GUIDELINES

Screening

Routine

a. We recommend that all patients should be screened for hepatitis B virus and hepatitis C virus prior to commencement of dialysis or when transferring from another dialysis facility. The serological screening panel should include serology for hepatitis B (HBsAg, anti-HBc, anti-HBs), and hepatitis C (anti-HCV) together with baseline liver function tests (1B).

b. We recommend that patients be screened for human immunodeficiency virus (HIV) if they are identified as having risk factors for HIV acquisition or have serological evidence of either hepatitis B or hepatitis C infection (1B).

c. We recommend that patients who are hepatitis B vaccinated with anti-HBs ≥10 mIU/mL have anti-HBs rechecked annually. For vaccine non-responders, with anti-HBs titres <10 mIU/mL, recheck HbsAg every six months (1C).

d. We recommend more frequent testing (every three months) in dialysis units with high-prevalence of hepatitis B (1C).

e. We recommend that those who are seronegative for hepatitis C have anti-HCV rechecked every six months. (1C).

Enhanced

f. We recommend that the local incidence and prevalence data for hepatitis B and hepatitis C be considered in determining the frequency of testing for aminotransferases (ALT/AST) (1C).

g. We recommend that all patients negative for hepatitis B receiving in-centre haemodialysis are rescreened for hepatitis B (HBsAg, anti-HBc and anti-HBs) if there has been a notification of a seroconversion of hepatitis B (HBsAg negative to positive) within the dialysis population. All patients who are non-immune should have repeat screening every two weeks for three months (1C).

h. We recommend that all patients associated with a dialysis centre undergo rescreening for hepatitis C (anti-HCV, HCV RNA) if there has been a seroconversion of hepatitis C (anti-HCV negative to positive) within the dialysis population, thence repeat screening every two weeks for three months (1C).

i. We recommend that all patients returning from holiday haemodialysis or haemodialysis at an alternative facility where the endemic rates of BBV is high and/or adherence to standard infection control precautions uncertain, be serologically screened on re-entry for hepatitis B (HBsAg, anti-HBc, anti-HBs), hepatitis C (anti-HCV, HCV PCR), and HIV (HIV Ag/Ab) and again at 6 weeks (1C).

Infection control precautions

Standard precautions

j. We recommend that dialysis staff should receive education in the implementation of standard precautions, in particular hand hygiene and aseptic technique and that adherence be routinely audited in centres undertaking haemodialysis (1B).

Patients

k. We recommend that hepatitis B non-immune haemodialysis patients receive a course of hepatitis B vaccination that is compliant with National Immunisation Guidelines (1B).

l. We suggest that HBsAg positive patients be dialysed in isolation or cohorted in an area that is separate to that where patients who are HBsAg negative receive dialysis (2C).
m. We suggest that HBsAg positive patients use a dedicated dialysis machine, and single use dialysers. When dialysers are to be reused, they should be decontaminated and disinfected (2C).

n. We suggest that patients with HIV or who are anti-HCV positive are not dialyzed in isolation, nor on a dedicated machine (2C).

o. We suggest that the isolation of anti-HCV positive patients and the use of a dedicated machine may be beneficial in a high prevalence setting (seroprevalence > 15%) or where an outbreak of hepatitis C has not been possible to contain (2C).

**Equipment**

**General – We recommend**

p. Single use items should be disposed of after use on one patient (1D).

q. Non-disposable items should be disinfected between patient use. If disinfection is not possible (for example, tourniquets and tape) then these devices should be dedicated for single patient use only (1D).

r. Physiological monitoring equipment such as thermometers and sphygmomanometers scales should be dedicated for use for each patient, when disinfection is not possible between uses (1D).

s. Medications and supplies should not be moved between patients. If multi-dose medications are to be used (multi-dose vials or requiring diluents dispensed from a multi-dose vial) then these should be prepared in a central designated area, and then dispensed to individual patients. No drugs or materials from the dialysis station should be returned to the preparation area (1C).

t. Needles should be dispensed into a sharps container. Containers should be designed to allow for non-touch technique (1D).

**Associated dialysis-related measures – We recommend**

u. After each dialysis session all surfaces should be wiped clean. Disinfection of the surface of dialysis machines should be undertaken according to the manufacturers’ specifications (type of disinfectant, contact time and concentration) (1C).

v. External circuits, once removed, should be transported from the dialysis station in a leak proof bag to a designated clinical waste area. If components require reprocessing or the circuit needs to be drained, then this should be undertaken in a dedicated area separate to treatment areas or areas used for the preparation of medications (1C).

w. Dialysis machine should be fitted with an external transducer protector to the pressure lines of external circuitry. The fit to the pressure monitor should be tight to minimise risk of wetting. If wetting occurs the transducer should be replaced (1D).

x. If fluid is evident on the machine side of the filter then the machine should be taken out of service, the internal filter changed and the internal housing disinfected (1D).

**UNGRADED SUGGESTIONS FOR CLINICAL CARE**

- We suggest that haemodialysis patients with chronic hepatitis B, hepatitis C or HIV infection be referred to an appropriate specialist for staging of their diseases and assessment for treatment.

- Patients with a high viral load for hepatitis B, hepatitis C or HIV may present a greater transmission risk. For patients with poorly controlled disease, initiation of antiviral therapy is important for reducing this risk. For patients with active hepatitis C or HIV viral infections and high viral load, consideration can be given to managing these patients as per hepatitis B (in isolation, on a dedicated machine).

- Patients or staff who have a high-risk exposure with a potential risk of transmission, should be assessed for post-exposure prophylaxis for hepatitis B and HIV where appropriate, and referred for hepatitis B, hepatitis C and HIV monitoring.

- We suggest that patients with chronic hepatitis C who have undergone hepatitis C treatment and achieved a test of cure (sustained virological response) should be managed the same as non-HCV infected patients in the dialysis setting. For patients with ongoing risks factors for hepatitis C infection in the community, more frequent testing may be required. Anti-HCV is unlikely to be a marker of reinfection in patients who have been cured of their disease, therefore use of hepatitis C PCR tests should be routine in the long-term surveillance of these patients.
• As an additional precaution, patients who do not consent to blood borne virus surveillance should be dialysed in a separate area unless prior hepatitis B immunity is confirmed (anti-HBs ≥ 10 mIU/ml). If patients who are known to be hepatitis B immune, and decline other blood borne virus surveillance, then they should be managed in the same way as patients with hepatitis C infection.

• Staff working with dialysis patients should be screened for HBsAg and anti-HBc, as well as anti-HBs. This avoids staff who have chronic hepatitis B receiving multiple unnecessary course of vaccine and being labelled as "non-responders". A diagnosis allows them to seek treatment and minimise risk of morbidity and mortality. For those who are hepatitis B non-immune (negative to HBsAg, anti-HBs and anti-HBc), should receive hepatitis B vaccination.

• Staff who are non-immune to hepatitis B, including vaccine non-responders, should not be assigned to the care of patients who are HBsAg positive.

• For patients with a documented history of hepatitis B vaccination and antibody response (anti-HBs ≥10 mIU/mL), we recommend a booster dose of hepatitis B vaccination if anti-HBs titres are subsequently < 10mIU/ml.

• Hepatitis B vaccine non-responders, including those not responding to a double dose or "dialysis" vaccine formulation, can be offered an intradermal vaccination schedule to stimulate sero-conversion. When these measures fail, "non-immune" status should be clearly documented.

• Hepatitis A vaccination is recommended in non-immune patients with chronic hepatitis B and hepatitis C. This is based on anecdotal reports of fulminant hepatitis A infection in those with pre-existing hepatitis C or hepatitis B.

• Patients with occult HBV (most commonly recognised by serologically undetectable HBsAg positive + anti-HBc, +/- anti-HBs) should be routinely monitored for evidence of HBV reactivation using six monthly assessments of aminotransferases (ALT/AST), and six monthly assessments of anti-HBs titres and HBsAg.

• We suggest that staff training should include education about maintaining and respecting patients’ privacy in the dialysis unit where possible, to protect confidentiality surrounding the diagnosis of a blood borne virus.

• We suggest that patients receive referral for counselling where appropriate, particularly following a positive diagnosis with a blood borne virus.

• In order to help reduce fear/confusion and alleviate the stigmatisation associated with a blood borne virus, we suggest that education be provided to patients and their carers regarding the level of risk of BBVs, and importance of the practice of isolation and cohorting in the management of blood borne viruses in the dialysis unit.

