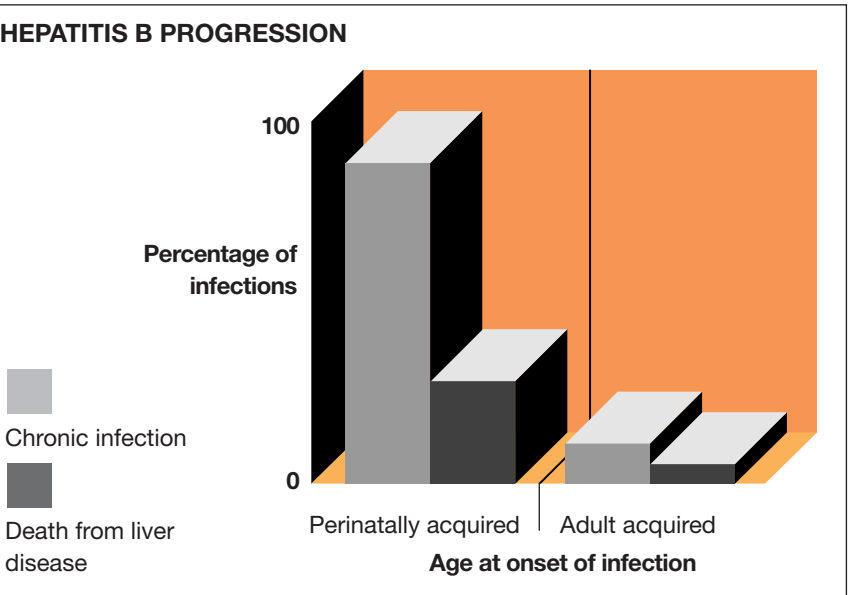

FIGURE 7.2 Prognosis according to age at onset of hepatitis B infection.

Early and/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

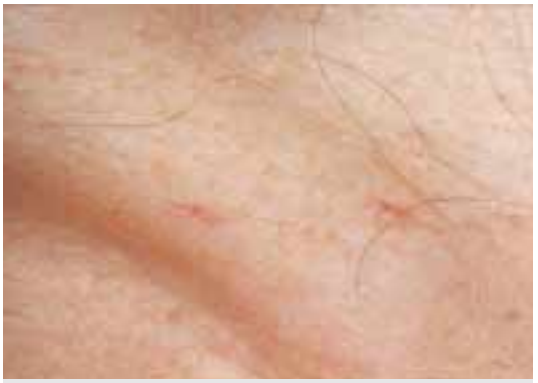

FIGURE 7.3 Spider naevi in chronic hepatitis

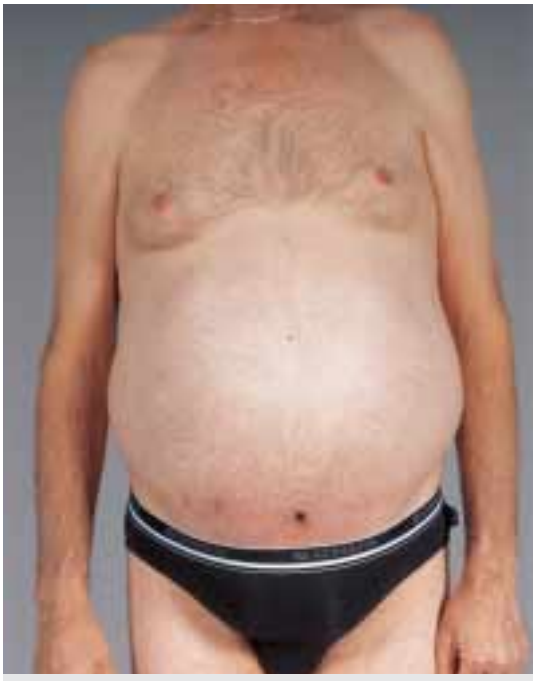

FIGURE 7.4 Decompensated cirrhosis secondary to hepatitis C

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 sex
• 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.

functioning, social functioning 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 and/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 ALT and 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

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, leuchonychia) 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, leuoconychia) 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)

'seroconvert', initially from HBeAg-positive (HBeAg+) to HBeAg-negative (generally with development of anti-HBe) and subsequent loss of HBsAg. People with frequent flares who have not seroconverted may experience faster disease progression and are at high risk of cirrhosis and/or HCC. Thus, people in this category should be referred to a hepatologist or liver clinic for assessment of stage of liver disease and possible therapeutic intervention. Antiviral therapy for chronic hepatitis B is most efficacious during this period through enhancement of clearance rates.[2]

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.

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.

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

Extrahepatic manifestations

Extrahepatic manifestations, although uncommon, represent clinically important aspects of hepatitis B and C. Specific treatment can be directed towards these conditions, some of which are listed in Table 7.3.

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.

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 10).

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 following acute infection or persist in a person who remains a carrier. Anti-HBs appears following the disappearance of HBsAg, and is a marker of both naturally acquired and vaccine-induced immunity. The presence of anti-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 5.5 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 some prognostic value with regard to response to antiviral therapy, and the HCV genotype is even more predictive of response. HCV viral genotyping is helpful in determining the likely response and optimal duration of antiviral treatment (Chapter 10).

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 and/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

TABLE 7.4 Investigations in chronic hepatitis

Investigation	Reason
HCV antibody (anti-HCV)	Exposure to HCV.
HCV RNA PCR	Detects presence of HCV.
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 (carrier).
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 markers 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.
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 markers 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	Definitive test for assessing severity of disease.

of the liver. Hypoalbuminaemia and prolonged prothrombin time indicate decompensated cirrhosis. Recent evidence from a cohort of people with chronic hepatitis C demonstrated that one of the strongest prognostic measures is 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/l.[7]

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 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.

Other investigations

Other tests are used to identify complications or coexisting 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 coexisting HBV, HCV or HIV may alter prognosis and treatment options. In treating hepatitis C, 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. Antinuclear antibody (ANA), anti-smooth muscle 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

The definitive test for the assessment and staging of disease is a liver biopsy.[8] Liver biopsy is usually offered to patients with abnormal ALT levels who may be considering antiviral therapy. It also greatly assists in determining prognosis over the short-to-medium term. 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.

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 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 is 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 14) 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.

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

8

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Introduction

Testing for HIV, HBV and HCV mandates pre-test and post-test counselling. The aims of pre-test and post-test counselling are to minimise the personal impact of diagnosis, to change health-related behaviour and to reduce anxiety, particularly when the patient has not initiated testing. Counselling thus requires the clinician to assess risk, educate the patient regarding risk of transmission, obtain informed consent and follow-up and arrange referrals as indicated.

The context of testing

Testing for HIV antibody has been available in Australia since October 1984. At that time, 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.[1] The widespread 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/AIDS remains a stigmatised condition and all people who are tested should be given detailed and sensitive pre-test and post-test counselling.

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 counselling, 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 individual about HCV transmission and natural history. As with HIV, the benefits of testing include interventions and treatments to improve clinical outcomes and 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 1, 7 and 10) still exists, and patients need to be suitably counselled.

Key points

- Pre-test counselling is essential for the patient to make an informed decision regarding HIV, HBV and/or HCV testing.
- Pre-test counselling 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 counselling should be adapted to an individual's knowledge and cultural understandings as appropriate. Testing should not be avoided because pre-test counselling is 'too hard'.
- In positive individuals, post-test counselling explores support and resources available to the patient and provides education regarding the infection and how to minimise the risk of transmission.
- In negative individuals, post-test counselling provides information on safe sex or injecting and addresses risk behaviour that led to the possible exposure.

The counselling process

During the counselling 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 (Table 8.1). Referring to a framework of key points ensures that the necessary information regarding blood-borne viruses is conveyed.

Within the context of general practice, clinicians may often recommend testing for HIV, HBV and HCV but rarely see positive results, particularly in relation to HIV. Consequently, detailed pre-test counselling may seem unnecessary. However, testing usually occurs because there is some level of risk and each case of testing for blood-borne viruses needs to be taken seriously. Pre-test counselling provides an opportunity for the clinician to educate patients in risk reduction while ensuring diagnostic vigilance is maintained.

TABLE 8.1 Summary of pre-test counselling

- Motivation/reason for test
- History of testing
- Psychiatric status and assessment of social supports
- Exposure/risk assessment
- Confidentiality
- Natural history and transmission
- Prevention of transmission
- Implication of a positive or equivocal test result, including availability of treatment
- Implications of a negative test result
- Explanation of the window period
- Advice on disclosure to family and friends
- Assessment of ability to cope with testing and possible diagnosis
- Support services
- Logistics of the HIV 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:

- upon patient request;
- upon identification of clinical symptoms or signs (Chapters 4–7);
- upon identification of risk factors in the patient history (Chapters 2–3);
- as part of a screening process;
- following a possible occupational or non-occupational exposure to the blood or bodily fluids of a person whose infection status is positive or unknown.

Screening may relate to antenatal testing, pre-surgical testing, military requirements, blood donation, and/or immigration or insurance requirements. Regardless of the reason for testing, pre-test counselling by the clinician and informed decision-making by the patient are essential.

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).

Other requests for testing may occur following an exposure, either in a medical context or occasionally in a public setting. Parents may present with young children who have inadvertently handled discarded syringes. In these circumstances, often the precise details of the exposure are unclear and the risk is difficult to assess.

Legal requirements

Some States and Territories have specific legal regulations relating to pre-test and post-test counselling for HIV and viral hepatitis, which may be used as a guide to minimum standards of care. Contact the relevant State or Territory health department for details (Chapter 14). Chapter 13 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 counselling

Pre-test counselling 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 safe sex and risk reduction measures;
- to prepare for a possible positive result.

History-taking and risk assessment

A non-judgemental counselling approach and a climate of openness and trust encourages 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 counselling

Table 8.1 lists topics to be addressed during pre-test counselling. In particular, the following points should be explored before the patient consents to testing:

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 13).

Medical consequences of infection

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

Information about prevention

Discuss the relative risks of transmission of HIV, HBV and HCV associated with various practices (Chapter 2). Explore the person's ability to practice 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 infected people can access.

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 sexually transmissible infections (STI). The clinician performs HIV pre-test counselling 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.

The benefits of HBV immunisation for household members and sexual partners may be relevant. Some individuals 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 equivocal result

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

The implications of a negative result

The absence of antibodies (the negative result) means either the person is not infected or that he/she is in the so-called 'window period' of infection, prior to the development of antibodies. The window period may be as long as three months from the date of initial exposure for HIV and six months for HBV and HCV.

Coping with the results

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 this process 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 14).

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/her result.

Summary

While pre-test counselling 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 clients. Not all of the issues listed above may be relevant to every patient each time he/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 counselling ensures that prevention measures are in place, the patient is prepared for his/her test results, and the clinician's ethical and legal obligations are met.

Post-test counselling

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.

Giving a positive result

The following points, summarised in Table 8.2, should be considered when providing post-test counselling in the event of a positive HIV, HBV or HCV test result.

Assess patient readiness to receive result

The person may be asked whether he/she has thought about the likely test result and its implications. If the person does not seem prepared, relevant issues covered in pre-test counselling may be reviewed. Alternatively, attendance may indicate the patient is ready to hear the result and it may be appropriate to give the result directly.

State the result clearly

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

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/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.

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/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 14). The ASHM website at www.ashm.org.au can provide contact details and links.

Managing a positive result

Much of the initial management of a new bloodborne 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 9 and 10 discuss initial and ongoing assessment, monitoring and management of patients with HIV and viral hepatitis.

Clinicians inexperienced in managing patients with blood-borne viral infections should collaborate with more experienced general practitioners and/or relevant specialists and specialist centres (Chapter 14 and the *ASHM Directory*).

Giving a negative result

The following points should be considered for discussion when providing post-test counselling for a negative HIV, HBV or HCV test result (Table 8.3).

Inform the patient of the result

Tell the patient that he/she is not infected. If appropriate, discuss the window period and make an appointment for re-testing.

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 14).

Offer vaccination

Hepatitis A and hepatitis B vaccination may be offered.

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 amongst young people, especially young men. Such responses need to be addressed.

Equivocal (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 need to consult pathology laboratory staff or the National Serology Reference Laboratory for specialist advice in interpreting equivocal 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 equivocal result.

A patient with an equivocal 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. Repeat HIV anti-

TABLE 8.2 Summary of post-test counselling: 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 next appointment
Subsequent consultations
• Treatment options, diet and exercise
• Effect of diagnosis on relationships (HIV-infected people are legally required to advise their sexual partners of their status)
• Issues of disclosure
• Travel to certain countries may be restricted for HIV-infected individuals
• Access to life insurance may be affected
• Workplace implications
• Impact of other issues (drug use, poverty, homelessness) on ability to access health care and treatments

TABLE 8.3 Summary of post-test counselling: giving a negative result

• Explain negative test result
• Reinforce education regarding safe behaviours
• Consider vaccination for hepatitis B and hepatitis A
• Further discuss anxiety or risk behaviours

body testing is generally offered at one month. If seroconversion is suspected, an HIV proviral DNA PCR assay may be used to determine HIV status (Chapter 4). Repeat HCV antibody testing may be offered using a different antibody test. Alternatively, a PCR assay may be used in consultation with a specialist centre to detect the presence or absence of virus.

A patient with high-risk behaviours, a history of recent exposure, clinical signs and/or specific types of equivocal results is at high risk of seroconverting. Upon repeat testing, these people usually test positive.

In populations of low seroprevalence of blood-borne viral infections, equivocal 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 one month, a second equivocal result is regarded as confirmation of negative status.

Special considerations

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 counselling.

Language barriers may be overcome by the use of an interpreter. Highlighting the need for confidentiality with the interpreter and reassuring the patient may be appropriate. Nevertheless, people of non-English speaking and indigenous backgrounds may hesitate to communicate through an interpreter due to fear that confidentiality will be breached. This may be particularly relevant in rural and remote settings where the interpreter may be closely connected with the patient's family.

Pre-test and post-test counselling may need to be adapted to suit the needs of a particular cultural group. In the Northern Territory, for example, changes to traditional pre-test counselling practices have occurred in conjunction with the training of community-based, Aboriginal health workers and the development of culturally appropriate resources and videos in indigenous languages. In addition, the term 'pre-test counselling' has been replaced by the term 'pre-test information' in an attempt to reduce clinician anxiety about pre-test counselling and to normalise HIV testing. However, any changes to pre-test and post-test counselling protocols should be undertaken in consultation with State or Territory public health authorities and appropriate specialist services or organisations.