Foot note

1 In some rarer circumstances occult HBV may be indicated by:

(1) A past infection indicated only by the presence of hepatitis B surface antibody (anti-HBs) without anti-HBc;

(2) Chronic hepatitis where there is a surface gene escape mutant that is not recognised by conventional assays;

(3) Where all seromarkers of hepatitis B infection are negative (seronegative occult HBV), but there are low levels of circulating HBV DNA.

IMPLEMENTATION AND AUDIT

• A competency based assessment of staff working in haemodialysis units that is aligned with recommendations outlined in this document. This includes hand hygiene, environmental cleaning, waste disposal, and disinfection and sterilising procedures for machines and equipment.

• Materials for education should be accessible (online or centralised location). Documents systems should enable version control. Training and education should aim to promote workforce awareness. Good governance should ensure a clear description of the personnel responsible for the collection, collation and reporting of surveillance data.

• Results of blood-borne virus screening should be recorded and noted in the patient medical record and a database of all serological results of and date of collection, maintained. Facility/workforce/unit managers should maintain records of the hepatitis B immune-status of staff working in, or planning to work in a haemodialysis centre. This includes clinical staff
(doctors, nurses, allied health personnel) and non-clinical staff (cleaners, hospitality/health service personnel)

- Dialysis unit managers should maintain a system for recording hepatitis B immune status and hepatitis B vaccination history in all dialysis patients. Those who are vaccine non-responders should have their vaccination status recorded.
- A program that includes workforce orientation and regular updates on standard precautions.
- The successful uptake of these guidelines can be evaluated by baseline survey of knowledge, awareness, with follow-up.

BACKGROUND

ABBREVIATIONS

HBV = Hepatitis B Virus
Anti-HBc = Hepatitis B core antibody
Anti-HBs = Hepatitis B surface antibody
HBsAg = Hepatitis B surface antigen
HBeAg = Hepatitis e antigen
HCV = Hepatitis C virus
Anti-HCV = HCV antibodies
HCV PCR/ NAAT = HCV polymerase chain reaction test or nucleic acid amplification test
HIV = Human Immunodeficiency virus

HEPATITIS C VIRUS (HCV)

The virus was discovered in 1989 and elucidated as a major cause of transfusion-related non-A, non-B hepatitis. Since this time hepatitis C (HCV) has been characterised as an enveloped single strand positive-sense RNA virus, consisting of a 9.6 kB genome that encodes three structural (core, E1, E2) and seven non-structural (p7-NS2, NS3, NS4A, NS4B, NS5A, NS5B) proteins. The non-structural proteins are the principal targets for the novel direct acting antiviral (DAA) therapies.

Natural history

The incubation period for HCV is 2-24 weeks (average 7-8 weeks). Of those acutely infected with HCV, 15-40% will clear the virus over the course of 6 months, and 60-85% will develop chronic infection. Of those with chronic HCV infection, 20-30% will progress to cirrhosis within 20-30 years, and of these a further 25% are will develop decompensated liver failure and/or hepatocellular carcinoma.

Epidemiology

The global prevalence of HCV is estimated at 2.3%, amounting to 185 million people worldwide with positive HCV antibody (anti-HCV). HCV prevalence varies widely within and between countries. In high-income countries HCV prevalence is between 1-2%, and in low to middle-income countries with the highest prevalence, 4-14% [1]. Genotype 1 has the widest worldwide distribution. In Australia, genotypes 1 and 3 account for 55% and 38% of prevalent genotypes, respectively [2].

In Australia, HCV has been a notifiable disease since the early 1990s. There are an estimated 314,000 adults with positive anti-HCV in Australia, giving a prevalence of 1.7%. The estimate of those who are HCV RNA positive is 1.2% [3]. A reduction in incident HCV cases has followed the screening of blood products in the early 1990s and improved harm reduction initiatives since early 2000, such as needle and syringe exchange programs and opioid substitution treatment programs. In 2014, there were 10,621 new HCV diagnoses in Australia, including people with acute and chronic HCV [4].

Between March and May 2016 a number of effective direct acting antiviral therapies with curative potential have been listed on the Pharmaceutical Benefits Scheme (PBS) in Australia. In 2016 it is estimated that 22,470 Australians with chronic HCV have received direct acting antiviral treatment [5].

Transmission risk

The main mode of HCV infection is percutaneous exposure to blood or by other fluids contaminated with blood. Most of the global transmission of HCV relates to a breakdown in hygiene. In high-income countries prior to 1990, HCV transmission was largely attributed to the contamination of blood supply. Since the routine screening of blood products was introduced in 1990 the risk of HCV acquisition has
been significantly reduced, and further still with the use of sensitive molecular methods such as HCV PCR for virus detection. With the combination of serology and molecular testing of blood donors, the risk of acquiring HCV from blood is less than 0.1 per 1 million units transfused [6]. Individuals with HCV that have been cured of their disease do not present a transmission risk, unless they become reinfected.

Haemodialysis (HD) units are a well-recognised setting for the transmission of HCV, due to the opportunities for people, surfaces and equipment to be contaminated with blood. Standard infection control precautions are therefore important in preventing contamination and interrupting the behaviours and practices that may propagate transmission, such as the reuse of syringes and the use of multi-dose drug vials.

HCV can survive on surfaces at room temperature for up to 16 hours [7], underscoring the importance of adequate surface decontamination and disinfection.

**Screening**

Screening for HCV infection is usually performed using a third generation enzyme immunoassays (EIA) test for HCV antibodies (anti-HCV), followed by the testing of reactive sera with HCV RNA by PCR. A negative RNA test in the presence of anti-HCV by EIA at least six months following a known exposure indicates a resolved infection. Alternative interpretations include a false positive anti-HCV EIA, a false negative HCV RNA, or exceptionally an intermittent or low level HCV viraemia. Anti-HCV by EIA may be negative in early infection, and usually becomes positive 6-8 weeks after of an acute exposure. In contrast HCV RNA can be detected within 2 to 3 days. HCV RNA may also be a more reliable screening test in those with impaired antibody production.

Monitoring aspartate transaminase (AST) and alanine transaminase (ALT) as evidence of an acute HCV infection may be insensitive as HD patients have lower aminotransferase levels when compared to non-HD counterparts. Using baseline ALT as the upper limit of normal and assessing fluctuations above this threshold may provide a more reliable measure of HCV infection [8-12].

**HEPATITIS B VIRUS**

Hepatitis B (HBV) is a 42nm partially double stranded DNA virus with a 3.2kb genome that has four proteins: core protein (HBcAg) is coded for by gene C. A preceding in-frame start codon (AUG) leads to production of a precore protein that is cleaved to form HBeAg. The S gene encodes for hepatitis B surface antigen and is divided into three sections leading to the production of small, medium and large polypeptides. The P gene encodes the DNA polymerase and X gene, a transcriptional activator. HBV is classified into eight well-known genotypes (A-H), and two more recently described genotypes (I, J). Genotypes A, C and D are the most common genotypes in Australia [13].

**Epidemiology**

There are an estimated two billion people globally that have been infected with HBV, of which approximately 240 million are HBsAg positive [14]. In areas where HBV is highly endemic (>8%), most infections are acquired in infancy and early childhood. The risk of becoming chronically infected with HBV is inversely related to age of acquisition. In low endemic settings (<2%), most disease is acquired during adulthood, through either sexual contact or injecting drug use.

Several factors have impacted the burden of HBV infection in the community. Firstly, the routine testing of blood donations for HBsAg was introduced in Australia and the United States of America (US) in the early 1970s. Secondly, the use of a highly effective inactivated vaccine against HBV in high-risk populations commenced in the 1980s, and has been scaled up over time to be increasingly inclusive of all those who could be at risk of HBV exposure in their lifetime. A national universal infant vaccination against HBV was therefore commenced in Australia in 2000 [15].

In 2014, an estimated 213,300 (range 175,000-253,000) people were identified as living with chronic HBV in Australia, of which 38% were born in the Asia-Pacific region, 9.3% were Aboriginal or Torres Strait Islanders, 5.7% were injecting drug users, 4.4% in men who have sex with men (MSM), and 4.3% were born in Sub-Saharan Africa [16]. The estimated prevalence of chronic HBV in these high-risk populations is 3-4%, and across the whole population, 1% [17].
In 2014 there were 6635 new notifications of HBV in Australia, giving a notification rate of 28 per 100,000 population. Highest age specific rates are reported in the 30-39 and 40 and over age group. The notification rate in indigenous Australian is almost twice that of the non-indigenous population [16].

Natural history
Acute infection with HBV is often asymptomatic. Young children in particular are often asymptomatic, and only 30-50% of adults will manifest signs of jaundice and systemic features including fever, arthralgia, rash, nausea, vomiting and abdominal pain.

The outcomes of an acute HBV infection include resolution, development of a chronic carrier state or chronic active infection. Up to 25% of chronic HBV cases will develop cirrhosis with decompensated liver failure, and up to 15% will develop hepatocellular carcinoma.

Transmission risk
The mechanism of HBV transmission is via percutaneous or mucosal exposure to infected body fluids, including blood, saliva, semen, vaginal secretions, pericardial, peritoneal, cerebrospinal fluid and synovial fluid.

The incubation period for HBV infection (i.e. time from exposure to symptom onset) ranges from 45-180 days (usually 60-90 days). The average time from exposure to HBsAg positivity is 30 days (range: 6-60 days). Those who are HBsAg positive with a high HBV viral load or a positive HBeAg are generally considered to be most infectious. A percutaneous injury with a 22 gauge contaminated needle contains approximately 1 microlitre of blood and up to 100 infectious HBV virions. The risk of becoming infected following percutaneous exposure to HBeAg blood is ~27-43%, and in HBsAg positive/HBeAg negative 6-10% [18].

Overall, HBV transmission from a high risk needle stick injury, involving a large volume of blood and/or high viral load in the source case, is 30-40%. The transmission risk associated with a HCV or HIV needlestick injury are comparatively less, at 1.8% and 0.3% respectively [18]. The virus can remain viable on surfaces for up to seven days and therefore environmental contamination with body fluids that carry the virus can be a source of indirect transmission [18, 19].

Persons with protective levels of anti-HBs antibodies (≥10mIU/ml) 4-8 weeks following a scheduled course of vaccination are deemed immune to HBV infection

Occult hepatitis B
Occult HBV is defined as patients with negative HBsAg with evidence of low detectable HBV DNA levels in serum. Occult HBV is increasingly recognised as a potential risk of HBV reactivation, especially in subjects receiving high-dose immunosuppression including monoclonal antibody therapy. HCV inhibits HBV replication, and therefore occult HBV may be more of an issue in HCV infected population. The only serological correlates of occult HBV are a positive anti-HBc with or without anti-HBs. Occult HBV may spread silently. There is moreover a potential association between HBV occult infection and lamivudine resistance. Generally occult HBV is associated with decreased replication fitness and low level viraemia. There are limited studies on occult HBV in the HD population. Estimates from Brazil indicate occult HBV affects 15% of the dialysis population and in other studies 0-36% of the population [20, 21]. Occult HBV has the potential to reactivate, with the emergence of positive HBsAg and HBV DNA as markers of chronic active HBV infection.

Screening
The diagnosis of HBV infection is established through serological testing. The diagnostic panel for HBV serology allows for the determination of susceptibility, active infection, or immunity through vaccination or past infection. The routine serological screening for HBV infection includes HBsAg (HB surface Antigen), anti-Hbc (anti-HB core) and anti-HBs (anti-HB surface) antibodies. HBeAg/anti-HBe serology and HBV DNA viral load are used to determine the phase of infection, the likelihood of progressive disease and need for treatment. Positive HBeAg and/or high HBV DNA viral load are markers that correlate with infectivity [22].
HUMAN IMMUNODEFICIENCY VIRUS

Human immunodeficiency virus (HIV), a retrovirus, was discovered in 1983. Subsequently two distinct species, HIV1 an HIV2, have been associated with the acquired immunodeficiency syndrome (AIDS). HIV1 accounts for the greatest burden of global disease.

Epidemiology

In 2013 there were 1.8 million new cases of HIV diagnosed globally, 35 million people living with HIV, of which approximately 70% were located in Sub-Saharan Africa, and 1.5 million AIDS-related deaths. A decline in the incidence of HIV has occurred over time, with over a million fewer new diagnoses in 2013 compared to 2001 [23].

In 2014 there were an estimated 27,150 (range 24,630-30,130) in those aged 15 years or older living with HIV in Australia, and an additional 3350 with the disease who remain undiagnosed, giving an overall prevalence of 0.14%. MSM have the highest burden of infection. In 2014, an estimated 17% of the MSM population were HIV infected, and 1-2% in injecting drug users attending needle exchange programs. New cases of HIV notified in Australia in 2014 numbered 1081, of which 70% reported MSM as a risk factor, 5% reported MSM and injecting drug use, 19% reported heterosexual transmission, and 3% reported injecting drug use [16].

Since 1985 all blood has been screened for HIV to prevent blood-borne transmission. As a result no known cases of blood borne virus (BBV) infection from transfusion have been detected since the late 1990s [16].

Natural history

Acute HIV infection can manifest as an acute mononucleosis-like syndrome with fever, lymphadenopathy and rash. Following acute infection, HIV infection can remain quiescent, with AIDS – defining opportunistic infections, correlating with increasing viral load and declining CD4 lymphocyte counts, developing over the course of 1-15 years.

Transmission

The main routes of transmission include mucosal trauma during unprotected sexual intercourse, vertical transmission from mother to child during pregnancy, delivery or breastfeeding and percutaneous exposure through the sharing of contaminated needles, syringes during injecting drug use. Prior to the serological and nucleic acid test screening of blood and tissue products, HIV transmissions occurred through infected donor transfusions and transplantation. Less important routes of transmission include exposure of abraded skin and mucosa to infectious body fluids, and skin piercing and tattooing with HIV contaminated equipment.

HIV screening is recommended in those with risk factors [24]. Current screening for HIV consists of 4th generation Ag/Ab test. Follow up confirmatory tests include nucleic acid amplification tests (NAAT) and/or Western blot.

Standard precautions

Standard precautions for all BBV includes hand hygiene before and after touching patients or equipment attached to the patient; the appropriate use of personal protective equipment including gloves, apron/gown, mask and eye protection during exposure prone procedures; the safe disposal and handling of sharps and clinical waste; the cleaning of spills; maintenance and cleaning of the patient care environment; the appropriate reprocessing of all reusable patient care equipment, and instruments, and linen; the use of aseptic non touch technique when inserting vascular devices.

SEARCH STRATEGY

Databases searched: MeSH terms and text words for haemodialysis were combined with MeSH terms and text words for chronic kidney disease, HBV, HCV, and HIV and then combined with text words for meta-analysis, randomised controlled trial, cross-over, case control, cross sectional and cohort. The search was carried out in Medline (1946 – November Week 3, 2014).

Date of search: 22 December 2014.
WHAT IS THE EVIDENCE?

Epidemiology of BBV in Australia-and New Zealand haemodialysis (HD) populations

HEPATITIS C VIRUS (HCV)

Prevalence of HCV in HD

The seroprevalence of HCV in Australian and New Zealand HD units has only been explored by a small number of very low to moderate quality studies. Globally, there has been a broader examination of HCV seroprevalence in HD units with high quality systematic reviews of observational studies available and various reports from a moderate-quality multi-national study conducted over three continents (Dialysis Outcomes and Practice Patterns Study (DOPPS)).

The largest study to examine the prevalence of HCV in Australian and New Zealand HD units involved an analysis of national and regional dialysis data registries from 10 Asia/Pacific countries (Australia, New Zealand, Japan, China, Taiwan, Korea, Thailand, Hong Kong, Malaysia and India) Period prevalent data was used, and longitudinal data was available from the Australia and New Zealand registry for all patients commenced on dialysis between 1995 and 2005. From an analysis of 201,590 dialysis patients across 10 registries, of which 172,788 were receiving HD, seroprevalence was significantly higher in HD compared to peritoneal dialysis (PD) patients (7.9% versus 3.0%; p=0.01). Lower HCV rates in PD may be explained by the lesser time spent on PD, and therefore period at risk. The highest HCV prevalence of 18% was reported in dialysis patients in India. In Australia and New Zealand there has been a steady decline in HCV seroprevalence from approximately 5.2% to 2% over the period from 1995 to 2005 [25] A retrospective review of the serological status for HCV, HBV, HIV and HTLV-1 in 440 HD patients from the Top End of the Northern Territory reported a HCV seroprevalence of 1.6%, which was lower than the prevalence for chronic HBV (8.9%) and HTLV1 (2.2%) [26]. The only other seroprevalence study from the Australian setting relates to a study from Western Sydney in the early 1990s that showed a 10% prevalence of anti-HCV. In this study, all patients had a history of prior blood transfusion [12].