HIV, HBV or HCV phobia

Occasionally the clinician will encounter an individual whose fear of infection with HIV or viral hepatitis is out of proportion with the actual risk of infection. Such individuals, 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 individuals who may have co-existing psychiatric morbidity, such as undiagnosed obsessive compulsive disorder, and may need referral for specialist counselling or psychiatric assessment.

HIV, HBV or HCV anxiety

Some people demonstrate extreme anxiety when presenting for testing. This anxiety may be due to behaviour, which the patient reports as 'out of character', that has resulted in risk of exposure to a blood-borne virus. For example, a married man may report guilt and fear of infection following protected sex with a sex worker. The anxiety may arise from the man's actions and may be exacerbated by his thoughts about the real or imagined interpersonal consequences of an infection, such as divorce from his partner and estrangement from his children.

CASE STUDY 2

A request for HIV testing may indicate anxiety not risk

AIDS 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 AIDS. 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.

Testing and pregnant women

Why test pregnant women?

The risk of perinatal transmission of HIV and HBV can be dramatically reduced by a range of 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 AZT (zidovudine, Retrovir™) monotherapy reduced mother-to-child transmission from 25% to 8%.[2,3,4] The use of combination therapy plus planned caesarean delivery and bottle-feeding has reduced HIV transmission to less than 2%.[5,6,7] Mother-to-child transmission of HIV has fallen dramatically in countries where antiretroviral therapy is available to pregnant women.[8]

Interventions to prevent HBV infection are well established and reference to the National Health and Medical Research Councils' Immunisation Handbook is advised.

A proven intervention for preventing perinatal transmission of HCV does not currently exist and the value of the universal offer of testing is unclear.[9] There is little risk of transmission via breast milk unless blood is present.

HIV testing during pregnancy

Pregnancy is a time when women are in contact with medical clinicians, and it provides an opportunity for detection of previously undiagnosed infections.

Australian health policy states that HIV testing of pregnant women should follow standard guidelines in regards to risk assessment, pre-test counselling and informed consent.[10] However, research shows that many women fail to report risk factors for HIV until after a positive diagnosis, and therefore standard risk assessment may be inadequate to determine who requires HIV testing.[11] When deciding whether to have an HIV antibody test, all women should be informed of the substantial benefits of determining HIV status in the prevention of mother-to-child HIV transmission.

HIV counselling during pregnancy

The issues to be discussed during pre-test counselling listed in Table 8.1 remain relevant for pregnant women.

Discussion of the implications of a positive test result should be extended to include the implications for the child and, in the case of HIV, should include discussion of treatment options and ways of preventing perinatal transmission. US and Australian guidelines on antiretroviral management in HIV-infected, pregnant women may provide the clinician with a detailed understanding of treatment, toxicity and mode-of-delivery issues in these women. To facilitate informed decision-making by the patient, consideration may be given to the risks as well as the benefits of interventions. For instance, although combination antiretroviral therapy is regarded as safe for infant and mother, there may be an increased risk of rare, life-threatening side-effects in the mother and birth abnormalities in the infant. The use of written information may aid the pre-test counselling process. Discussion of an equivocal result may also be considered, given that pregnancy may slightly increase the likelihood of an indeterminate result.

Post-test counselling of positive tests results should involve all of the points listed in Table 8.2. 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. Counselling 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 www.aidsinfo.nih.gov
- Australian testing guidelines and standards of care for pregnant women with HIV can be found at http://www.health.gov.au/hfs/pubhlth/ancard
- The Commonwealth Department of Health and Ageing has developed guidelines for HCV testing which can be linked via the ASHM website at www.ashm.org.au.

Summary

Pre-test and post-test counselling for HIV and viral hepatitis provides the clinician with the opportunity to review and reinforce prevention

and risk reduction messages. It also protects human rights by facilitating the individual's ability to make an informed decision 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 counselling deals primarily with psychosocial issues and early follow-up is recommended.

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

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Primary care management of HIV disease

9

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Introduction

The course of HIV infection has been altered significantly by the use of potent antiretroviral therapy and treatments for HIV-related opportunistic illnesses in developed countries. In the era of combination antiretroviral therapy, many HIV-infected patients 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 HIV-infected patients. 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/AIDS 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 HIV-infected patients. Signs and symptoms of HIV disease are discussed in Chapter 6.
- Combination antiretroviral therapy is available for the treatment of HIV/AIDS. Long-term suppression of HIV replication occurs in approximately 60% 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 HIV-infected patients 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 HIV-infected patients, 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/AIDS 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/or 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/she is comfortable with HIV-infected patients (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.

TABLE 9.1 Checklist: Initial assessment of the HIV-infected patient

- General assessment including medical history, family history, drug and alcohol history, smoking history
- Full psychosocial assessment
- Targeted physical examination including weight, cardiovascular status, oral and dental health, skin and general systems examination
- Sexual health review and a pelvic/anogenital examination
- Screens for infections such as toxoplasmosis (Toxoplasma IgG), tuberculosis (Mantoux test and chest X-ray), cytomegalovirus (CMV IgG), syphilis, and hepatitis B and A (HAV IgG, HBsAg, anti-HBs, anti-HBc)
- Screen for hepatitis C (anti-HCV, HCV PCR) for patient with risk factors and a CD4 <350 cells/µl
- Blood tests, including HIV RNA viral load, CD4 count, CD4 percentages, 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 an 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 HIV-infected patients. Both Fluvax and Pneumovax are recommended as per NHMRC guidelines.[1]

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 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 T-lymphocytes falls. Average time 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 disease. Early symptoms of immune deficiency begin to appear when the CD4 count falls below normal levels (Figures 1.1 and 6.1). As the CD4 count decreases to levels below 200 cells/µl, the patient is at greater risk of several 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 78 for further details.

Assessment and monitoring

Assessment and monitoring of the HIV-infected patient relates to general physical health, psychosocial wellbeing, as well as immune and virological status.

Initial assessment

During initial consultations with an HIV-infected patient, a comprehensive medical and psychosocial assessment should be conducted. General discussion concerning the impact of HIV/AIDS on the patient, issues of sexuality and social support will build rapport and facilitate appropriate management and referral. The patient's priorities with regard to HIV disease and his/her knowledge of HIV/AIDS need to be established prior to discussion of 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.

Initial medical assessment concerns establishing the stage of HIV disease and assessment of comorbidities. A comprehensive range of blood tests, serological tests and clinical examination should be conducted (Table 9.1).

Chapter 8 addresses how to deliver a positive HIV result to a patient and conduct early follow-up. In the context of 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 HBV or HCV is associated with greater risk of chronic liver disease and cirrhosis, 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 10).

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 HIV-infected people. 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 count and HIV viral load are prognostic markers of likely disease progression and clinical illness in HIV disease. As can be seen from Table 9.2, 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.

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). 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 carinii* pneumonia (PCP), cerebral toxoplasmosis, 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

TABLE 9.2 Surrogate markers and risk of progression to AIDS

CD4 cell count	Viral load copies/ml	% AIDS progression in men over 3 years	over 9 years
<200/µl	<10,000	14%	64%
	10,000 – 30,000	50%	90%
	>30,000	86%	100%
200-350/µl	10,000	7%	66%
	10,000 – 30,000	36%	85%
	>30,000	64%	93%
>350/µl	<10,000	7%	54%
	10,000 – 30,000	15%	74%
	>30,000	40%	85%

Adapted from Multicenter AIDS Cohort Study[1,2]

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 an individual'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) can be measured by two different technologies – branched chain DNA (bDNA) or reverse transcriptase polymerase chain reaction (RT PCR). The two commercially available methods have a strong correlation at the population level but results may differ by up to 1 log in an individual, so it is not recommended that the two assays are used interchangeably in a single individual.

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 9.3 and Case Study 1). The lower limit of detection of the assays is currently at 40–50 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 levels of CD4 cells), to monitor the response to antiretroviral therapy and to identify treatment failure.

Monitoring HIV infection

The Australian National Council on AIDS, Hepatitis C and Related Diseases (ANCAHRD) has produced a document: *Model of Care for HIV Infection in Adults*, which sets out the recommended schedule of monitoring for HIV infected adults, both treated and untreated. It is available for downloading at www.ashm.org.au. Patients will require more regular reviews if they are more immunosuppressed 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.[5] Graphs and summary pages contained in the *Model of Care* are essential tools to assist the clinician and the patient in monitoring changes in viral load and immune function, as well as general health maintenance.

Psychosocial assessment

Effective management of HIV-infected individuals 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. The cumulative grief experienced by many HIV-positive people who have lost close friends to HIV should be considered when conducting psychosocial assessment. Social, emotional and educational support is available through AIDS Councils and HIV-positive people's groups in each State and Territory (Chapter 14).

Psychosocial assessment and management involves consideration of the following issues:

- self-esteem and body image;
- stigmatisation and discrimination;
- family and social relationships/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/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/or HIV status, their reaction to this information and/or the patient's reasons for not telling them. Friends may also provide an invaluable support network.

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 14).

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 HIV-infected women, 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 8). For a woman who already has children, there may be concerns that her children are HIV-infected. Most

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.

TABLE 9.3 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
5,000	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

infants with HIV develop signs of immune deficiency within the first year of life and antiretroviral therapies are available to children, although adherence to therapy can present difficulties. For HIV-infected women requiring support, referral to Positive Women's groups is recommended (Chapter 14).

In the era of combination antiretroviral therapy, patients may wish to address issues of returning to work, education or relationships in light of their 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/or sexuality.

Psychological assessment[6]

Several Australian studies indicate a high prevalence of major depressive symptoms and dysthymia among HIV-infected people,[7,8,9] with particularly high rates among patients with fewer social supports and lower income. Depressive symptoms may impact on the individual'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 HIV-infected people 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 give to the mental health implications of immune status. In addition, depressive, neuropsychological side-effects may be caused by antiretroviral agents, most commonly efavirenz.

Health promotion

Prevention

It is important that HIV-infected people 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/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 may be reiterated, such as prevention of sexually transmitted infections. Unprotected sex between HIV-infected individuals may carry the risk of re-infection with a drug-resistant or more aggressive virus, which may accelerate disease progression.

Post-exposure prophylaxis (PEP)

In cases of exposure (e.g. through condom breakage), PEP may help patients prevent transmission of HIV to their partners. As described in detail in Chapter 4, PEP involves taking antiretroviral medication within 72 hours of a high-risk exposure to HIV. Knowledge of this intervention can help to increase the confidence of HIV-infected people 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 PEP for non-occupational exposure have been produced – 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 highly sophisticated understanding of their situation.

The clinician has a central role in interpreting test results and providing the patient with an understanding of his/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 individuals. 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 (Chapter 10), low levels of stress and regular exercise are recommended. Potential drug-related harms and drug interactions with antiretroviral therapy should be discussed.

TABLE 9.4 Assessment and monitoring of the HIV-infected patient

Three-monthly reviews in all HIV-infected patients:

- Collection of history and symptom review
- General physical monitoring
- Weight, blood pressure, oral and dental checks
- Full blood count
- Liver function tests and amylase
- CD4 cells and percentage
- Viral load
- Psychosocial assessment and support
- Patient education (transmission prevention and treatment updates)
- Health promotion (alcohol avoidance for HCV co-infected patients, smoking cessation, dietary adjustment)

Six-monthly reviews in all HIV-infected patients:

- Ophthalmological assessment if CD4 cell count is below 50 cells/ml (rule out asymptomatic CMV retinitis)
- Pap smears in women with previous evidence of cervical dysplasia. Anal smears are performed by some GPs but predictive value of subsequent anal carcinoma is unproven.

Annual reviews for all HIV-infected patients:

- Assessment of immunity to hepatitis B
- Vaccinations
- Cervical cytology by Pap smear in women

Additional monitoring for patients taking antiretroviral therapy

Treatment-related monitoring is primarily conducted by the antiretroviral prescriber

Frequent review during the first month of treatment:

- Monitoring for severe side-effects (e.g.hypersensitivity, Stevens-Johnson syndrome, CNS toxicity)
- Management of treatable side-effects (e.g. nausea, diarrhoea)
- Adherence monitoring and support. Tips to maximise adherence. Consideration of change of medication. Referral.

Three-monthly reviews:

- Assessment of potentially adverse effects of treatment (e.g. peripheral neuropathy, lipoatrophy, lipodystrophy)
- Ongoing adherence monitoring and support

Six-monthly reviews:

- Fasting cholesterol (including HDL and LDL), triglycerides, insulin and oral glucose tolerance
- Monitoring of serum lactate, particularly in symptomatic patients, to detect lactic acidemia related to nucleoside analogue therapy (the utility of this monitoring remains unclear)

Annual reviews:

- Physical assessment for lipodystrophy, including DEXA scan for assessment of fat and bone mineral density
- Assessment of cardiovascular risk factors (family history, smoking, hypertension, hyperlipidemia, insulin resistance)

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 providing information for clinicians and patients which is regularly updated. Treatment information for patients is also available from community organisations (Chapter 14).

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.[10] The relationship between viral load and treatment benefit from antiretroviral therapy has been analysed in over 5,000 patients enrolled in 18 clinical trials. These studies have shown that:[11]

- 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. Viral load reductions are always greater in treatment-naive individuals.

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 in Australia and overseas to guide decisions about commencing and switching treatment.[12,13]

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).[14] 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 30,000 copies/ml by bDNA (or greater than 55,000 copies/ml by RT-PCR).

Deferral is generally recommended if a patient's CD4 cell count is greater than 350/µl and viral load is lower than 30,000 copies/ml bDNA (or 55,000 copies/ml by RT-PCR).

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/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 14.

Treatment regimens

There are three classes of approved antiretroviral medications: nucleoside analogue reverse transcriptase inhibitors (NRTIs); non-nucleoside reverse transcriptase inhibitors (NNRTIs) and protease inhibitors (PIs). These antiretroviral drugs inhibit one of two viral enzymes – reverse transcriptase or protease. Anti-HIV medications and their side-effects are summarised in Table 9.5.

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 or 'start up' (e.g. headache), persistent (e.g. diarrhoea) or long term (e.g. lipodystrophy).[15] Each antiretroviral drug has its own particular side-effect profile with which the primary care clinician should be familiar (Table 9.5).