Incidence of HCV in HD

The incidence of HCV globally has been examined in numerous prospective studies with small sample sizes of very low to low quality. Studies specific to the Australia-New Zealand HD setting are lacking. A systematic review of all observational studies conducted between 1990 and 2012 [27] provides the best estimate of the global incidence of HCV in HD units, although the risk of bias of the included studies was not assessed. In this systematic review the estimate of HCV incidence between 1990 and 2012 was 1.47 per 100 patient years. Subgroup analysis and meta-regression identified a country's development level and baseline HCV prevalence as the strongest determinants of HCV incidence. In low to middle income countries incidence rate (IR) was 4.44 per 100 patient years and in high income countries, 0.97 per 100 patient years [27].

Mortality associated with HCV in HD

Systematic reviews of observational studies provide the clearest picture of the effect of HCV on mortality in patients on HD. None of these studies however are specific to the Australian setting. Although, in several systematic reviews [28-30] the findings for the HD patients were unable to be distinguished from the PD patients, as the analysis involved both groups of patients. The estimates of HCV effects on survival and morbidity in HD is of relevance in determining the potential gains in dialysis outcomes that may accrue from the prevention or treatment of HCV.

A meta-analysis of four clinical trials, three prospective cohort studies and one case-control study compared mortality rates in those on HD with those who were HCV negative. Adjusted all-cause mortality was significantly increased in those with HCV infection (relative risk 1.57; 95% CI 1.33, 1.86) [28]. A follow-up systematic review of seven observational studies that included 11,589 participants, demonstrated an adjusted relative mortality risk of 1.34 (95% CI 1.13, 1.59) in HCV positive HD patients. Sub-analyses showed a statistically non-significant increase in infection and cardiovascular mortality in patients with HCV, and a significantly increased risk of liver-disease related mortality (RR 3.75; 95% CI 2.02, 6.96) [29]. An updated systematic review of 14 observational studies involving 145,608 dialysis (HD and PD) patients demonstrated that patients infected with HCV have a
significantly increased all-cause mortality risk (RR 1.32; 95% CI 1.25, 1.39), increased cardiovascular mortality risk (RR1.26; 1.10, 1.45), increased infection-related mortality risk (RR1.53 95% CI 1.11, 2.12) and increased liver-disease related mortality (RR 3.18; 95% CI 2.08, 4.84) [30]. A systematic review and meta-analysis examining the survival advantage of kidney transplantation over dialysis in patients with HCV, revealed a pooled risk of death in those on dialysis with HCV of 2.19 (95% CI: 1.50, 3.20). Cardiovascular disease in this population was a major cause of death after controlling for the effects of age and gender [31].

Risk factors associated with HCV in HD
Risk factors associated with incident and prevalent HCV have been highlighted across low quality prospective and retrospective observational studies, few of which relate directly to the Australian-New Zealand setting. Multiple risk factors have been associated with HCV seroconversion and the independent effects of infection control interventions in reducing incident HCV made difficult by the fact that such interventions are often delivered as a bundle.

Haemodialysis as compared to PD is associated with a higher rate of incident HCV. From registry data the incidence ratio adjusting for years on dialysis, in PD versus HD is estimated to be around 0.33 [25]. In another observational study, incidence HCV was reported in 0.86% of HD patients as compared to 0.53% of PD patients [32] The increased risk of HCV acquisition is possibly related to the increased hospital contact of HD patients, and the increased requirement for blood products in the HD population. The geographic setting where HD occurs is further associated with HCV acquisition. Rates of HCV were more than four-fold higher in low-to-middle income countries as compared to high-income countries, with an incidence rate of 4.44 per 100 patients in low-to-middle income countries compared to 0.97 per 100 patients in high-income countries [27].

The background prevalence of HCV in HD units is a significant risk factor for HCV acquisition [31, 33-36]. In one multicentre study, incident HCV was correlated with background HCV prevalence and HCV incidence increased when HCV prevalence exceeded 20%. In centres where prevalence was >60%, the incidence was 23 fold higher than in centres where prevalence was <20% [32]. In a meta-regression analysis of published studies, centres with a HCV prevalence of <15 % had an incidence of HCV of 0.56, which was a quarter of that observed in centres where the HCV prevalence was ≥15% [27]. A prospective multi-centre Italian study, demonstrated a background prevalence of ≥30% in the HD population to be independently associated with incident HCV (odds ratio 4.6; 95% CI 1.4, 16.0) [37]. In a US study of fifty-three facilities and 2933 patients, a HCV prevalence of ≥10% was associated with a significantly increased odds ratio of HCV antibody and/or HCV RNA (odds ratio 3.0; 95% CI 1.8-5.2) [38]

The requirement for blood transfusions has been associated with an increased risk of HCV in HD patients [32, 38-43]. In a prospective multi-centre German study, the timing of blood transfusion showed a significant association with being HCV positive. For those receiving blood products prior to 1991 (the time at which HCV screening of blood products was mandated) compared to those receiving blood products after 1991, the risk of HCV was significantly increased (odds ratio 5.39; 95% CI 2.67, 10.89) [39]. In a US study, blood transfusions received before 1986 (the year surrogate marker screening for Non A Non B hepatitis was introduced) was associated with an increased odds of HCV (odds ratio 2.1; 95% CI 1.2, 3.7) on univariate analysis. This association, however, was not significant after adjusting for years on HD [33]. In a meta-analysis, 997 Chinese HD patients who had received a transfusion had an odds ratio of 5.65 for HCV (95% CI 3.69-8.66; p<0.00001) as compared to the 529 HD patients that were not transfused [34]. In a multi-centre French study, the rates of anti-HCV positivity was significantly higher in those not receiving erythropoietin stimulating agents (odds ratio 2.1; 95% CI 1.2, 3.5; p<0.01) [44].

In addition to blood transfusions, HD patients have an increased requirement for invasive procedures. A significantly increased independent risk of acquiring HCV was observed in patients undergoing a surgical intervention in the preceding six months, including creation of arteriovenous fistulae, inguinal hernia repair, gynaecological surgery, and surgical treatment of complicated skin wounds (odds ratio 16.5; 95% CI 2.6, 105.7) [37]. Prior receipt of a renal allograft was another intervention independently associated with an increased risk of being anti-HCV positive (odds ratio 4.0; 95% CI 2.4, 6.8; p<0.0001) [44].
Dialysis-specific interventions such as the use of dedicated machines, the isolation of patients with HCV from the non-HCV infected and reuse of dialysers have been assessed in a number of observational studies. The use of dedicated machines has been associated with a lower prevalence of HCV in a high prevalence setting. In a randomly selected sample of 12 dialysis units in Tehran, involving 593 patients, four centres used dedicated dialysis machines for HCV positive patents and eight centres used non-dedicated machines. All machines were located in general dialysis wards and infected patients were not physically isolated. Only patients confirmed to be HCV RNA positive were considered HCV infected.

HCV prevalence in the dedicated centres was 10.1% (range: 4.6%-13.2%), and in the non-dedicated centres 7.1% (range: 4.2%-16.8%). Patients (n=442) were followed for nine months and 281 cases for an additional nine months. No significant differences in loss to follow-up due to death, transplantation or transfer to another facility were noted between the groups. In the first follow-up period the incidence of HCV infection was 1.6% in the dedicated group and 4.7% in the non-dedicated group (p=0.05). In the second follow up period HCV incidence in dedicated and non-dedicated groups were 1.3% and 5.8%, respectively (p<0.05) [40]. In a prospective study conducted over five years, involving four HD centres (n=135), a strict cleaning regimen was compared to the use of dedicated dialysis machines. The strict cleaning strategy involved all HD monitors being systematically disinfected after each dialysis session with sodium hypochlorite and peracetic acid, in addition to a disinfection clean three times per week. This was compared to the use of dedicated dialysis machines in addition to strict cleaning. The strict cleaning regimen alone was associated with a seroconversion rate of 0.54% per year and with the additional measure of using dedicated machines, the seroconversion rate was 0.36% per year. The study concluded that dialysing patients with dedicated machines demonstrated no statistically significant benefit over and above strict cleaning [41].

In a systematic review of three observational studies, lower rates of HCV were observed when dialysers were not reused [34]. In contrast, a Belgian study involving 15 HD units showed no association between reuse of dialysers [43]. This has also been supported by a US national survey of dialysis related diseases in the US. In 2002, 63% of centres surveyed reported reusing dialysers, with 94% of centres reprocessing the dialysers in their own facility. Dialyser reuse showed no association with HCV incidence or prevalence across the US dialysis centres surveyed. The authors also noted that from 1983 to 2002 an increasing proportion of dialysers were treated with peracetic acid and a declining proportion with formaldehyde [35].

Isolation of HCV from non-HCV infected patients has shown the greatest benefit in high prevalence settings [29, 35, 42, 45-50]. The independent benefit of isolation has been difficult to tease out from other interventions that have been bundled such as improved compliance with universal precautions [42]. Even in a high prevalence setting, however, isolation has demonstrated no additional benefit when strict adherence to infection control standards are applied as shown in a prospective observational study involving a single dialysis centre in Buenos Aires conducted over six years (1994-2000). In the first year of this study, 53 patients were on HD, and by 2000 this number had increased to 82 patients. Measures to increase strict adherence to universal precautions were implemented in 1993 and anti-HCV testing of blood donors in 1994. Neither separate rooms nor separate machines were used for anti-HCV positive patients. Prevalence of HCV decreased from 41.5% in 1994 to 8.5% in 2000. Yearly seroconversion rates were 0.5% from 1994-1996 and 0.4% during the period 1998-2000. The authors conclude that standard precautions without isolation measures could achieve reductions in HCV prevalence, and low incidence in a high prevalence setting [51]. In low prevalence setting for HCV, adherence to strict universal precautions has been shown to prevent transmission when no isolation policies have been applied. A multi-centre German prospective study, randomly selected six HD units to have their population (n=435) sequentially sampled for GBV-C RNA, a non-pathogenic virus that can be used as a surrogate marker of blood borne transmission, and therefore a means of assessing breaches in infection control. Twenty-eight GBV-C RNA positive subjects were also anti-HCV negative. These patients were not managed in isolation, but were subject to the strict implementation of universal hygiene standards. Over the two sampling periods three de novo GBV-C infections were identified, but none were phylogenetically related to the prevalent GBV-C infections using sequence analysis, indicating that no cross transmission of infection had occurred in haemodialysis patients who were not managed in isolation [39]. In a prospective Belgian study, involving 15 participating dialysis units, a dialysis cohort was followed for 54 months, from 1991-1995, and were observed to achieve a sustained decrease in HCV seroconversions. In the first 18 month study period, seroconversions occurred at a rate of 1.4% and by study conclusion no seroconversions had occurred in the preceding 18 months. None of the patients with HCV were isolated during dialysis. Prevention of HCV transmission was attributed to the improved compliance with universal precautions [52]. Similarly, in the DOPPS study,
there was no association between HCV seroconversion and HD centres that implemented isolation in patients with HCV [53]. A Swedish HD centre further described a decrease in HCV seroprevalence from the baseline survey (1991) compared to the second survey period (December 1996-January 1997). Of note isolation of HCV patients had been discontinued after the initial survey period, without an associated increase in seroprevalence or HCV transmission within the unit. The authors conclude that routine hygienic practices were sufficient to reduce HCV transmission [54].

Other studies have examined the spatial relationships that are associated with HCV transmission by looking at transmission events in patients dialysing in the same area, on the same day, or on the same shift as HCV positive patients. In all of these studies, a breach of standard infection control precautions has been suggested. A case control study of a HCV outbreak investigation in a French HD unit identified a number of risk factors associated with seroconversion including receiving dialysis immediately after a patient infected with genotype 2a/2c or sharing a dialysis room with a patient with 2a/2c. Observed breaches in infection control that may have facilitated transmission included wetting of transducer protectors with blood and contamination of machine parts not accessible to routine cleaning [55].

In a longitudinal observational study in a single dialysis centre in France, 70 patients were prospectively followed with systematic virological and biochemical tests, including monthly ALT and three-monthly anti-HCV and HCV RNA to ascertain nosocomial transmission. At baseline 26 of 70 patients were anti-HCV positive giving a baseline prevalence rate of 37.1%, of which 85% were also confirmed HCV RNA positive. Eleven de novo infections were identified over 12 months. Three clusters of HCV in this study were associated with patients dialysing in the same area and or during the same shift. After implementation of enhanced universal precautions, two further new cases were identified, which prompted the use of separate rooms and dialyser machines for HCV positive patients [36]. In a retrospective cohort study, a structured audit of medical records and HD logs were analysed. Internal protocols were reviewed and healthcare workers interviewed to identify practice breaches. HD patients were also interviewed to assess for other potential risk factors. Ten of 13 incident cases were phylogenetically typed and all of these were reported as genotype 2c. Eleven of the 13 cases who seroconverted had all dialysed on the same afternoon. A prevalent HCV case, identified as the index case, had dialysed in the unit on the same morning and had difficulties with their arteriovenous fistula, requiring extra doses of heparin. Multiple regression analysis of risk factors for HCV acquisition identified patients receiving dialysis on the same shift and same days to HCV positive patients to be at significantly increased risk of HCV seroconversion. The postulated mode of spread was from contaminated 250ml saline diluent or multi-dose heparin vials used on a known HCV prevalent case in the morning shift [43]. A phylogenetic study from Japan identified five HCV clusters among 20 of 48 patients that dialysed on 17 consoles during three separate shifts in the same room. The study ascertained that cluster cases were more likely to dialyse in the same shift, and that dialysing at a console nearby was less of a risk factor [45].

Work force capacity has been identified as a risk factor for HCV. Dialysis centres with a personnel/patient ratio of <1:28.2 had an increased and independent risk of incident HCV cases (odds ratio 5.4; 95% CI 1.4, 19.2) [37]. In a US study of 53 facilities involving 2933 patients, a patient to staff ratio of ≥7 to 1 had a significantly increased odds of patients with positive HCV antibody and/or HCV RNA (odds ratio 2.4; 95% CI 1.4-4.1) [38]. A cross-sectional survey of 13 dialysis centres in Khartoum State Sudan assessed staff working in these units on their knowledge of HBV and HCV infection, transmission and prevention. In addition, a cohort of 1011 patients dialysing in these facilities consented for interview and medical record review, capturing serological and HBV vaccination status. Centre characteristics that were significantly associated HCV seroconversion included assigning more than three patients per dialysis nurse (odds ratio 12; 95% CI 1.2-123; p=0.03) [56]. The quality of staff training has been identified as an additional risk factor. In the DOPPs study, centres with highly trained staff (defined as staff with at least two years of formal nurse training) showed a significantly decreased HCV prevalence. A 10% increase in trained staff was associated with an odds ratio for HCV prevalence of 0.93 (p=0.003) [53].