The patient should be supported through initial side-effects, most of which are very common and usually short-term (www.medscape.com/Medscape/HIV/Treatmentsupdate). 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. The mechanism underlying this syndrome and its treatment is currently under investigation.[16]

It is important to recognise a potential increased cardiovascular risk in patients with the development of insulin resistance and hyperlipidaemia. Appropriate management and attention to other risk factors such as hypertension and smoking is required.

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. These can be found at the following websites:
www.hiv-druginteractions.org and
www.georgetown.edu/departments/pharmacology/davetab.html.
Always check these 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 ecstasy by people taking PIs.

Drugs contraindicated with concomitant use of PIs and delavirdine 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 protease inhibitor ritonavir.

TABLE 9.5 Antiretroviral medications

Nucleoside/nucleotide analogue reverse transcriptase inhibitors*

Nucleoside analogue	Dose (adults)	Adverse effects
abacavir	300 mg bd	Hypersensitivity reaction (potentially lethal if rechallenged), headache, malaise, GI intolerance
Combivir (AZT/3TC)	300mg/150mg bd	See AZT and 3TC above
didanosine (ddI)	400 mg daily	GI intolerance, diarrhoea, taste disturbance,pancreatitis, peripheral neuropathy
dideoxycytidine (ddC)	0.75 mg tds	Stomatitis, oropharangeal ulceration, pancreatitis, peripheral neuropathy
lamivudine (3TC)	150 mg bd	Headache, nausea, diarrhoea
stavudine (d4T)	40 mg bd	Headache, GI intolerance, peripheral neuropathy, pancreatitis
tenofovir	300mg daily	Headache, GI intolerance, rare renal toxicity
Trizivir (abacavir, AZT/3TC)	300mg/300mg/150mg bd	See AZT, 3TC and abacavir above
zidovudine (ZDV, AZT)	250 mg bd	GI intolerance, malaise, headaches, macrocytosis bone marrow suppression, anaemia, 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.

Non-nucleoside reverse transcriptase inhibitors (NNRTIs)*

NNRTI	Dose (adults)	Adverse effects
efavirenz	600 mg qd	Rash, insomnia, somnolence, psychiatric disturbances, vivid dreams/nightmares, abnormal liver function tests, hyperlipidemia
nevirapine	200 mg bd	Rash, Stevens-Johnson syndrome, hepatitis
delavirdine	600 mg tds	Rash, headaches, abnormal liver function tests

Protease inhibitors (PIs)*

Protease inhibitor	Dose (adults)	Adverse effects
amprenavir (APV)	1,200 mg bd or 600 mg with 100 mg RTV bd	GI intolerance, rash, headache
atazanavir (ATZ)	400 mg daily or 300 mg/ 100mg daily with RTV	Elevated bilirubin, jaundice, nausea
indinavir (IDV)	800 mg td (fasting) or 800 mg bd with RTV 100 mg bd	Elevated bilirubin, GI intolerance, nephrolithiasis, ingrown toenails, dry skin, mouth and eyes, hair loss, diabetes, hepatitis
lopinavir/ritonavir (LPV)	400 mg/100 mg bd	GI intolerance, abnormal liver function, tests
nelfinavir (NFV)	1,250 mg bd	Diarrhoea, GI intolerance.
ritonavir (RTV)	100-200 mg bd as a pharmacokinetic enhancer of other ARV agents	GI intolerance, diarrhoea, hepatitis, abnormal liver function tests,
saquinavir (SQV)	1,200 mg tds or 1600 mg with 100 mg RTV once daily	GI intolerance, diarrhoea, headache

* Drug information current at March 2004. See ASHM website www.ashm.org.au for updated information.

Compliance 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/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.[17] Unfortunately, there is often significant cross-resistance within the same class of antiretroviral drugs[18] 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 domicillary 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.[19] 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 may be recommended to prevent some common opportunistic infections. Table 9.6 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.[20] For patients who have instituted prophylaxis and then experience immune reconstitution, 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 mark.

AIDS-related illness

Symptoms in the HIV-infected patient 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 symp-

TABLE 9.6 Recommended prophylaxis during HIV infection

Opportunistic infection	First-line prophylaxis	Alternative	CD4 cell count
Pneumocystis carinii pneumonia	cotrimoxazole 1 tab qd	dapsone nebulised pentamidine	200 cells/µl
Toxoplasmosis	cotrimoxazole 1 tab qd	dapsone/pyrimethamine	200 cells/µl
Mycobacterium avium complex	azithromycin 1,200 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

toms 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/or 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/AIDS primary management.

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10 Primary care management of chronic viral hepatitis

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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 some patients.
- For patients with chronic hepatitis C, the rate of progression to cirrhosis is usually very slow and antiviral treatment is not 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, between 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 30–50% 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.

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 diagnosis

The initial approach of the clinician must include consideration of the non-viral and viral aetiologies for hepatitis (Table 10.1). 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. 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 HBsAg, HCV antibody (anti-HCV) and HIV antibody (anti-HIV), as appropriate, following pretest counselling and informed consent (Chapter 8). 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.

TABLE 10.1 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 and 5.5)
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	

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 ALT are at higher risk of significant liver damage and disease progression, even patients with normal liver enzymes may be at risk of progressive disease.

Patients with positive anti-HCV and persistently normal ALT 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 Tables 10.2 and 5.5 for a summary of serological and virological markers.

TABLE 10.2 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 HCC.

For patients with chronic hepatitis C, ongoing monitoring is recommended every six to twelve 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 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 (low platelet count or 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, desire for pregnancy, et cetera.

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 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/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 14).

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 10.3 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/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.

Hepatocellular carcinoma is becoming a major clinical problem in patients with HCV-associated cirrhosis. The current recommendations regarding screening for hepatocellular carcinoma include ultrasound and alpha-fetoprotein 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 infected 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 immuneclearance phase, and some can continue to have hepatitic 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 10.2) 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/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 $<10^4$ copies per 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.

TABLE 10.3 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

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 alpha-fetoprotein;
- liver ultrasound if cirrhotic or family history of HCC.

HBsAg+, HBeAg-negative females 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, males 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 alpha-fetoprotein 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>2 times 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, bloodborne 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.

There clearly is a risk of transmitting HCV from mother to child, although the risk is low (approximately 5%).[4] This risk is significantly higher if the mother is coinfected with HIV.

Currently, there is no indication for elective caesarean section in HCV-positive mothers.

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[5], 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 HBV-infected individuals are migrants who contracted infection as infants.

With universal HBV vaccination of neonates and administration of hepatitis B immunoglobulin to infants of HBV-infected mothers, there are very few new cases of vertically acquired HBV in Australia.

TABLE 10.4 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

Most cases are acquired sexually or through direct blood-to-blood contact. HBV-infected individuals 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/infection is discussed in detail in Chapter 2. Communication of safe sex and safe injecting messages is covered in Chapter 3 and Appendices.

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 7-8 standard drinks (70-80 grams alcohol.[6] 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 10.4. Individuals with cirrhosis should be encouraged to stop drinking alcohol.

Individuals 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 the focus of attention, rather than the presence of chronic hepatitis B or C. Referral to treatment programs and support groups may be appropriate.

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.[7] 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 fall 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

Coinfection 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 coinfection tend to be more likely to progress to cirrhosis and to develop hepatocellular carcinoma. 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 14).

Referral to counselling or support services may be indicated for patients with complex emotional, family/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 14).

TABLE 10.5 Treatments for hepatitis B and C. Section 100 Highly Specialised Drugs Program of the PBS*

Treatment	Condition	Criteria	Caution
Lamivudine (Zeffix) 100 mg daily taken orally	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	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	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 viral positive at week 12 but have attained at least a 2-log drop in 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.	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) 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.	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+	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.

*Details correct at April 2006.

**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.

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.[8,9]

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 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. 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 and normal ALT values 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 10.5.

The combination of pegylated interferon and ribavirin produces an overall SVR of greater than 50%,[10,11] 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/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). 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 twelve months' duration, depending on HCV genotype.[12] When discussing the benefits and risks of treatment, the general practitioner 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 a significant number 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/HBV coinfection, HCV/HIV coinfection, chronic renal failure, cryoglobulinaemia and with HCV recurrence after liver transplantation.

HIV/HCV coinfection

HIV/HCV coinfection is associated with higher HCV viral load and an accelerated rate of HCV disease progression.[13] There is no fundamental difference to the management of HCV in the presence of HIV. Patients with HIV/HCV coinfection who have stable CD4 cell counts on antiretroviral therapy, with ongoing evidence of active HCV, may be considered for combination pegylated interferon plus ribavirin. Such management s difficult, particularly in patients already taking multiple medications, as side-effects, drug interactions and poor tolerability are common.[14]

Who should be treated for hepatitis C?

Antiviral therapy is currently reimbursed for patients who are 18 years or older with:

- anti-HCV positive;
- detectable serum HCV RNA;
- compensated liver disease;
- no prior 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 10.5 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/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 s100 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

The first treatment available for patients with chronic hepatitis B was interferon alfa (see Table 10.5). Currently, the nucleoside analogue lamivudine is available for the treatment of hepatitis B

through Section 100 of the PBS.[15,16] Pegylated interferon alfa 2a, adefovir dipivoxil (a nucleotide analogue) and entecavir (a nucleoside analogue) are also approved for the treatment of patients with chronic hepatitis B.

A 4- to 6-month course of interferon is associated with HBeAg loss in 30–40% of patients and, in early trials, approximately 10% lost HBsAg.[17,18] 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 but is ineffective against HBeAg-negative mutant HBV. 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.[19,20]

Lamivudine (100 mg daily) is highly effective in suppressing HBV replication and improving liver histology. The rate of HBeAg seroconversion after 12 months of lamivudine therapy is comparable to that after 4 to 6 months of interferon, and increases with longer treatment to over 70% at four years.[21] It is very effective against HBeAg negative mutant HBV and is useful in both compensated and decompensated cirrhosis. Cessation of lamivudine treatment is, however, frequently associated with virological and biochemical relapse. Unfortunately, lamivudine therapy is also associated with the emergence of resistant strains (YMDD variants), and 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.

Lamivudine is extremely well tolerated, with a side-effect profile that is no different from placebo. However, the emergence of lamivudine resistance may be associated with a flare of hepatitis, during which the patient may develop symptoms of tiredness, right upper quadrant discomfort and possibly jaundice and hepatic decompensation.

Patients with lamivudine resistance should continue to take lamivudine, as its cessation may result in a severe flare of wild-type infection. Addition of adefovir dipivoxil is extremely effective in patients with lamivudine resistance.[22] 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. Lamivudine and adefovir should be given together for at least three months. Adefovir monotherapy may be associated with emergence of drug-resistant mutants which may be associated with a clinical flare of hepatitis. In HIV-HBV co-infected patients with lamivudine resistance, tenovir is extremely effective at suppressing HBV replication and improving hepatic function. Other antiviral agents are currently in clinical trials.

Recently adefovir and entecavir have been approved for use in patients with chronic hepatitis B. Both drugs are associated with low rates of antiviral drug resistance, offering significant advantages over lamivudine. It should be noted that adefovir is only available as an Section 100 alternative if lamivudine has failed and entecavir is not reimbursed for treatment of HBV.

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 six to twelve 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 long-term treatment.

Patients who are HBeAg-negative with abnormal LFTs should have an HBV DNA performed.

If this is positive, then liver biopsy and treatment with lamivudine 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 hepatocellular carcinoma. Detailed management of end-stage liver disease is beyond the scope of this publication but management of some specific complications is discussed in Chapter 11.

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 general practitioners, specialists and referral centres is required for optimal patient management.

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11 Palliative care

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Introduction

The introduction of combination antiretroviral therapy has improved the prognosis of individuals with HIV/AIDS and reduced the number of AIDS-related deaths, although progression to advanced disease and death still occurs among people with HIV. In the context of treatment optimism, symptom management and palliative care of people with advanced HIV/AIDS provides new challenges, both medical and psychosocial, to health professionals.

The impact of antiviral therapy on mortality due to chronic viral hepatitis is as yet unclear. A substantial number of individuals with cirrhosis and a number with hepatoma are in need of appropriate symptom management, complication control and palliation.

People in the advanced stages of disease often have concerns that there will inevitably be severe pain, loss of independence and loss of dignity. The aim of palliative care is to improve quality of life by focusing on the management of symptoms and the provision of physical, psychological, social and spiritual support. Good symptom management and psychosocial support, embodying the principles of palliative care, will enable most people to maintain independence and enjoy life even with very advanced disease.

Key points

- Shared care is crucial to the management of palliative care for people with advanced and terminal AIDS and viral hepatitis. The care team may comprise the general practitioner, relevant specialists, a social worker or counsellor, a palliative care nurse specialist and clergy. The patient, family members and other carers may be included in the care team.
- Individual palliative needs are best met in the context of supportive partners and family, who also need consideration. Support and counselling for family, partners and friends may be undertaken by the GP or other members of the care team.
- Stigma and fear associated with HIV/AIDS and viral hepatitis may influence the needs of the patient in relation to psychosocial support and preparations for death.
- The patient should be encouraged to attend to his/her affairs prior to advanced disease by writing a will and by granting 'power of attorney' to a trusted individual.
- Assessment and management of pain are important features of palliative care, regardless of a patient's use of recreational or illegal drugs.
- Treatment of specific conditions may relieve pain and suffering and improve quality of life.

Issues impacting on provision of palliative care

Clinicians caring for people with HIV/AIDS and viral hepatitis should be aware of the following issues which may impact on the patient, his/her carers and family.

'Positive living' philosophy

The opportunity should be given to patients to discuss dying if they are ready to do so. However, individuals with very real fears of dying may not want to talk about death, particularly in the era of optimism associated with modern treatments. In addition, the cycles of health and ill-health common in HIV/AIDS may make the identification of end-stage disease difficult for patients, family and health professionals. It is quite possible for individuals to experience improved health after medical interventions associated with palliative care. This is illustrated in Case study 1.

Fear, stigma and confidentiality

Patients may not wish family and/or community support agencies to be aware of their HIV or hepatitis status due to fear of discrimination or rejection. Confidentiality issues may be of

particular concern in rural and remote areas, and in some cultural groups. These concerns may extend to consideration of the certified cause of death on the death certificate. The clinician may provide reassurance and assistance with appropriate disclosure, and explain the process of certification of death to assist individuals deal with these fears.

Sexuality and legal issues

A substantial proportion of people with HIV/AIDS in the developed world are gay men and issues of 'ownership' of person and property can be a source of conflict between a gay man's family and his lover, particularly around the time of death. All patients should be encouraged to attend to their affairs prior to advanced disease by appointing a 'legal guardian' (who is empowered to make treatment decisions if the patient becomes incapable of such decisions) and by making a will and leaving instructions regarding funeral and burial/cremation arrangements. Legal provisions relating to 'power of attorney' exist at the State and Territory level and referral to appropriate legal advice may be obtained from local community groups such as AIDS Councils (Chapter 14).

Grief and loss issues

Many gay men, drug users and haemophiliacs with HIV and/or viral hepatitis have been exposed to multiple losses, with family members, friends and partners pre-deceasing them. Cumulative grief responses may manifest in many ways, such as unexpected and extraordinary reactions to what are seemingly trivial events. This sense of cumulative loss may impact on the person's ability to cope and may complicate fears relating to his/her own death. The provision of psychosocial and counselling support is vital. Following a death, referral to community projects, such as the AIDS Memorial Quilt, may be offered to partners, family members or friends to assist them to cope with their grief. Referral to a bereavement counselling service may sometimes be indicated if risk factors for a complicated bereavement are present.

Complexity of treatments and disease

People with advanced HIV/AIDS often require concurrent and continuous treatments for several AIDS-related conditions with a wide range of drugs with potential interactions and side-effects.[1] The complexity of advanced HIV disease, due to coexistent opportunistic infections, malignancies, adverse events and/or metabolic disorders, may present a challenge for patients and their families in understanding disease processes and making treatment decisions. The question of when to cease combination antiretroviral therapy is difficult and must be negotiated with the patient. Some individuals choose to continue with active treatments until they are very close to death but these do not preclude treatments to alleviate distressing symptoms and pain management.

CASE STUDY 1

Palliative care: antiretroviral treatment can lead to recovery

Recovery following 'palliative care'

A male patient with severe wasting in the advanced stages of AIDS is prescribed morphine and midazolam for relief of discomfort and anxiety. After assessment by a general practitioner experienced in HIV/AIDS, the patient is admitted to an HIV/AIDS specific palliative care unit. On discussion, it is evident that he is keen to pursue life-prolonging treatments including enteral feeding and antiretroviral combination therapy. Under the joint management of infectious diseases and palliative care specialists, his condition improves to the point where he is discharged with community supports. The man remains well in the community three years after his time as a palliative care patient.

Recreational or illicit drug use

The use of substitution drugs may be required when a person is admitted to a hospital or palliative care unit to avoid the effects of withdrawal or unmasked pain.[2] Because individuals with HCV, HBV or HIV may have injected drugs, coexistent or past drug addiction may be an issue in their palliative care. It is well recognised that undertreatment for pain, anxiety or psychological stress has been a feature of the management of individuals thought to be addicted to, or potentially addicted to, alcohol, opiates or benzodiazepines.

The fact that patients have used or continue to use recreational or illegal drugs should not preclude the effective use of appropriate analgesics after careful evaluation. High doses may be required to provide effective pain relief in individuals with a history of opiate usage.[3,4] Acknowledgement of the equal intensity of symptoms and the right to relief of those symptoms in all patients are fundamental principles of palliative care. Consequently, assessment of an increased need for opiates and effective dosing in tolerant individuals is appropriate.

TABLE 11.1 Opiates and drugs for pain relief in palliative care

Opiates used in palliative care
• Morphine
• Diamorphine
• Methadone
• Hydromorphone
• Oxycodone
• Fentanyl
Drugs used for neuropathic pain
• Methadone
• Ketamine
• Antidepressants, e.g. amitriptyline, sertraline
• Anticonvulsants, e.g. carbamazepine, gabapentin, sodium valproate
• Anti-arrhythmics, e.g. mexiletine, flecainide
• Clonidine

Cannabis may be used by patients with AIDS wasting to reduce pain and nausea, and to stimulate appetite. The potential benefits of marijuana (e.g. weight gain) should be seen within the context of risk (e.g. bacterial lung infection), particularly among individuals with severe immune suppression.[5]

Caring for patients who use illicit drugs may be complicated by factors such as homelessness, poverty and mistrust.

Loss of autonomy

A patient may nominate a partner, friend or family member as his/her advocate or 'legal guardian' in the event of cognitive impairment or coma. Such a person may be empowered to make treatment decisions on behalf of the patient. This may be particularly appropriate where the patient is alienated from the next-of-kin ('Sexuality and legal issues' page 97).

Euthanasia

Some patients with terminal disease consider self-deliverance in the form of euthanasia or suicide.[6] Euthanasia may be seen as a legitimate answer to the relentless progress of the disease, loss of independence and to the perception of being a burden to carers, lovers and families.

Acknowledgement of the patient's consideration of euthanasia as an option can provide significant reassurance. Psychiatric evaluation and support should be routinely offered, as a depressive illness may warrant treatment and psychological support.

Doctors and health professionals should be prepared to discuss requests for euthanasia and must determine their own responses to such requests. They may perhaps be prepared to refer patients to a clinician experienced in euthanasia issues if uncomfortable with euthanasia themselves.[7] Euthanasia is currently illegal in Australia.

A collaborative approach to providing palliative care

As can be seen from the kinds of issues described above, people in the terminal phase of HIV/AIDS or viral hepatitis require access to a continuum of care encompassing symptom management, respite care, rehabilitation, terminal care and psychosocial support. Such care can be provided in a range of settings including the home, an acute medical unit, an AIDS-specific continuing care or palliative care unit and in a general hospice or palliative care in-patient unit.

It is important that this care is provided in conjunction with an appropriate range of medical and psychosocial specialists. The primary care clinician may take an active role in coordinating a patient's care team by liaising with local services such as support groups, home-care services, and hospital- or hospice-based social workers, nurses and specialists.

Palliative care physicians, HIV specialists, hepatologists and general practitioners may assist each other with:

- assessing the pathophysiology of symptoms;
- managing palliative therapeutics;
- clinical decision-making in advanced disease;
- managing nutritional deficiency and fluid retention in end-stage liver disease;
- identifying and responding to the psychological, social and spiritual components of suffering, and making appropriate referrals;
- breaking bad news to patients and families;
- liaising between hospital and home care;
- other medical management of the terminal phase.

Pain management

Pain is common in advanced disease and is often underestimated and undertreated.[8] Common types of pain in people with HIV/AIDS are peripheral neuropathy, headache, abdominal pain, perianal pain and mouth pain. Side-effects of treatment may lead to the need for pain relief.

Pain needs to be carefully assessed using patient self-rating and monitoring tools to isolate causes and facilitate treatment and intervention. There is a strong association between psychosocial status and pain intensity, hence the existence of potentially helpful non-pharmaceutical pain management strategies such as clinical hypnosis and emotional and spiritual support.

Drugs for pain management

Analgesic drug use should follow the World Health Organization (WHO) analgesic ladder progressing from mild analgesics (e.g. paracetamol) to a combination of mild analgesics with a weak opioid (e.g. paracetamol plus codeine) or possibly tramadol before using strong opiates. Other drugs may be more effective for specific types of pain including: nonsteroidal anti-inflammatory drugs; antidepressants (principally tricyclics); anticonvulsant drugs; antispasmodic drugs; local anaesthetic, and ketamine. Opiates used in pain management include morphine, methadone, hydromorphone, oxycodone and fentanyl (Table 11.1). The main indication for substituting other opiates is where morphine is not well tolerated. With the exception of methadone for neuropathic pain, other opiates are unlikely to provide improved analgesia where morphine has failed.

Routes of administration include oral, subcutaneous, transdermal (fentanyl) and (very rarely) intrathecal (Case study 2). Advice from specialists in the field may be useful for primary care clinicians who are unfamiliar with the drug combinations, dosage ranges and methods of administration which are routine in palliative care.

Neuropathic pain

Painful peripheral neuropathy is common in HIV/AIDS, occurring in up to 30% of patients, and post-herpetic neuralgia, while less common, can be equally disabling.[9] Abolishing pain completely without unacceptable side-effects may be extremely difficult but the use of anticonvulsants, antidepressants, morphine and other opiates, sometimes in relatively high doses, can result in significant improvement.[10] The total daily dose of morphine may be as much as 3,000 mg or more.

The use of adjuvant drugs such as tricyclic antidepressants, anticonvulsants, local anaesthetic anti-arrhythmics (such as mexiletine) in conjunction with analgesics can improve management; however, the response of individual patients is unpredictable and often disappointing.[11] Methadone or ketamine may provide improved analgesia (associated with NMDA receptor antagonist activity) but advice regarding their use should be sought from specialists in pain management or palliative medicine.[12] There is increasing interest in the role of the anticonvulsants gabapentin and lamotrigine in neuropathic pain management, and intrathecal or epidural morphine is a recognised treatment option for intractable pain, but there are no published studies of its use in patients with HIV/AIDS.[13]

Management of other symptoms

AIDS and opportunistic illnesses

Other symptoms in patients with advanced HIV/AIDS may include debility and weight loss, fatigue, anorexia, nausea, depression, diarrhoea, constipation, dyspnoea, cognitive impairment, dysphagia and neurological deficits.[14,15,16]

Symptoms due to opportunistic infections such as candidiasis, herpes simplex, *Mycobacterium avium* complex, *Pneumocystis carinii* pneumonia, toxoplasmosis or cryptococcosis are best

CASE STUDY 2

Palliative care: use of intrathecal morphine

Severe peripheral neuropathy

A patient with advanced HIV disease presents to his GP complaining of severe peripheral neuropathy. The man's health improves following commencement of combination antiretroviral therapy but his peripheral neuropathy persists. After careful consideration and joint assessment by a palliative medicine consultant, an infectious diseases physician, a pain management anaesthetist and a neurologist experienced in the use of intrathecal morphine, the patient has an intrathecal drug administration system implanted. Three years later the intrathecal morphine dose remains stable at 30 mg per 24 hours and his oral morphine daily dose, which has previously been as high as 2,500 mg, has been reduced to 200 mg daily. His quality of life is much enhanced.

alleviated by treatment with appropriate antibiotics. Some drugs used for symptom management such as cisapride, non-sedating antihistamines, midazolam and carbamazepine may have significant interactions with antiretroviral drugs, particularly protease inhibitors. Where there is concern about a particular drug, discussion should be sought with physicians or pharmacists.

Diarrhoea

Diarrhoea which persists after appropriate assessment and/or treatment by an infectious diseases physician and gastroenterologist warrants pursuit of symptomatic management. Dietetics advice may assist where there appears to be intolerance to specific foods or supplements. Drugs which may alleviate symptoms include loperamide, diphenoxylate, codeine phosphate, opiates and bulking agents. A trial of a somatostatin analogue (e.g. octreotide) may be considered.

End-stage liver disease

Treatment is available for several conditions associated with end-stage liver disease. For patients who are not transplant candidates, dramatic improvements in quality of life may occur following dietary intervention or treatment for ascites or encephalopathy.

Malnutrition is prevalent during end-stage liver disease, compounding fatigue, wasting and weakness. Dietary interventions may include increased calorie intake (e.g. night snacks) and consumption of proteins and protein supplements such as Sustagen or branch chain amino acids. Consultation with a dietitian may be considered.

Fluid retention or ascites is another common feature of end-stage liver disease that impacts on nutrition and mobility of the individual. Management may be dietary (e.g. salt restriction), medical (e.g. diuretics) or surgical (e.g. paracentesis). For intractable ascites, consideration may be given to insertion of TIPSS (transjugular intrahepatic porto-systemic shunt) or to a peritoneovenous shunt.

Chronic encephalopathy may improve upon protein restriction but the laxative lactulose is the mainstay of management. Long-term prophylactic treatment with the antibiotic norfloxacin may improve or prevent bacterial translocation across the bowel wall and prevent spontaneous bacterial peritonitis, as well as improve encephalopathy and reduce the risk of gastrointestinal bleeding.

TABLE 11.2 Pharmacological treatment of terminal restlessness

Useful drugs	Single dose range
clonazepam	0.5 mg to 5 mg
midazolam	2 mg to 15 mg
diazepam	2 mg to 40 mg
haloperidol	2 mg to 20 mg
morphine	2.5 mg to 400 mg
phenobarbitone	100 mg to 400 mg

N.B. Very high doses are necessary only in exceptional circumstances. The correct dose is the lowest effective dose.

Terminal care

Health care professionals, families and other carers may find it difficult to make the transition from active care to terminal palliative care, even if the patient is unconscious or heavily sedated. Discussing the withdrawal of hydration and/or nutrition, for example, requires great sensitivity and flexibility. The patient may need strong advocacy and the patient and family may need intensive pastoral support throughout this period.

Of paramount importance is the relief of any pain or other distressing symptoms. Causes of distressing symptoms should be explored and treated if appropriate and consistent with treatment objectives. Investigations should be kept to a minimum and only performed if the information obtained is likely to result in improved symptom management. Patients often state their acceptance of drug treatments for relief of symptoms even if their level of consciousness becomes impaired.

Restlessness or delirium may be a cause of considerable distress to the patient, his/her family and health care professionals, and it is essential to relieve such symptoms. Restlessness in most patients can be well managed with benzodiazepines including midazolam, clonazepam and diazepam but may require large or escalating doses (Table 11.2). In addition, consideration should be given to alleviating the causes of restlessness (such as pain, retention of urine, constipation and faecal impaction, psychotic symptoms and anxiety).

Patients in the terminal phase of their illness must have the option of absolute and continuous relief of distressing symptoms. If there is any doubt as to the adequacy of symptom management, consideration should be given to transferring the patient to a specialist palliative care unit or seeking assessment by a palliative medicine

physician or clinical nurse specialist. The use of regular, preferably continuous, drug administration will be necessary to avoid fluctuation in levels of symptom management. Ready access to nursing and medical support is essential.

Counselling (by social workers, clergy or other appropriately trained health care workers) may assist partners, families and friends to deal with their grief at this stage and throughout the final weeks of illness.

The proper management of terminal care will assist in the grieving processes of those who are left behind. Ongoing support should be available as necessary throughout the bereavement period, and those showing signs of abnormal grieving identified and referred for specialist support.