The duration of HD or dialytic years has been shown to be an independent risk factor for HCV acquisition across several studies [27, 31, 32, 36, 38, 40-42, 52]. In a systematic review and meta-analysis of Chinese dialysis centres, 593 long-term (>1 year duration) HD patients had an odds ratio of 7.62 for HCV (95% CI 5.42-11. 59; p<0.0001) when compared to 265 short-term (<1 year duration) HD patients [34]. An equal probability, two stage cluster sampling was used to survey 87 US HD facilities from Medicare-approved providers that treated 30-150 patients. Fifty-three facilities and 79% of
A number of observational studies have explored the role of environmental contamination and poor adherence to standard infection control precautions as risk factors for HCV transmission [30, 36, 39, 40, 57-61]. Contamination of inanimate objects in the dialysis environment by HCV and HBV was examined across three HD centres in Rome, Italy. Prevalence of HCV (anti-HCV) in the three centres was 44% (Centre A), 16% (Centre B), and 11% (Centre C). All centres routinely had HCV patients dialyse in the same room as non-HCV infected patients, but on dedicated machines. Samples were collected from environmental surfaces, machines and items after interdialysis cleaning and disinfection and these were tested for HCV RNA. Negative controls using swabs moistened in a sterile buffer without contact with the dialysis environment were tested simultaneously. One of 64 environmental samples (1.6%) were positive for HCV RNA. The positive sample was found on the external surface of the dialysate (inlet-outlet) connector of the dialysis machine used for a HCV negative patient in Centre C [62]. Hand hygiene is important for reducing transmission risk of blood borne viruses and other nosocomial pathogens. A virological study of HCV contamination of healthcare worker hands was undertaken in a single-centre HD unit in Riyadh, Saudi Arabia. The study involved the washing of hands with one litre of sterile water, and capturing the fluid for HCV RNA sampling within three hours of collection. Three groups were sampled including 80 washings from healthcare personnel who dialyzed HCV positive patients, 100 washings from personnel who dialyzed HCV negative patients and 60 samples from a control group, taken before entering the dialysis unit. Significant differences were identified in HCV RNA on hands of those working with HCV positive dialysis patients (23.7%), compared to those working with HCV negative patients (8%) (p<0.003). The authors concluded that the hands of healthcare workers are a potential mode of HCV transmission, emphasising the importance of adherence to standard precautions including strict hand hygiene in the healthcare setting [46]. The strict implementation of standard precautions, including hand hygiene, the wearing and changing of disposable gloves; the cleaning and disinfection of dialysis machines between use; the routine cleaning and disinfection of equipment; the use of individual supplies, dedicated staff for patients with HCV, and a clean area for the preparation of medications have been associated with lower HCV prevalence in the HD setting. The odds of prevalent HCV, after adjusting for transfusion history and years on HD was significantly increased (odds ratio 4.9; 95% CI 2.5-9.6; p<0.001) in centres that did not routinely adhere to standard precautions when compared those that did [47]. In a study of European HD centres a total of 4724 patients with baseline and follow-up serology at 12 months resulted in the identification of 13 seroconversions. These seroconversions occurred in seven hospitals in five different countries (Austria, Israel, Belgium, Switzerland, Italy). One centre that reported four seroconversions had multiple risk factors including a distance of <0.5 metres between dialysis stations, dialysis machines only being washed between acute dialyses, the lack of routine screening for HCV, with screening only being done upon indication, chairs being washed at the end of a shift and not between patients and the lack of personal protective equipment such as aprons [48]. The priming of dialysis machines, handling of blood specimens and preparation and delivery of medications have been identified as risks for HCV transmission. Dialysate priming in US HD centres was observed to carry a significantly increased risk of incident HCV when the priming solution was discarded into a non-disposable container attached to the machine, as compared to a disposable container discarded after each treatment (HCV incidence 0.39% versus 0.18%; p<0.05) [35]. In another US survey of patient-care practices, risk factors independently associated with higher HCV prevalence included the reuse of priming receptacles without disinfection (odds ratio 2.3; 95% CI 1.4, 3.9), handling blood specimens adjacent to medications and clean supplies (odds ratio 2.2; 95% CI 1.3, 3.6) and using mobile carts to deliver injectable medications (odds ratio 1.7; 95% CI 1.0, 2.8) [38].

The importance of enhanced screening and infection control procedures for patients returning after dialysis in a high prevalence, or resource poor setting has been highlighted by two studies. In a European study, three of seven centres reported seroconversions that involved patients who had dialysed in another country beforehand. It was estimated that travelling abroad contributed to 3 out of the 13 patients seroconversions. However, the reliance on self-report and variations between centres made it difficult to determine the likely infection control breaches that contributed to HCV acquisitions [48]. In a retrospective UK study, 16 new cases of HCV following dialysis abroad were identified in two large HD units in Birmingham, UK. These cases constituted 16/36 (44%) of all new HCV acquisitions. The study underscored the importance of enhanced screening and infection control procedures for patients returning after dialysing in resource poor settings [63].
HEPATITIS B VIRUS (HBV)

Prevalence of HBV in HD

There have been few studies that have examined the prevalence of HBV in Australia and New Zealand HD units, and prevalence estimates are at best inferred from large international cohort studies. Globally there have been a number of national surveys, international multi-centre studies and single-centre retrospective studies all of very low quality because of concerns of reporting bias and potential confounding.

The only Australian multi-centre study reporting on HBV prevalence and incidence in the HD setting is from the Top End of the Northern Territory. In this population, past infection with HBV (anti-HBc) was reported in 42.7% of 440 HD patients, and the prevalence of HBsAg was 8.9%, making HBV the most prevalent of all BBV [26]. A large registry-based study from the Asia-Pacific region reported prevalence of HBsAg from seven Asian-Pacific countries including Japan, China, Malaysia, Hong Kong, Thailand, Taiwan and Korea. Prevalence ranged from 1.3% to 14.6%. Unlike HCV, rates of HBsAg were comparable between PD and HD in five countries, whereas Japan and Taiwan reported higher rates of HBV in PD compared to HD patients. The prevalence of HBV in Australian and New Zealand was not reported in this study [25]. A national survey of specific diseases and practices of all US chronic HD centres was conducted in 2002. A total of 4035 centres participated (96% total) with a total sample population of 263,820 patients. The reported HBsAg prevalence was 1% and incidence was 0.12%. Twenty-seven per cent of centres reported having one or more patients with prevalent HBV, and 2.8% reported incident cases [35]. In a study of eight European HD centres (n=21,861) the overall HBV prevalence was 1.9%, with the highest HBV prevalence reported in the Czech Republic (3.1%), with Slovakia, Greece, Italy and Belgium all reporting a prevalence of approximately 2%. The lowest HBV prevalence of < 1% was reported from Norway, Scotland and England. All participating centres reported screening for HBV in their dialysis population on a routine basis (at least yearly). Sixty-six per cent of all dialysis centres reported isolating patients who were HBV positive [49]. A cross-sectional study examining both HCV and HBV prevalence in 2120 HD patients from 20 HD units in Beijing, found the prevalence HBsAg to be 7%, and anti-HCV 6.1%. HBsAg prevalence in the HD population was close to that reported in the general population from a national serosurvey in 2006. Whereas, the significant risk factors associated with HCV included dialysis duration, blood transfusion and attending more than one dialysis centre, the risk factors for HBV included sociodemographic factors including older age, having a household contact with HBV, previous surgery. A large number of HBsAg in this study were associated with Infectious Diseases Hospitals, and it was likely that such patients were referred to these centres with a known positive HBsAg status prior to commencement of dialysis [50].

Incidence of HBV in HD

Of the studies that have examined seroconversion of HBV in HD units, most have also investigated the introduction of various standard precautions on nosocomial transmission. A moderate-quality systematic review and meta-analysis of prospective studies and a low-quality international multi-centre observational have examined the incidence of HBV in haemodialysis units, these are discussed below: Dialysis units are the most common settings in which HBV outbreaks have been described. In a systematic review of 33 HBV outbreaks reported between 1992 and 2007, a total of 471 patients contracted HBV, and of these 16 died. Dialysis units accounted for 30.3% of all outbreaks described [64]. Data from DOPPS, a cross-sectional prospective observational study was conducted to examine patterns of prevalence and seroconversion for HBV. A random sample from 308 representative dialysis facilities from five European countries (France, Germany, Spain, Italy and UK), US and Japan were surveyed between 1997 and 2001. The sample included 8615 patients. Mean unadjusted HBV prevalence was 3.1%, and median 2.0%. The highest prevalence was reported in Italy (6.6%) and lowest in US (2.8%). Overall 78.5% of dialysis centres that were randomly sampled had HBV prevalence ≤5% and 78.1% had a seroconversion rate of 0 per 100 patient years. The overall HBV seroconversion rate was 0.78 per 100 patient-years. HBV prevalence showed a positive association with years on dialysis. This association may have been confounded by the observation that longer term HD patients potentially started dialysis in an era when the routine methods for screening of blood products was less reliable, and the transfusion avoidance strategies such as erythropoietin were not available or in wide use [65].
Mortality associated with HBV in HD
Studies that specifically address HBV mortality in HD populations are lacking. In one systematic review and meta-analysis of dialysis-associated HBV outbreaks, no HBV associated deaths were reported. Deaths from HBV reported in other non-HD outbreak settings were observed in patients with underlying neoplasia [64].

Risk factors associated with HBV in HD
The transmission risk with HBV is much greater than with either HCV or HIV, and routes of nosocomial spread have been linked to needle stick injuries, transfusions, cross contamination of multi-dose vials, poor environmental cleaning and contamination of equipment. As with HCV, multiple risk factors have been associated with HBV transmission and the independent effects of infection control interventions in reducing incident HBV made difficult by the fact that such interventions are often delivered as a bundle. There is low to moderate quality evidence examining various risk factors for HBV acquisition in the HD population.

HBV outbreaks in HD units are well-described [64, 65]. In a systematic review of 33 nosocomial outbreaks of HBV between 1992 and 2007, dialysis units were implicated in 10 outbreaks, 30.3% of all episodes. Other settings included nursing homes, surgical and medical wards and outpatient clinics. Outbreaks in dialysis centres were of significantly shorter median duration (3.5 months versus 9 months; p=0.02), and median numbers of patients acquiring HBV fewer (4 versus 11; p=0.024) when compared to other settings. The transmission sources in HD related HBV outbreaks have included multi-dose vial use (five outbreaks), multiple deficiencies in standard precautions (one outbreak), and blood transfusion (one outbreak). In three outbreaks the transmission source was not defined [64].

The evidence for isolating patients with HBV infections is sparse. Data from the DOPPS study examined practice patterns and facility characteristics for their associations with HBV prevalence and seroconversions. Factors that were significantly associated with HBV prevalence, after adjusting for covariates, included isolation of patients (odds ratio 1.58, p=0.047) and number of patients to dialysis stations (odds ratio 1.11 for each additional patient dialyzing at a dialysis station, p=0.01) [65]. The finding of the increased association between isolation and HBV prevalence likely reflects the response of centres with prevalent HBV to have isolation protocols in place. In a prospective study from Zhejiang province in China, all 6182 registered HD patients from 150 units were recruited in 2007 and followed for four years. Provincial quality control standards were implemented in 2007 and included a policy of isolation in HBV infected patients, single use dialysers, HBV and HCV serological screening prior to entry on dialysis and every six months on maintenance dialysis, attention to hand hygiene, single use HD care packages for disposal after use, disinfection protocols for machines and fixtures, staff training, data reporting and regular audits. Over the four years of the study, the proportion of units that were isolating or segregating the HBV/HCV patients had increased from 25% to 90%, and HBV seroconversion from 0.66% to 0.26%. The background prevalence of HBV in the HD population was 8.3%, and HCV was 6.6% [66].

As with HCV, there is no strong evidence against dialyser reuse. The UK, US and Spain were three countries in the DOPPS study that reported using reused dialysers. A comparison of HBV prevalence and seroconversion rates in centres that reused dialysers and those that did not, showed no significant difference [65].

The dialysis environment with particular reference to medication preparation, delivery of medications and environmental cleaning are among the standard measures to reduce HBV transmission. US centres with dedicated medication rooms or a medication preparation area separate from the dialysis treatment area had a significantly lower incidence of HbsAg, when compared to centres that used medication carts or prepared injectable medications within the dialysis treatment area (0.06% versus 0.27%; p<0.05) [35]. The environmental contamination of HBV, in addition to HCV was examined across three dialysis centres in Rome, Italy. Prevalence of HBV (HbsAg) was 15% (Centre A), 0% (Centre B), and 4% (Centre C), and all centres routinely had HBsAg patients dialysed in a separate room on a dedicated machine. Samples were collected from environmental surfaces, machine and items after interdialysis cleaning and disinfection and tested for HbsAg. Negative controls using swabs moistened in a sterile buffer without contact with the dialysis environment were tested simultaneously. One of 64 environmental samples (1.6%) were positive for HbsAg. The positive sample was found on
the internal surface of the blood pressure monitor cuff used on a HBsAg-positive patient room in Centre A [62].

The administration of HBV vaccination to non-immune HD patients is another measure to protect patients from HBV infection. A multicentre randomised placebo controlled trial recruited 1311 patients from 41 US dialysis centres [67]. Of these, 650 were randomised to the vaccine group and 651 to placebo. In this study, overall antibody responses to vaccines was poor. Moreover, 4 vaccine responders with protective post vaccination antiHBs titres went on to become HBsAg positive at least 18 months after receipt of their vaccination. One vaccine failure was explained by a patient receiving immunosuppression for a transplant. In another subject, HBsAg positivity was transient. In the remaining two subjects, antiHBs levels had declined to <10 before they developed positive HBsAg. In a case-control study involving 98 US HD centres, 111 case patients were identified, defined as those who seroconverted from HBsAg negative to positive in 1995. Controls (n=12,500) were those were HBsAg negative, and had not seroconverted, and had dialysed in the same centre as a patient who had seroconverted. Case patients had significantly lower rates of HBV vaccination (unadjusted odds ratio, 0.39; 95% CI, 0.22, 0.72). After controlling for dialysis centre location, adjusted odds of vaccination uptake were found to be even lower (odds ratio, 0.30; 95% CI, 0.18, 0.50). This study concluded that HBV vaccination had a significant protective effect against HBV acquisition in chronic HD patients [68]. The implementation of a HBV protocol, inclusive of isolation, screening, trained staff and vaccination was associated with a lower HBV seroconversion rates (risk ratio 0.44, p=0.03). Vaccination was independently associated with an increased rate of seroconversion (odds ratio 11.2, p=0.007). In this observational study, the authors concluded that centres experiencing high rates of seroconversions were more likely to vaccinate their non-immune haemodialysis patients. [65].

HUMAN IMMUNODEFICIENCY VIRUS (HIV)

There have been relatively few studies that have examined HIV in the HD population. The studies are of very low quality because of concerns regarding the sample size and potential reporting bias due to the reliance on centre-based questionnaires and surveys.

Prevalence of HIV in HD

In a retrospective review of BBV serology in the top end of the Northern Territory, no cases of HIV were reported in the 440 patients included in the analysis [26]. In 2002, 39% of US centres reported treating patients with HIV infection, and the prevalence of HIV in the chronic HD population was 1.5%, and those with AIDS, 0.4% [35]. In an EDTNA/ERCA project involving eight European countries/region, HIV prevalence in the dialysis population ranged from 0-0.4% [49]. A US survey of 1324 long-term HD patients from 28 dialysis centres in 1986, showed a low overall prevalence of HIV (0.98%). Rates of HIV by dialysis centre reflected community incidence trends, and those with HIV were more likely to report risk factors independent of their dialysis, such as a history of injecting drug use. [69].

Incidence of HIV in HD

In the abovementioned US survey, none of the seronegative HIV HD patients had seroconverted over the course of one year. These results suggested that standard infection control measures were sufficient to minimise risk of HIV transmission. A limitation of this study was that it involved voluntary participation, and 50% of those in the incidence phase of the study, were lost to follow-up. At the time of this study being conducted, the prevailing recommendation was that HIV patients did not require isolation from the general dialysis population [69].

Mortality associated with HIV in HD

Studies are not available that specifically address HIV-related mortality in those on HD, and how this compares to HIV patients not receiving HD.

Risk factors associated with HIV in HD

Much of what is known about preventing HIV in HD is extrapolated from other nosocomial settings. A single retrospective cohort study in Colombia from January 1992 to December 1993 identified nine HIV seroconversions in 23 patients with stored sera who were receiving HD. All cases were linked to a dialysis patient with known HIV undergoing HD in the same centre. Two patients had potentially acquired their infection from a high-risk sexual contact. Access needles were reprocessed by soaking them in a common container with a low level disinfectant. It was therefore concluded that the likely
mode of transmission in this outbreak related to improperly reprocessed patient care equipment, most notably access needles [57].

**SUMMARY OF THE EVIDENCE**

**HEPATITIS C VIRUS**

The prevalence and incidence of HCV in HD has been explored using data from retrospective and prospective cohort studies, and systematic reviews. Multicentre studies, systematic reviews and longitudinal studies have enabled an examination of risk factors associated with seroprevalence and incident cases. The prevalence of HCV in HD is observed to vary considerably between countries, with rates ranging from 1% [49] to >40% [34, 70]. A decline in the prevalence and incidence of HCV in chronic haemodialysis patients has been documented across multiple geographic regions over the last two decades. In Australia and New Zealand, a decline in HCV prevalence from 5.2% to 2% has been reported over the decade 1995 to 2005 [59]. The incidence of HCV in high-income countries is currently estimated to be less than 1 per 100 patient years [27]. Much of the decline in HCV burden in HD patients has been the result of decreased use of blood transfusions in the era of erythropoietin stimulating agent (ESA), and the availability of screening tests and the mandated screening of blood products.

Risk factors for HCV acquisition in HD patients include dialysis duration, or dialytic years, a history of blood transfusion, a history of holiday dialysis, dialysing in a unit with high HCV prevalence and poor compliance with universal infection control precautions. The role of dedicated machines and isolation of patients with HCV to prevent transmission is more contentious, with these strategies showing greater success in settings with a high HCV prevalence. The strict implementation of universal precautions and cleaning protocols have been shown to be sufficient to interrupt HCV transmission and achieve reductions in HCV incidence even without isolation measures and the use of dedicated machines [39, 60].

**HEPATITIS B VIRUS**

The prevalence of HBV in HD patients in the Asia-pacific region is 1.3%-14.6% [59] and in Europe 1%-3% [49]. Available data from the Top End of the Northern Territory Australia has reported a seroprevalence of 8.9% in HD patients [26]. The prevalence of HBV in HD has shown a decline since the early 1970s, due to the successful screening of blood products, the availability of an effective vaccine, and improved compliance efforts with universal precautions. HBV incidence has shown a decline over time with these measures, with seroconversion rates in HD populations being reported at <1%.