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12 Standard precautions and infection control

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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 conceptualised, based on the US CDC 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 reduce the potential for stigma and discrimination. They 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, as well as some other infections. Standard precautions should be implemented universally, regardless of information or assumptions about infection status. Transmission based precautions are further measures required to prevent transmission when a particular infection, that has a different transmission route, is established or strongly suspected, such as in the case of tuberculosis.

This chapter provides a summary of the most recent Australian infection control guidelines published by the National Health and Medical Research Council (NHMRC) and draws on the *HIV Guidelines for GPs* published by the Royal Australian College of General Practitioners, as well as other guidelines.[1,2,3,4] The NHMRC guidelines describe in detail the practices and procedures necessary to prevent transmission of blood-borne infections, including HIV, HBV and HCV and review of these guidelines is strongly recommended for individuals implementing infection control procedures. In addition, compliance with relevant State and/or Territory guidelines is mandatory

Implementation of standard precautions minimises the risk of transmission of blood-borne and some other infections from health care worker to patient, from patient to health care worker and from patient to patient. Some clinicians or health care workers may feel uncomfortable about implementing standard precautions, which they believe may alienate patients. If this is the case, the health care worker may reassure the patient that protective procedures and equipment are normal protocol which exist to protect both patients and staff. Clinic-based infection control protocols, recommended by the NHMRC, should be developed and consulted where staff are not following appropriate procedures.

Infection control guidelines are relevant in social and domestic contexts as well as occupational settings. The clinician should be ready to answer questions from patients about a clinic's infection control policies and provide advice for

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: aseptic technique; barrier protection; safe disposal systems; correct sterilisation and disinfection processes, and the appropriate use of instruments and equipment.
- Vaccination is an important infection control strategy for HBV and HAV; all health care workers should be aware of their vaccination 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.
- Referral should be made to the most recent NHMRC Infection Control Guidelines and relevant State and Territory guidelines.

patients in relation to infection control in their daily environment.

Transmission

Modes of transmission are outlined briefly in Table 12.1 and risk of transmission is discussed in more detail in Chapter 2. In the health care setting, incidents involving blood-to-blood contact with infected individuals are associated with a marked risk of transmission, with the greatest risk being associated with:

- the presence of a large quantity of blood, indicated by visible contamination;
- placement of a needle directly into a vein or artery or deep injury;
- advanced HIV disease, high HIV viral load, positive HCV PCR, or HBeAg in the source.

In relation to HCV, patient-to-patient transmission has been associated with endoscopic procedures and a failure to comply with recommended cleaning and disinfection protocols.[6,7,8,9]

TABLE 12.1 Mode of transmission and recommended precautions[5]

Disease	Mode of transmission	Recommended precaution
HAV	Contact (oral-faecal route)	Standard precautions Additional precautions for incontinent patients
HBV	Direct contact with blood or body substances	Standard precautions
HCV	Direct contact with blood or body substances	Standard precautions
HIV	Direct contact with blood or body substances	Standard precautions Additional precautions for complications, e.g. TB

Standard precautions

Standard precautions should be applied in the handling of:

- blood (including dried blood);
- all other body fluids, secretions and excretions (excluding sweat) regardless of visible blood;
- non-intact skin;
- mucous membranes.

Standard precautions, including high levels of cleanliness, generally provide staff and patients with adequate protection against blood-borne viruses. Standard precautions include aseptic technique, barrier protection, safe disposal systems and the appropriate use of instruments and equipment, as outlined below.

Hand-cleaning and skin integrity

Hand-cleaning must occur:

- before and after each clinical client contact;
- before and after eating;
- after using the toilet;
- before and after use of gloves;
- after contact with used equipment;
- immediately following contact with body fluids.

Hand jewellery, ideally, should be removed and hands cleaned with cleaning solution (detergent with or without disinfectant) and water for 15–20 seconds, followed by drying with a single-use towel. Healthy, unbroken skin provides a valuable 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 standard precaution and must be used when:

- handling any blood or body fluids;
- performing venepuncture;
- touching mucous membranes;
- touching non-intact skin;
- handling contaminated sharps;
- performing any invasive procedure;
- cleaning body fluid spills or any equipment (instruments) or materials (linen) or surface that may have been contaminated by body fluids.

NHMRC guidelines provide detailed instructions on appropriate use of sterile and non-sterile gloves.

Other protective clothing

Additional protective clothing is required in the following circumstances:

- face masks and/or goggles if splashes are likely;
- gown and/or plastic apron if soiling is likely;
- footwear should be enclosed and protective against injury if sharp items are being used.

TABLE 12.2 Exposure-prone procedures[10]

Risk	Procedure
High-risk or 'exposure-prone' procedures	• Any submucosal invasion with sharp, hand-held instruments or procedures dealing with sharp pathology/bone spicules, usually in poorly visualised or confined spaces (e.g. orthopaedic surgery, trauma, internal cavity surgery)
Variable-risk procedures	• Minor dental procedures (excluding examination), routine dental extractions • Internal/instrument examination/biopsy (e.g. endoscopy, vaginal examination, laparoscopy) • Minor skin surgery
Low-risk procedures	• Interview consultation, dental examination • Non-invasive examinations or procedures (aural testing, electrocardiograph, abdominal ultrasound) • Intact skin palpation (gloves not required) • Injections/venepuncture (gloves required)

Needle-stick injury prevention

To minimise the risk of a needle-stick injury, sharps and clinical waste should be handled carefully. Specifically:

- Minimise handling of sharps and clinical waste.
- Do not bend or recap needles.
- Do not remove needles from disposable syringes.
- A safe needle-handling system should be provided including rigid containers for disposal. These should be kept out of the reach of toddlers and small children.
- 'Sharps' containers should be at point of use or in close proximity to work sites to aid easy and immediate disposal.

Health care workers

Vaccination

Vaccination is an important infection control strategy for HBV and HAV. The NHMRC and some State and Territory health departments provide guidelines on the screening and vaccination of health care workers. All health care workers and other staff who may come into contact with blood or body fluids should be aware of their HBV vaccination status and be vaccinated if appropriate. Health care workers who are unable to demonstrate HBV immunity after supplementary doses of HBV vaccine may need to be advised regarding the risks relating to their professional practice. (Chapter 5 provides a detailed discussion of exposure management and vaccination regarding viral hepatitis.) Demonstration of active antibody production after vaccination is now viewed as conferring lifelong immunity to the vaccinated, immune-competent adult.

HAV vaccination is recommended for health care workers at increased risk of exposure, such as those working with people with intellectual impairment, children, or people from rural and remote indigenous communities. Serology can be used to assist in the assessment of the need for HAV vaccination.

No vaccination is available for HIV or HCV.

Testing

The mandatory testing of health care workers (including general practitioners) for HIV and viral hepatitis is not warranted, due to the low risk of transmission if standard precautions are followed. NHMRC guidelines state that testing should only be undertaken on the basis of clinical assessment or where testing is in the interests of patients and health care workers (e.g. a needle-stick injury). Clinicians and other health care workers who regularly perform exposure-prone procedures (Table 12.2) have a responsibility to be regularly tested for HIV, HCV and HBV if not immune. The provisions of confidentiality, privacy and consent for testing should be applied.

Infected health care workers

Health care workers who are aware that they are infected with a blood-borne virus should consult state regulations to determine what restrictions are placed on their practice. In general it is recommended that they do not perform procedures that carry a high risk of transmission of the virus from health care worker to patient. Table 12.2 details the level of risk associated with specific procedures.

Infection control in the clinic

The NHMRC infection control guidelines provide detailed information relating to specific issues, 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.

Points that relate to prevention of 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 single-use only. 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 razors blades must 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.

Incident management

Body fluid spills (includes blood and body substances)

Management of spills will depend on the nature of the spill, likely pathogens, type of surface and the area involved. A spills kit of cleaning equipment can be assembled to assist in urgent situations. In general:

- All spills must be dealt with as soon as possible.
- 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.
- Use cold water if blood is present, to prevent coagulation.

Injury

If an injury or incident occurs where body fluids come into contact with non-intact skin/ membranes, the following action should be taken:

- Wash exposed membrane or injury with cleaning solution and water (chlorhexidine as a disinfectant can be used on the skin).
- If eyes have been exposed, rinse eyes with tap water or saline.
- If mouth has been exposed, rinse mouth with water and spit out.
- Seek medical advice immediately, as post-exposure prophylaxis (PEP) treatments are available for HIV and HBV.
- If it is a significant exposure and if the source is known, he/she should be approached regarding consent for HIV antibody, HCV antibody and HBsAg testing in conjunction with PEP.

For more information, contact the NSW 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 needle-stick injury or other occupational exposure.

In cases of accidental exposure to blood or body substances, testing procedures and all follow-up treatment should be fully documented.[3]

Post-exposure prophylaxis (PEP) in the health care setting

Treatments given as soon as possible within 72 hours of exposure may 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 get appropriate advice, as this area is constantly changing. Blood should be taken prior to or shortly after administration of PEP to check for prior exposure or infection. Chapters 4 and 5 contain further details.

HIV PEP in the health care setting

- HIV PEP is recommended for significant percutaneous exposure to blood involving a high risk of HIV transmission.
- HIV PEP is offered (but not actively recommended) for ocular mucous membrane or non-intact skin exposure to blood or body fluids.
- HIV PEP is not offered for exposure to any non-bloody urine, saliva or faeces.[2]

HBV PEP in the health care setting

- If the exposed person is not immune to HBV, or is of unknown immune status, HBV immune globulin 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 (Chapter 5).

There is currently no PEP for HCV

Legal and ethical issues

Legal liability may occur if inadequate care has been taken to prevent the transmission of infection. Regulatory authorities (e.g. environmental protection) and Commonwealth, State, Territory and local governments enforce laws and regulations relating to infection control and waste disposal. Their requirements can vary considerably throughout Australia and such requirements should take precedence over the general information presented in this chapter. Contact State and Territory health departments and medical and other professional boards for further details (Chapter 14). Legal issues are considered in greater detail in Chapter 13.

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 perceived risk, infection control procedures must be followed in all clinical settings to minimise the risk of accidental transmission of these diseases.

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Legal responsibilities

13

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Introduction

The legal responsibilities of clinicians in relation to blood-borne viral infections are shaped by two key principles: the protection of public health and the protection of individual rights. These principles are embodied in practices such as obtaining informed consent before testing, complying with notification requirements, ensuring the maintenance of confidentiality and the provision of non-discriminatory care. In some situations, a clinician may face conflicting responsibilities and be required to balance duty to the community at large with duty to the individual patient. For example, a breach of the duty of confidentiality to an individual patient may be necessary to protect the broader community from harm. Generally, however, respecting the rights of the individual patient optimises public health outcomes.

This is the principle that was expressed by Justice Michael Kirby when he described the 'AIDS paradox':

> *My basic thesis is that, paradoxically, the protection of the human rights of persons at risk is the most effective way of arresting or slowing the spread of the virus. This is the AIDS paradox.*
>
> *By a paradox, [it is meant that] one of the most effective laws we can offer to combat the spread of HIV, which causes AIDS, is the protection of persons living with AIDS, and those about them, from discrimination. This is a paradox because the community expects laws to protect the uninfected from the infected.*[1]

The law can, as part of an integrated approach involving treatment, education, patient advocacy, appropriate media coverage and changing community understanding, provide a supportive environment to minimise the spread of blood-borne viruses and to encourage effective responses to treatment and containment. This not only benefits the lives of those infected but also limits the effects of HIV, HBV and HCV on the wider community.

Public health laws are generally of two types: punitive or protective. Punitive laws criminalise or punish certain types of behaviour. There are also laws that require certain actions to be carried out, such as notification of prescribed diseases. Protective laws are those that protect or promote certain behaviours; for example, anti-discrimination laws or laws that ensure equal access to health care. Other than the *Quarantine Act 1908* (Cth), which does not apply to blood-borne viruses, there is no Commonwealth legislation that deals with public health. Instead, the States and Territories have their own legislation. These laws are generally similar in content. In addition to legislation or 'statutory' laws, the 'common' law plays a significant role in health law. The common law is law made by judges as they decide individual cases.

Key points

- Clinicians are responsible for:
  - obtaining informed consent before testing for blood-borne viruses and facilitating informed decision making by patients;
  - complying with notification requirements;
  - ensuring the maintenance of confidentiality;
  - providing non-discriminatory care for those infected;
  - warning a patient, if a doctor or another patient is a potential hazard to the patient.
- Clinicians have a duty of care to their patients to diagnose HIV and viral hepatitis as well as a duty of care to protect the sexual partners of these patients from infection.
- Clinicians must follow-up patients when test results are positive.
- Clinicians have a duty to prevent foreseeable harm.
- Full documentation of pre-test and post-test counselling, recommendations and follow-up is required and may be used to assist the defence in the event of a legal challenge.

Testing

Given that the consequences for the patient of either being tested or not being tested for a blood-borne virus may be considerable, it is wrong to treat tests for such pathogens as 'standard' or 'routine', if that term implies the lack of a need for informed consent specific to each test. Principles of medical ethics, as well as laws, require that all medical procedures, including testing for HIV, HBV and HCV, be carried out only after the patient has provided informed consent for the procedure. Consent is valid only if it is given without coercion by an informed and competent patient. In some jurisdictions and with respect to some diseases (most notably HIV), these obligations are made explicit by statute. The provision of treatment without consent constitutes a trespass. However, where consent has been obtained in broad terms that is, the patient has been informed about the nature and general purpose of the proposed procedure, but there was a failure to disclose material risks, there is no trespass but there is negligence. Whilst commonly referred to as 'failure of informed consent', this is more properly described as 'disclosure negligence'.

In addition to the statutory obligations imposed on clinicians that either specifically or generally impact on the management of patients infected with blood-borne viruses [most specifically Section 7 (s.7) *HIV/AIDS Preventive Measures Act 1993* (Tas)], there also are common law obligations.

The doctor must provide sufficient information to ensure the patient's right of 'self-determination' has been satisfied. The concept of 'informed consent' is too narrow when 'informed decision making' is required. A patient may decide to accept or reject the doctor's advice. A decision to refuse the doctor's advice must be seen to be as fully 'informed' as one to accept the advice, both ethically and as a matter of law. When a clinician advises testing for HIV, HBV or HCV, the patient must be provided with sufficient information, in a form that he/she is capable of understanding, to enable the patient to make an informed decision whether or not to be tested. The doctor has a duty to provide information to each individual patient in a style and manner such that that particular patient is able to absorb it as knowledge. Information must be fairly balanced; that is, both the benefits of testing and the possible negative sequelae must be discussed. Both positive framing (an overemphasis on benefits) and negative framing (an overemphasis on risks) can unduly influence the patient's decision.[2] The doctor has no duty to the patient to ensure that he or she makes a 'wise' decision. Indeed, it is a fundamental principle of the patient's right of self-determination and bodily integrity that he/she makes his/her own decisions, regardless of whether a third party perceives the decision to be 'wise' or not. Detailed documentation of pre-test and post-test counselling (Chapter 8) is recommended as evidence of proper information disclosure in case of legal challenge.

Based on the High Court's decision in *Rogers v Whitaker*[3], in which a woman undergoing eye surgery was not warned of a rare side-effect of surgery that left her almost totally blind, the following tests apply to information disclosure. These tests are additive, not alternative.

The 'Reasonable Patient' test

All the information that any reasonable person would think material or relevant to making a decision regarding testing must be provided.

The 'Reasonable Doctor' test

The additional information that any reasonable doctor would or should add, due to its relevance to the particular patient, must be provided. Any reasonable doctor would know that a sex worker, for example, is a special case in relation to HIV testing, as is a patient who is already immunocompromised.

The 'Individual Patient' test

Any additional information that the patient requests must be provided. Additional information needs to be solicited by open-ended questions such as 'Is there anything else you would like to know?'

These 'legal tests' also apply to the treatment and care of patients infected with blood-borne viruses. The High Court has recently reconsidered and upheld these principles in *Rosenberg v Percival*.[4]

Confidentiality

There is a distinction between different types of disclosure in a medical setting. There is disclosure of information where public health issues are concerned (where confidentiality is usually protected) and general disclosure (where confidentiality is often not protected).

In each State and Territory, HIV, hepatitis B and hepatitis C are notifiable diseases and

clinicians are required to provide the relevant health authorities with information regarding these infections. In some legislation and regulations, HIV/AIDS attracts stricter guidelines relating to notification and disclosure than those established for other infectious diseases such as hepatitis B and hepatitis C. In New South Wales, South Australia, Victoria and Tasmania, notification of cases of HIV/AIDS must be in coded form, ensuring anonymity and confidentiality. Coded notification of HIV/AIDS may also occur in Queensland.

The second type of disclosure or breach occurs where the health care worker discloses medical or other information (e.g. positive HIV status) about a person in addition to the person's name, address or other identifying characteristics. The basic principle is that a health care worker, like any person, has a duty not to breach confidentiality when he/she comes into possession of information that is confidential. In some circumstances, there is an implied waiver of the right to have the matter kept confidential. For example, matters directly related to the immediate health care of the patient are likely to be communicated to others directly involved in the provision of that health care. The implied waiver applies only to information transferred in the patient's interest required directly for that episode of care. Passing information for the purpose of protecting other health care workers may not satisfy this test.

If confidentiality is breached, the patient may sue for damages and/or complain to the local medical disciplinary authority, health complaints' authority or, in some jurisdictions, the local privacy authority. For example, if a health care worker disclosed someone's HCV status in a small country town and that person was forced to move, the patient may have a successful action for damages for removal costs as well as for pain and suffering, loss of enjoyment of life and emotional stress. A concurrent complaint to that health care worker's registration authority may lead to disciplinary sanctions.

There have also been legislative attempts to discourage such disclosure. There are general obligations in New South Wales, Victoria, Queensland and South Australia stating that certain categories of health care professionals (primarily those employed by public hospitals) are required not to disclose medical information obtained during course of their duties [s.22 *Health Administration Act* 1982 (NSW); s.141 *Health Services Act* 1988 (Vic); s.49 *Health Act* 1937 (QLD); and s.64 *South Australian Health Commission Act* 1976 (SA)].

A breach of confidentiality in New South Wales, Tasmania and the Australian Capital Territory is a criminal offence [s.17 *Public Health Act* 1991 (NSW); s.19 *HIV/AIDS Preventive Measures Act 1993* (Tas); and s.110 *Public Health Act 1995* (ACT)]. The duty of confidentiality in New South Wales extends to any service provider not just health workers (s.17). However, s.17 (3) of the *Public Health Act* 1991 (NSW) provides that 'information about a person's HIV status can be disclosed to a person who is involved in the provision of care to, or treatment or counselling of the other person if the information is required in connection with providing such care, treatment or counselling...' It should be noted that s.17 protects patients' confidentiality regarding information about HIV and AIDS but not viral hepatitis. The duty of confidentiality in Tasmania is confined to HIV testing and there is a list of circumstances in which the duty does not apply.

Victorian legislation imposes a criminal penalty on health professionals if they do not have an appropriate system for protecting the privacy of people tested for HIV (*Health Act 1958* (Vic) s.128). In South Australia, s.42 of the *Public and Environmental Health Act* 1987 (SA) protects confidentiality by imposing a fine for breaches of confidentiality. Under Queensland legislation any person, body corporate and/or association of persons may suffer penalties for a breach of confidentiality.

In general, clinicians have both ethical and legal obligations to establish and maintain systems for protecting the confidentiality of information about their patients. This is not just a matter of self-protection from the risk of litigation, it also builds the confidence of patients and potential patients in the integrity of clinicians, their institutions and their staff.

Privacy

In addition to longstanding common law and ethical and statutory confidentiality obligations, health care workers must now abide by a raft of privacy laws that have been enacted by the Commonwealth Government and by a number of State Governments. Those laws recognise that 'health information privacy' is perhaps the most sensitive information of all and deserves special treatment and protection. The privacy laws will require health care workers and the organisations that employ them to undertake and to be seen to have undertaken, a range of practices aimed at enhancing and respecting confidentiality, privacy, security, open-

ness and transparency. The relevant legislation affecting the private sector throughout Australia is the *Privacy Amendment (Private Sector) Act* 2000 (Cth). It applies to all private sector 'health providers' and came into effect on 21 December 2001. Some States have sought to address health privacy through 'health-specific' privacy legislation, which extends to both the public and the private sectors. For example, the Victorian Government enacted the *Health Records Act* (2001) which came into force on 1 July 2002.

Notification

In all States and Territories, hepatitis B, hepatitis C and HIV/AIDS are notifiable conditions. This requires clinicians to notify the relevant health authorities when a new case is diagnosed. Legislation has attempted to strike a balance between preserving the privacy of the individual and the greater public interest in curbing the spread of notifiable conditions.

New South Wales, Queensland, Northern Territory, South Australia, Tasmania and the Australian Capital Territory require clinicians to report any incidence of a notifiable disease as soon as is practical [s.14(1) *Public Health Act* (NSW); s.32A(1) *Health Act* (QLD); s.6 *Notifiable Diseases Act* 1981 (NT); s.102(3) *Public Health Act* (ACT); and s.30 *Public and Environmental Health Act* (SA)]. The definition of what is practical will depend on the facts of the specific case. In most States and Territories, pathology laboratories may also undertake notification of notifiable diseases.

Under Western Australian legislation the obligation of notification rests with both the clinician and the occupier of the house where a person is found to be suffering from an infectious disease [s.276 *Health Act* 1911]. In contrast, Victoria requires clinicians to notify the relevant health authorities immediately by telephone and then send written confirmation within seven days of confirmation of original diagnosis [Schedule 2, *Health (Infectious Diseases) Regulations* 1990]. Referral to State and Territory health departments is recommended for full details of notification requirements (Chapter 14).

Non-discrimination

The Commonwealth and all States and Territories have legislation making discrimination illegal on the grounds of disability or perceived disability, impairment and handicap.

In each State or Territory where legislation exists, except South Australia, HIV and hepatitis C status falls within the definition of 'disability' in the anti-discrimination legislation. Thus, it is illegal to discriminate on the basis of a person's actual or perceived HIV or hepatitis status. In other words, it is illegal to discriminate against someone whom a person believes to be HIV-infected, whether or not they are actually HIV-infected. In South Australia, the law prohibits discrimination on the ground of impairment. 'Impairment' is defined in such a way that it covers AIDS and symptomatic (but not asymptomatic) HIV infection.

Historically, the greatest source of complaint about HIV discrimination has been health care settings. Hepatitis B and hepatitis C pose similar issues. The most common type of unlawful discrimination relevant to blood-borne viruses has been on the ground of an attribute considered by the health care worker to be a risk factor for disease, such as homosexuality (or perceived homosexuality). In this context, it should be noted that recent case law recognises drug dependency as a disability that is protected from unlawful discrimination.

The definition of discrimination varies in the different legislation. Generally, discrimination on the ground of disability occurs when one person treats another person less fairly than he/she would someone without that disability, or harasses another person because of his/her disability.[3,5] Likewise, discrimination on the ground of homosexuality (or, in New South Wales, of being a transgender person) occurs when, on that ground, a person is treated less fairly than a person without the attribute of homosexuality (or being transgender).

In situations where a person's disability poses real issues, such as a health risk, the policy of anti-discrimination statutes is to encourage employers and service providers to take reasonable steps to accommodate the person's disability. This can be done by adopting recognised measures for infection control, by making reasonable adjustments in practice, in scheduling and so on. A failure to reasonably accommodate a person's disability will be taken into account in deciding whether or not an act of discrimination was unlawful.

New South Wales differs from the other States and Territories, as it is the only state that outlaws vilification on the grounds of HIV/AIDS, 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.

Infected health care workers

The requirements for information disclosure also apply to the ethical and legal obligations of health professionals infected with blood-borne viruses. If a doctor or another patient is, for any reason, a potential hazard to a patient, the patient has the legal right to be warned of that hazard. This is because the *Rogers v Whitaker* High Court judgement underscored the patient's right to be informed of all 'material risks'. Even a small risk of contracting HIV, HBV or HCV infection from a health care worker or another patient may be perceived as 'material'. A health care worker infected with a blood-borne virus has a duty to assess whether, in the context of his or her practice, there is a material risk that HIV, HBV or HCV infection could be transmitted to a patient. If there is, and the health care worker continues in that practice, then there are both legal and ethical burdens requiring disclosure of that risk.

In this context, the health care worker will take into account factors such as:

- the magnitude of the harm that transmission would cause;
- the degree of risk of transmission involved in the procedure or other contact;
- the infection control procedures to be adopted or in place;
- the advice received from a clinician skilled in such assessments.

Risk of transmission in the health care setting is discussed in Chapter 12. Infected health care workers can consult relevant professional or public health authorities for clarification of risk and relation to professional practice.

Diagnosis malpractice

A doctor's duty of care to diagnose HIV and chronic viral infections applies to patients and their sexual partners, following the judgement in *BT v Oei* (Case study 1). In this case, the doctor was found negligent in not advising testing for HIV and the court agreed that this negligence led to BT becoming HIV infected.

Another form of diagnosis malpractice is the failure to follow-up a positive test result. In *Kite v Malycha*[7] , Justice Perry found a surgeon negligent for not informing a patient that a fine-needle aspiration biopsy of a breast lump showed cancer cells. The surgeon did not have a system for detecting that the patient had not received the test result. Part of his defence was that the patient did not follow his advice to phone for the result in a few days and return for review in a few weeks. However, Justice Perry stated in his judgement that: "[Mrs Kite] was entitled to assume that if the outcome of the testing of the biopsy gave cause for concern, she would be informed." Thus he rejected an argument that Mrs Kite contributed to or caused her own damage through her failure to carry out the surgeon's advice regarding follow-up.

Because testing for HIV antibody status is largely anonymous (that is, the blood sample is often sent without patient identification but with a code assigned by the referring doctor), the

CASE STUDY 1

Diagnosis malpractice, negligence and duty of care

Failure to recommend HIV testing

In a NSW case, *BT v Oei* [6], the defendant doctor was found to have a duty of care to a patient's sexual partner, even though the partner was not herself a patient of the doctor. The case involved a man (AT) who reported a flu-like illness in late 1991 and developed acute hepatitis B and a urinary tract infection in early 1992. A woman called BT subsequently formed a sexual relationship with AT and became infected with HIV.

Despite Dr Oei's testimony to the contrary, the court found that Dr Oei did not recommend HIV testing. As a result, AT was unaware of his HIV status and subsequently passed the virus to BT. BT sued the doctor claiming that his failure to diagnose AT's HIV infection was negligent. BT asserted, and the court agreed, that the doctor should have advised AT to have a HIV test when AT first presented. The doctor certainly owed a duty of care to AT. The question asked of the court, and answered in the affirmative, was whether he also owed a duty of care of BT.

Justice Bell, in finding for BT, took note of the provisions of the *Public Health Act 1991* (NSW), which requires a doctor who believes a patient is HIV-infected to inform that patient of the danger he/she poses to others and to advise the measures he/she should take to protect others from cross-infection. Justice Bell found the doctor negligent in not suspecting the presence of HIV infection. If he had suspected HIV infection and had followed the dictates of the *Public Health Act* then, on the balance of probabilities, AT's HIV status would have been diagnosed early enough for him to have practised safe sex with BT and BT, again on the balance of probabilities, would not have contracted HIV infection. Thus, Dr Oei was found negligent and his negligence was found to have caused BT's 'damage'.

judgement in *Kite v Malycha* makes it probable that a doctor who does not have a system to check that results are received for all requested/referred tests and that those results are communicated to the relevant patient, will be held to be negligent.

The *BT v Oei* judgement would suggest that the liability in negligence will extend both to the patient and to anyone else unwittingly infected by that patient in the belief that no communication from the doctor meant that the test must have been negative. If Justice Perry's judgement in the Supreme Court of South Australia is supported in other State jurisdictions (or by the High Court of Australia), then patients referred for HIV antibody testing will be seen to be legally entitled to assume that 'no news is good news'. That is, if the doctor does not contact them about the test, it must have been negative.

Another recent NSW judgement (*PD v Dr Nicholas Harvey & 1 Ors* [2003] NSWSC 487), handed down in June 2003, reinforces this point. A couple attended a GP together for pre-marital counselling and STD 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. It transpired later that he told her that his result was negative, they had unprotected intercourse, and she became infected with HIV. She sued the doctors involved. In his judgement Cripps AJ 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 that the GPs were in breach of their statutory duty (under NSW's *Public Health Act 1991*) 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 legislated power to intervene. Further, the judge found that 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 such 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.

Prevention of foreseeable harm

A clinician could be found liable in negligence to a third party if he/she knows that an HIV-infected patient is recklessly putting others at risk, but does not warn that third party or the relevant health authorities.

Though there is doubt as to its relevance to Australian law, the 1976 Californian case *Tarasoff v The Regents of the University of California*,[8] centred on this point. A psychologist was found to have been negligent in not warning the ex-girlfriend of a patient that the patient had expressed to the psychologist, an intent to kill the ex-girlfriend. The patient subsequently did murder the girl and her parents sued successfully for 'failure to warn'.

A similar case could succeed in relation to a patient with a blood-borne virus, either where a specific individual is placed at risk (for example, the much-debated scenario in which an HIV-infected man refuses to tell his wife his HIV status and refuses to practise safe sex with her – a situation very similar to that is *PD v Harvey*) or where the community at large is placed at risk (for example, an HIV-infected sex worker who admits to providing sexual services without a condom to attract higher fees). In the latter case, if a doctor did not report those circumstances to the health authorities, a person who later contracted HIV infection from that sex worker might well bring a successful action in negligence against the doctor. In the former case, even if the patient's spouse is not a patient of that doctor, the duty to prevent foreseeable harm might require the doctor to ensure the spouse is protected from the risk of harm, even if specifically instructed by the patient not to contact the spouse. The doctor's duty of confidentiality to the patient can often be reconciled with the duty to prevent foreseeable harm by taking advantage of facilities offered by health departments for dealing with such cases – the point made by Cripps AJ in *PD v Harvey*. In cases where experienced sexual health counsellors are available, it may often be better to involve them in

the task of reducing the risk of harm of transmission to a patient's partner.

In general, it is preferable for the doctor to report directly to public health authorities rather than attempt to make contact with the person thought to be at risk.

See Chapter 14 for contact information for services able to advise on legal issues.

References

1 *Law Discrimination and Human Rights – Facing up to the AIDS paradox*. Third International Conference on AIDS in Asia and the Pacific. Chiang Mai, Thailand; 1995.
2 McDonalds market a new range of fast foods under the slogan '97% fat free'. That's positive framing. The converse would be to label them '3% fat'.
3 *Rogers v Whitaker* (1992) 175 CLR 479; 109 ALR 625 (HCA).
4 *Rosenberg v Percival* (2001) 8 HCA 18.
5 *New South Wales Anti Discrimination Act* (1991) s.49B.
Queensland Anti Discrimination Act (1991) s.10.
South Australian Equal Opportunity Act (1984) s.66.
Victorian Equal Opportunity Act (1995) s.7.
Tasmanian Anti Discrimination Act (1998) s.14.
West Australian Equal Opportunity Act (1984) s.66A.
Australian Capital Territory Discrimination Act (1991) s.8.
Northern Territory Anti Discrimination Act (1992) s.20.
6 *BT v Oei* [1999] NSWSC 1082.
7 *Kite v Malycha* (1998) 71 SASR 321.
8 *Tarasoff v The Regents of the University of California* 1976 CA 131 Cal Rptr 14, 551 p2d 334 CA Supreme Court.

14 Contact and referral information

The following list provides phone numbers and websites (if applicable) for a range of national and state services that will be useful to both clinicians and patients. Please also consult the *ASHM Directory* (available from the ASHM office and online at www.ashm.org.au) for further details of HIV/AIDS and hepatitis C specialists and services to assist you in making appropriate referrals.

	Phone number	Website
GENERAL CONTACTS		
Australasian Society for HIV Medicine (ASHM)	02 9368 2700	www.ashm.org.au
Commonwealth Department of Health and Ageing (Population Health Division)	02 6289 1555	www.health.gov.au/ www.health.gov.au/pubhlth/
Ministry of Health – New Zealand	0011 64 496 2000	www.moh.govt.nz/moh.nsf
National Health and Medical Research Council (NHMRC)	02 6289 9184	www.nhmrc.gov.au
National Drug & Alcohol Research Centre (NDARC)	02 9398 9333	www.med.unsw.edu.au/ndarc/

STATE/TERRITORY HEALTH DEPARTMENTS					
ACT	02 6205 5111	www.health.act.gov.au/dept.html	SA	08 8226 8800	www.health.sa.gov.au/
NSW	02 9391 9000	www.health.nsw.gov.au/	TAS	03 6233 3185	www.dhhs.tas.gov.au/
NT	08 8999 2400	www.nt.gov.au/	VIC	03 9616 7777	www.dhs.vic.gov.au/
QLD	07 4920 6953	http://www.health.qld.gov.au/	WA	08 9222 4222	www.health.wa.gov.au/

Many useful NSW health department circulars can be found at: http://www.health.nsw.gov.au/fcsd/rmc/cib

PROFESSIONAL BODIES		
Australasian Society for HIV Medicine (ASHM)	02 9368 2700	www.ashm.org.au/
Australian College of Ambulance Professionals		www.acap.org.au/
Australian College of Rural and Remote Medicine	07 3352 8600	www.acrrm.org.au
Australasian College of Sexual Health Physicians (ACSHP)	02 9382 7457	www.acshp.org.au/
Australian Dental Association	02 9906 4412	www.ada.org.au/
Australian Division of General Practitioners	02 6251 3380	www.adgp.org.au/
Dietitians Association of Australia	02 6282 9555	www.daa.asn.au/
Gastroenterological Society of Australia (GESA)	02 9256 5454	www.gesa.org.au/
Hepatology Nurses Group	02 9828 5906	
International Association of Physicians in AIDS Care (IAPAC)	312 759 4930	www.iapac.org/
Royal Australian College of General Practitioners (RACGP)	03 9214 1414	www.racgp.org.au/index.htm
Royal Australian College of Physicians (RACP)	02 9256 5444	www.racp.edu.au/
Royal College of Nursing Australia	02 6282 5633	www.rcna.org.au/
Royal College of Pathologists of Australasia	02 8356 5858	www.rcpa.edu.au/
Social Workers in AIDS (SWAIDS)	02 9843 3124	

	Phone number	Website
MEDICAL AND PATHOLOGY SERVICES		
Australian Infection Control Association	0414 422307	www.aica.org.au/
Australian Red Cross Blood Service (to connect to local blood banks)	13 14 95	www.giveblood.redcross.org.au
National Serology Reference Laboratory	03 9418 1111	www.nrl.gov.au/
Victorian Infectious Diseases Reference Laboratory (This website has an excellent links page for infectious diseases/serology information)	03 9342 2636	www.vidrl.org.au
HIV/AIDS CONTACTS		
National		
Australian Federation of AIDS Organisations (AFAO)	02 9281 1999	www.afao.org.au/
Australian Research Centre in Sex, Health & Society (collaborating with the NCHSR)	03 9285 5382	www.latrobe.edu.au/www/arcshs/
National Association of People Living With HIV/AIDS (NAPWA)	02 9281 2511	www.napwa.org.au
National Centre in HIV Epidemiology and Clinical Research	02 9332 4648	www.med.unsw.edu.au/nchecr/
National Centre in HIV Virology Research	02 9845 9005	www.hiv.edu.au/
National Centre in HIV Social Research (NCHSR)	02 9385 6776	www.arts.unsw.edu.au/nchsr/
New Zealand AIDS Foundation	0011 64 9303 3124	www.nzaf.org.nz
AIDS Councils		
AIDS Action Council of the ACT	02 6257 2855	www.aidsaction.org.au/
AIDS Council of NSW	02 9206 2000	www.acon.org.au/
Northern Territory AIDS Council	08 8941 1711	www.octa4.net.au/ntac/
Queensland AIDS Council	07 3017 1777	www.quac.org.au
AIDS Council of South Australia	08 8362 1611	www.aidscouncil.org.au/
Tasmanian Council on AIDS and Related Diseases (TasCAHRD)	03 6234 1242	www.tascahrd.org.au
Victorian AIDS Council/Gay Men's Health Centre (VAC/GMHC)	03 9865 6700	www.vicaids.asn.au/
Western Australian AIDS Council	08 9482 0000	www.waaids.com
People Living with HIV/AIDS (PLWHA) groups		
Body Positive Inc (New Zealand)	0011 64 9309 3989	www.bodypositive.org.nz
PLWHA ACT	02 6257 4985	http://www.aidsaction.org.au/plwha/
PLWHA NSW	02 9361 6011	http://www.plwha.org.au/
PLWHA NT	08 8941 1711	info@ntac.org.au
Positive People (QLD)	07 3844 1990	
PLWHA South Australia	08 8293 3700	http://www.hivsa.org.au/
Positive People Tasmania	03 6234 1242	www.tascahrd.org.au
PLWHA Vic	03 9865 6772	http://www.gaynet.com.au/plwha/
WA – see Western Australian AIDS Council	08 9482 0000	www.waaids.com
Positive women		
AIDS Council of NSW Positive Women's Support	02 9206 2012	www.acon.org.au/
Information on Children, Parenting and Pregnancy Paediatric AIDS Unit, Sydney Children's Hospital	02 9382 2222	www.health.nsw.gov.au/publichealth
Ladies Into Positive Support (LIPS) (QLD)	07 3846 3939	www.quac.org.au/qpp
Positive Women Victoria	03 9276 6918	www.positivewomen.org.au
Women's Health Statewide HIV/AIDS Project (SA)	08 8267 5366	

continued >

14 Contact and referral information

	Phone number	Website
Positive heterosexuals		
HIV Positive Heterosexuals (NSW)	Freecall 1800 812 404	02 9515 3095
Straight Arrows (VIC)	03 9267 3792	http://www.straightarrows.org.au
Services for young people		
ACON Fun and Esteem	02 9206 2077	
Second Storey Youth Health Service (SA)	08 8326 6053	
Toehold in Queensland	07 3844 1990	
VAC Young and Gay	03 9865 6700	www.vicaids
There is also a useful directory of Australia-wide services for people living with HIV/AIDS at: www.hivaids.webcentral.com.au/text/dir.html		
Other community contacts		
AIDS Dementia and HIV Psychiatry Service (ADAHAPS) (NSW)	02 9339 2078	www.digitalmetworkmanagement.com/adahps/
Australian IV League (AIVL)	02 6279 1600	www.aivl.org.au
Bobby Goldsmith Foundation	02 9283 8666	www.bgf.org.au/
Haemophilia Foundation of Australia	03 9885 7800	www.haemophilia.org.au
Transfusion-related AIDS (TRAIDS): Medically Acquired Hepatitis C and HIV, Counselling, Support and Advocacy Centre	02 9843 3143	

HEPATITIS CONTACTS

National organisations					
Australian Hepatitis Council (ACH)			02 6232 4257		www.hepatitisaustralia.com/
Hepatitis C Councils and support networks					
ACT	02 6253 9999	www.acthepc.org	SA	08 8362 8443	www.hepccouncilsa.asn.au
NSW	02 9332 1599	www.hepatitisc.org.au	TAS	03 6234 1242	
NT	08 8941 1711	www.ntac.org.au	VIC	03 9380 4644	www.hepcvic.org.au
QLD	07 3229 3767	www.powerup.com.au/~hepcq	WA	08 9328 8538	www.users.highway1.com.au/~hepccwa/

Alcohol and Drug Information Services (ADIS)			
These are 24-hour services unless otherwise specified:			
ACT	02 6205 4545		
NSW	02 9361 8000		
NT	08 8981 8030	1800 629 683	8.30am to 4.30pm Monday to Friday
QLD	07 3236 2414	1800 177 833	
SA	08 8363 8618		
TAS	03 62336722	1800 811 994	
VIC	03 9416 1818	1800 136 385	131570 (Drug Info)
WA	08 9442 5000	1800 198 024	

			Phone number	Website
NEEDLE AND SYRINGE PROGRAMS / METHADONE PROGRAMS				
Information on these services can be obtained from either ADIS (page 115) or the following drug user groups:				
ACT		Canberra Injector's Network (CIN)	02 6262 5299	
NSW		New South Wales Users and AIDS (NUAA)	02 9557 1476	1800 644 413
NT	(Darwin)	Health for Injectors in the NT (TUF)	08 8941 1711	www.ntahc.org.au
	(Alice Springs)	Central Australia Injectors Network (CAIN)	08 8953 6503	
QLD		Queensland Intravenous AIDS (QuIVAA)	07 3252 5390	1800 172 076
SA		South Australian Voice for IV (SAVIVE)	08 8362 9299	
TAS		Tasmanian Users Health and Support (TUHSL)	03 6234 1242	www.tascahrd.org.au
VIC		Victorian Drug Users Group (VIVAIDS)	03 9419 3633	
WA		WA Substance Users Assocation (WASUA)	08 9227 7866	
A useful website with links to many services can be found at the Alcohol and Drug Information Network (ADIN): http://www.adin.com.au/				

EDUCATION AND TRAINING CONTACTS		
AIDS Dementia and HIV Psychiatry Service (ADAHP)	02 8382 1810	www.health.nsw.gov.au/adahps
Albion Street Centre	02 9332 9600	www.sesahs.nsw.gov.au/albionstcentre/
Australasian College of Sexual Health Physicians (ACSHP)	02 9382 7587	www.acshp.org.au/
Australasian Society for HIV Medicine (ASHM) – HIV Continuing Medical Education Project	02 9368 2700	www.ashm.org.au/
Australian Centre for Health Promotion	02 9351 5129	www.achp.health.usyd.edu.au/
Australian Research Centre in Sex, Health and Society	03 9285 5382	www.latrobe.edu.au/www/arcshs/
Centre for Community Welfare Training (CCWT)	02 9281 8822	www.acwa.asn.au/ccwt/
FPA Health (formerly Family Planning Australia)	02 6230 5255	www.fpa.net.au
NSW Health Workforce Development Program/ Hepatitis C Workforce Development Project	02 9368 2724	www.wdp.nsw.gov.au/
Royal Australian College of General Practitioners (RACGP)	03 9214 1414	www.racgp.org.au/
Royal College of Nursing Australia	02 6282 5633	www.rcna.org.au/
See also State and Territory Health Departments listed above.		

LEGAL SERVICES				
Anti-discrimination bodies				
	ACT	Human Rights Office	02 6207 0576	http://www.hro.act.gov.au
	NSW	Anti-Discrimination Board	02 9268 5555	www.lawlink.nsw.gov.au
	NT	Anti-Discrimination Commission	08 8981 3813	www.adc.nt.gov.au
	QLD	Anti-Discrimination Commission	07 3247 0960	www.adcq.qld.gov.au
	SA	Equal Opportunity Commission	1800 188 163	www.eoc.sa.gov.au
	TAS	Anti-Discrimination Commission	03 6233 4841	
	VIC	Equal Opportunity Commission	03 9281 7110	www.home.vicenet.net.au
	WA	Equal Opportunity Commission	08 9264 1930	www.equalopportunity.wa.gov.au
HIV/AIDS Legal Centre (NSW)			02 9206 2060	www.halc.org.au
Human Rights and Equal Opportunity Commission			02 9284 9600	www.hreoc.gov.au
Guardianship Tribunal (NSW)			02 9555 8500	

continued >

INTERNET RESOURCES

Below is a selection of useful and interesting websites on both HIV/AIDS and Hepatitis.
This list is not intended to be comprehensive.

HIV/AIDS:

Australian

- **www.ashm.org.au** – Australasian Society for HIV Medicine (ASHM):
  The peak representative professional body for medical practitioners and other health care workers who work in HIV and related disease areas. The site contains education, training and conference information as well as ASHM publications and clinical updates.
- **www.ancahrd.org** – Australian National Council on AIDS, Hepatitis C and Related Diseases (ANCAHRD):
  Site lists details of committees of ANCAHRD, including Clinical Trials and Research Advisory Committee (CTARC) and links to CTARC news.
- **http://www.latrobe.edu.au/www/arcshs/** – Australian Research Centre in Sex, Health & Society:
  ARCSHS is a collaborating centre to the National Centre in HIV Social Research and is affiliated with the University of Melbourne. It aims to undertake multidisciplinary research into social and behavioural aspects of sexually transmissible diseases, their prevention and consequences.
- **www.burnet.edu.au** – Macfarlane Burnet Institute for Medical Research and Public Health:
  Australia's largest virology and communicable disease research institute, the Burnet Institute investigates some of today's most serious viral infections such as HIV/AIDS, hepatitis and measles.
- **www.med.unsw.edu.au/nchecr/** – National Centre in HIV Epidemiology and Clinical Research:
  NCHECR is one of Australia's leading medical research centres and is recognised internationally as a leader in the field of research into HIV/AIDS and viral hepatitis.
- **www.arts.unsw.edu.au/nchsr** – National Centre in HIV Social Research:
  NCHSR conducts research which describes and analyses the social understandings, meanings and practices of peoples, institutions and communities in relation to HIV, STDs and other communicable diseases.
- **www.hiv.edu.au/** – National Centre for HIV Virology Research:
  The National Centre for HIV Virology Research is in the process of being re-organised into the new Australian Centre for HIV and Hepatitis Virology Reasearch (ACH2), which is to be a broadly inclusive, collaborative national virology research organisation focused on HIV and Hepatitis C.
- **www.med.unsw.edu.au/ndarc/** – National Drug and Alcohol Research Centre:
  NDARC is a clearinghouse for a wide range of drug-related research and publications.

International

- **http://www.aegis.com/** – AEGiS (AIDS Education Global Information System):
  The largest HIV/AIDS website in the world. AEGiS is a non-profit, charitable and educational corporation with information for the medically educated and layperson alike, with an easily used search engine and useful online forum.
- **http://www.aidsmap.com/** – AIDSmap:
  This site is produced by the National AIDS Manual (NAM Publications) in collaboration with the British HIV Association and provides extensive information on treatments and a searchable database. Includes The Wheel – an interactive pill planner for consumers and health professionals.
- **www.aids/org** – AIDS.ORG:
  This US site offers quality HIV/AIDS treatment information and resources .
- **www.thebody.com/index.shtml** – The Body: an AIDS and HIV Information Resource:
  The Body aims to use the Web to: lower barriers between patients and clinicians; demystify HIV/AIDS and its treatment; foster community, and improve patients' quality of life.
- **http://www.hivdent.org** – HIVdent:
  Comprehensive coverage of HIV issues and dentistry; also hepatitis C information.
- **http://hivinsite.ucsf.edu/InSite** – HIVInSite:
  Treatment, prevention and policy information from the University of San Francisco California.
- **www.hopkins-aids.edu** – The Johns Hopkins AIDS Service:
  This website is provided by the Johns Hopkins University as a resource for physicians and other health care professionals in providing care and treatment to patients with HIV/AIDS.
- **www.hiv-druginteractions.org** – Liverpool HIV Pharmacology Group (LHPG):
  This website has been designed for use both by clinicians and patients as a straightforward, up-to-date reference on anti-HIV drugs.
- **www.medscape.com** – Medscape HIV/AIDS:
  Medscape is the leading interactive, multi-speciality commercial Web service for clinicians and consumers. Includes free access to the MEDLINE, AIDSLINE and TOXLINE databases and the HIV/AIDS Clinical Calculator of drug-drug interactions. http://hiv.medscape.com/Medscape/HIV/DrugInteractions/index.cfm
- **www.nzaf.org.nz** – New Zealand AIDS Foundation.
- **www.unaids.org** – UNAIDS: The Joint United Nations Program on HIV/AIDS:
  As the main advocate for global action on HIV/AIDS, UNAIDS leads, strengthens and supports an expanded response aimed at preventing the transmission of HIV, providing care and support, reducing the vulnerability of individuals and communities to HIV/AIDS, and alleviating the impact of the epidemic.

INTERNET RESOURCES

HEPATITIS :

Australian

- **http://www.health.gov.au/pubhlth/strateg/hiv_hepc/hepc/index.htm** – part of the Australian Government Department of Health and Ageing site, outlining the national response to HCV and providing links to epidemiological and statistical information, as well as the Australian hepatitis C research register (http://www.health.gov.au/pubhlth/strateg/hiv_hepc/hepc/register/index.htm)
- **www.hepatitisaustralia.com** – Australian Hepatitis Council:
  An information resource primarily for people with hepatitis C, their families, friends and carers.
- **www.acthepc.org** – ACT Hepatitis C Council
- **www.hepatitisc.asn.au** – Hepatitis C Council of Queensland
- **www.ntahc.org.au** – Northern Territory AIDS & Hepatitis Council
- **www.hepccouncilsa.asn.au** – Hepatitis C Council of South Australia
- **www.taschard.org.au** – Tasmanian Council of AIDS, Hepatitis and Related Diseases (TasCAHRD)
- **www.hepcvic.org.au** – Hepatitis C Council of Victoria
- **www.hepatitiswa.com.au** – Hepatitis C Council of Western Australia

The following organisations can provide information and assistance about hepatitis C and related issues

- **www.aivl.org.au** – Australian Injecting and Illicit Drug Users League (AIVL)
- **www.adf.org.au** – Australian Drug Foundation
- **www.multiculturalhivhepc.net** – Multicultural HIV/AIDS and Hepatitis C Service

International

- **www.hepfoundation.org.nz** – Hepatitis Foundation of New Zealand
- **www.h-r-n.org** – Hepatitis Resources Network provides physicians with high-quality, balanced educational resources and access to clinical trials with the goal of improving the quality of life for people living with chronic viral hepatitis C.
- **www.who.int** – World Health Organization.

Appendix 1

Patient information - Natural history and transmission of HIV

What is HIV?	HIV (Human Immunodeficiency Virus) 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, approximately 20,000 people have been diagnosed with HIV. Over 6,200 people in Australia have died of AIDS.
How is HIV transmitted?	HIV is present in certain bodily fluids of infected people (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 (Chaper 3); • safe injecting using only sterile equipment (needles, syringes, swabs, spoons, fillers, 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 12).

Appendix 2

Patient information – Natural history and transmission of HBV

What is HBV?	HBV is a virus that can cause hepatitis. Hepatitis means inflammation of the liver.
What does the liver do?	The liver is one of the largest organs in the body 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 is infected by HBV, his/her body produces tiny proteins called antibodies in an attempt to eliminate the virus. During the first 45 to 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 infected babies (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 infected adults develop chronic infection. A person with 'chronic hepatitis B' infection is often called a 'hepatitis B carrier' and may be infected 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?	Approximately 1 out of every 100 Australians carries the hepatitis B virus. This rate is higher amongst men who have sex with men, injecting drug users and people of certain nationalities. Around 1–2% of people from Mediterranean countries, parts of Eastern Europe, and the former USSR have chronic HBV infection, while this figure is as high as 10% in some Australian Aboriginal, 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?	HBV is spread through sexual contact or through infected blood or sexual secretions (semen, vaginal fluids) entering someone else's bloodstream. Transmission can occur via skin piercing (e.g. injecting drug use or tattooing) or the sharing of toothbrushes and razorblades. 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 required for newborn infants of infected mothers and those acutely exposed to HBV. In addition, HBV transmission is prevented by: • safe sex (Chapter 3); • safe injecting (Chapter 3 and Appendix 4); • standard precautions (Chapter 12).

continued >

Appendix 3

Patient information – Natural history and transmission of HCV

What is HCV?	HCV is a virus that can cause hepatitis. Hepatitis means inflammation of the liver.
What does the liver do?	See Appendix 2.
How does HCV affect people?	When someone is infected by HCV, his/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 and/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 25–30 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, the skin and the kidneys.
How many people have HCV?	Approximately 1–2 in every 100 Australians is HCV antibody positive. In Australia, about 80% of people acquire HCV by injecting drugs. Others have acquired HCV from blood transfusion prior to 1990. HCV is more common in some ethnic groups.
How do people know what is happening to their liver?	See Appendix 2.
How is HCV transmitted?	HCV is spread through infected blood entering someone else's bloodstream (e.g. by sharing 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?	HCV transmission is prevented by: • safe injecting (Chapter 3 and Appendix 4); • standard precautions (Chapter 12).

Appendices 1–3 written by Paul Andrews et al, authors of Chapter 8.

Appendix 4

Safe injecting and cleaning injecting equipment

The sharing of injecting equipment is the single greatest risk factor for contracting 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, 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/ 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 3.5 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 infected with HIV, 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 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 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/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.

continued >

3. When you have cleaned your fit follow the 'Guidelines for safer injecting' (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 the Australian Intravenous League's *Guide to Cleaning Fits*, 1999, Australian Intravenous League, Canberra.

Glossary of terms

Ab	antibody
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 Intravenous 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
Anti-HAV IgM	antibody to HAV Igm signifies recent exposure to HAV
Anti-HBc IgM	antibody to hepatitis B core antigen signifies recent exposure to HBV
Anti-HBe	antibody to hepatitis Be
Anti-HBs	antibody to hepatitis B surface antigen associated with non-replicative phase
Anti-HCV	antibody for HCV indicating 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
BD	twice daily
B-cell	a type of immune cell
BBV	blood-borne virus
BCG	Bacille Calmette-Guerin (tuberculosis vaccine)
b-DNA	branched deoxyribonucleic acid
CAH	chronic active hepatitis
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
CMV	cytomegalovirus
CNC	clinical nurse consultant
DHAC	Commonwealth Department of Health and Aged Care
DNA	deoxyribonucleic acid
EBV	Epstein Barr virus
EIA	enzyme immunoassay
ELISA	enzyme linked immunosorbent assay
FBC	full blood count
GESA	Gastroenterological Society of Australia
GGT	gamma glutamyltransferase
GI	gastrointestinal
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
HAART	highly active antiretroviral therapy
HAV	hepatitis A virus
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
HIV	human immunodeficiency virus
HPV	human papilloma virus
HSV	herpes simplex virus
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
LFT	liver function test
LKM	liver kidney microsomal
MAC	*Mycobacterium avium* complex
MAI	*Mycobacterium avium* intracellulare
ml	millilitre
mmol	millimole
NCHECR	National Centre in HIV Epidemiology and Clinical Research
NHMRC	National Health and Medical Research Council
NNRTI	non-nucleoside reverse transcriptase inhibitor
NAPWA	National Association of People Living with AIDS
NRTI	nucleoside analogue reverse transcriptase inhibitor
OI	opportunistic infection
p24	a core HIV protein, the primary protein detected by the superceded HIV antigen test
PBS	Pharmaceutical Benefits Scheme
PCP	*Pneumocystis carinii* pneumonia
PCR	polymerase chain reaction
PCT	porphyria cutanea tarda
PEP	post-exposure prophylaxis
pg/ml	picogram per millilitre
PI	protease inhibitor
PML	progressive multifocal leucoencephalopathy
Qd	once daily
RACGP	Royal Australian College of General Practitioners
RACP	Royal Australian College of Physicians
RF	rheumatoid factor
RNA	ribonucleic acid
RT	reverse transcriptase
SBP	spontaneous bacterial peritonitis
Section 100	a section of the Pharmaceutical Benefits Scheme which provides access to highly specialised drugs
SMA	smooth muscle antibody
SR	sustained virological response (negative HCV RNA and normal ALT six months after completion of therapy for HCV)
SSRI	selective serotonin re-uptake inhibitors
STI	sexually transmissible infection
T-cell	white blood cell or lymphocyte
Td	three times daily
µl	microlitre
U & E	urea and electrolytes
VZV	varicella zoster virus
WHO	World Health Organization

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Note: Italic type indicates information is part of a table or illustration.

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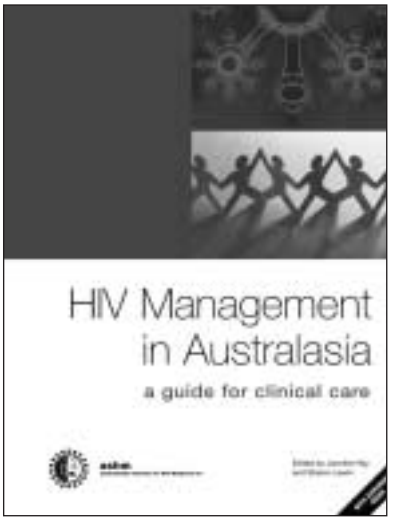

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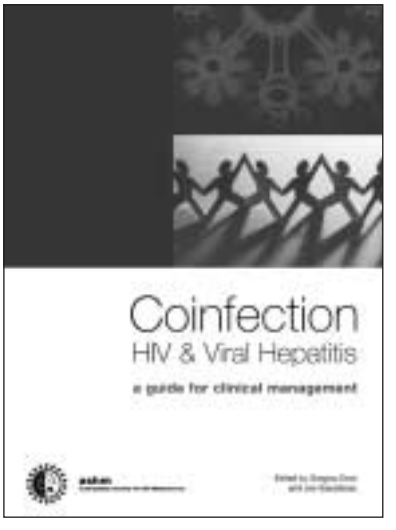

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