HBV is notable for its increased transmissibility when compared to either HCV or HIV and its capacity to remain viable on inanimate objects for up to seven days. HD units are the most common setting for nosocomial HBV outbreaks [64]. Breaches in infection control, the use of multi-dose vials and inadequate environmental cleaning are important risk factors for disease transmission in HD units. In addition to universal precautions, the use of dedicated machines and a spatial segregation or isolation of HBV cases is advocated to mitigate transmission risk, though there is much less observational data to underpin this recommendation when compared to the published data for HCV.

HBV vaccination is an effective strategy for reducing HBV transmission risk, and therefore increased uptake can serve to reduce HBV transmission and disease burden in the HD setting.

**HUMAN IMMUNODEFIciency VIRUS**

A single study documenting HIV transmission in the HD setting related to the reuse of contaminated needles reinforces the importance of strict adherence to universal infection control. Screening patients for HIV prior to commencement of HD should be guided by host risk factors for the disease as there are no data to indicate dialysis is a risk factor for HIV, and HD patients are not a recognised risk group for HIV acquisition. The prevalence of HIV in the dialysis population has ranged from 0% to 1.5%. 
Recommendations

Screening

Routine

a. We recommend that all patients should be screened for hepatitis B virus and hepatitis C virus prior to commencement of dialysis or when transferring from another dialysis facility. The serological screening panel should include serology for hepatitis B (HBsAg, anti-HBc, anti-HBs), and hepatitis C (anti-HCV) together with baseline liver function tests (1B).

b. We recommend that patients be screened for human immunodeficiency virus (HIV) if they are identified as having risk factors for HIV acquisition or have serological evidence of either hepatitis B or hepatitis C infection (1B).

Transmission of HCV and HBV has been described in low and high prevalence HD settings. Baseline serological screening is important for establishing baseline HBV and HCV prevalence within a dialysis population, recognising that prevalence is a significant risk factor for transmission, and dialysis units are the most frequent nosocomial setting for HBV outbreaks. Of those who are serologically screened and have positive seromarkers of infection for HBV and HCV, referral and assessment for treatment of their infection may prevent long term complications. Baseline liver function tests are an important adjunct for staging viral hepatitis. For patients who are negative for all HBV seromarkers (anti-HBs, anti-HBc, and HBsAg), HBV vaccination should be offered.

c. We recommend that patients who are hepatitis B vaccinated with anti-HBs ≥10 mIU/mL have anti-HBs rechecked annually. For vaccine non-responders, with anti-HBs titres <10 mIU/mL, recheck HbsAg every six months (1C).

We recommend more frequent testing (every three months) in dialysis units with high prevalence of hepatitis B (1C).

Anti-HBs titres HBs ≥10 mIU/mL are generally regarded as protective following vaccination and sufficient to elicit an anamnestic response if re-exposure to HBV occurs. Titres below this threshold may not be protective. Those who do not mount an adequate vaccination response are regarded as non-immune and should be rescreened at least every 6 month for infection using HBsAg. More frequent screening in non-immune HBV patients is recommended in high prevalence settings.

d. We recommend that those who are seronegative for hepatitis C have anti-HCV rechecked every six months. (1C).

HCV has an incubation period that can be up to 6 months. It is therefore reasonable to suggest that new infections, using serological markers, would be identified in this timeframe.

Screening

Enhanced

e. We recommend that the local incidence and prevalence data for HBV and HCV be considered in determining the frequency of routine testing for aminotransferases (ALT/AST) (1C).

Monthly liver function tests monitoring has been used in one prospective study to identify new HCV infections in a HD centre where prevalence was 37%. The combination of monthly ALT used in conjunction with 3 monthly HCV serology and HCV RNA, identified 11 de novo HCV infections [62]. Less frequent LFT monitoring is likely to be more cost effective in a low prevalence setting.
f. We recommend that all patients negative for hepatitis B receiving in-centre haemodialysis are rescreened for hepatitis B (HBsAg, anti-HBc and anti-HBs) if there has been a notification of a seroconversion of hepatitis B (HBsAg negative to positive) within the dialysis population. All patients who are non-immune should have repeat screening every two weeks for three months (1C).

g. We recommend that all patients associated with a dialysis centre undergo rescreening for hepatitis C (anti-HCV, HCV RNA) if there has been a seroconversion of hepatitis C (anti-HCV negative to positive) within the dialysis population, hence repeat screening every two weeks for three months (1C).

h. We recommend that all patients returning from holiday haemodialysis or haemodialysis at an alternative facility, where the endemic rates of BBV is high and/or adherence to standard infection control precautions uncertain be serologically screened on re-entry for hepatitis B (HBsAg, anti-HBc, anti-HBs), hepatitis C (anti-HCV, HCV PCR), and HIV (HIV Ag/Ab) and again at 6 weeks (1C).

Enhanced serological screening for HBV and PCR testing for HCV are important measures to assist in early outbreak identification, risk assessment and implementation of infection control measures. HD units are the most common settings in which nosocomial HBV outbreaks have been described. The recognition of new cases of BBV infection is a sentinel event that should prompt investigation of any breaches in standard infection control measures.

**Infection control precautions**

**Standard precautions**

i. We recommend that dialysis staff should receive education in the implementation of standard precautions, in particular hand hygiene and aseptic technique and that adherence be routinely audited in centres undertaking haemodialysis (1B).

Environmental contamination and poor adherence to standard infection control precautions have been well described risk factors for HCV [30, 35, 36, 39, 40, 46, 48, 71], HBV [62, 64-66, 72] and HIV infection [57]. The strict implementation of standard precautions, including hand hygiene, the wearing and changing of disposable gloves; the cleaning and disinfection of dialysis machines between use, the routine cleaning and disinfection of equipment; the use of individual supplies, and a clean area for the preparation of medications have been associated with lower reductions in HBV and HCV in the HD setting.

**Patients**

j. We recommend that hepatitis B non-immune haemodialysis patients receive a course of hepatitis B vaccination that is compliant with National Immunisation Guidelines (1B).

**Ungraded suggestions for clinical care**

- For patients with a documented history of HBV vaccination and antibody response (anti-HBs ≥10 mIU/mL), we recommend a booster dose of HBV vaccination if anti-HBs titres are <10mIU/ml on follow-up screening.

Australian Immunisation guidelines [15] currently recommend that non-immune dialysis patients be vaccinated with either 20µg in each arm at each schedule point, and that they receive a four dose schedule at 0, 1, 2 and 6 months or a single H-B-VaxII (dialysis formulation) at 0, 1 and 6 months). Limited data are available for vaccinated haemodialysis patients with waning immunity. In one RCT, patients with protective anti-HBs titres post vaccination developed HBV infections (positive HBsAg) when protective anti-HBs titres had fallen to < 10 mIU/ml [67]. A booster dose of HBV vaccine is currently recommended for renal failure, including haemodialysis patients, and those who are immunocompromised when anti-HBs is < 10IU/m [15, 73].

- We suggest that HBsAg positive patients be dialysed in isolation or cohorted in an area that is separate to that where patients who are HBsAg negative receive dialysis (2C).
- We suggest that HBsAg positive patients use a dedicated dialysis machine, and single use dialysers. When dialysers are to be reused, they should be decontaminated and disinfected (2C).
The higher transmission risk of HBV compared to HCV and HIV, and the recognition that this virus remains viable on surfaces for up to 7 days has led to the recommendation of managing these patients away from the non-infected HBV population, on dedicated machines. Available studies have supported the use of dialyser reuse in HBV patients provided appropriate disinfection is carried out before reuse [27, 60].

- We suggest that patients with HIV or who are anti-HCV positive are not dialysed in isolation, nor on a dedicated machine (2C).
- We suggest that the isolation of anti-HCV positive patients and the use of a dedicated machine may be beneficial in a high prevalence setting (seroprevalence > 15%) or where an outbreak of hepatitis C has not been possible to contain (2C).

HBV presents a higher risk of transmission, in part due to its longer viability on environmental surfaces [7, 18, 19]. The isolation of patients with HCV in HD units has been supported from a number of studies in high prevalence settings or in an effort to control an outbreak. There are no data correlating HCV or HIV transmission to HCV and HIV viral load, respectively, in the HD setting. A high viral load in a patient who is either failing treatment or has not been initiated on effective antiviral therapy may present an increased risk of transmission. Such patients can be managed in the same way as HBV infected patients (dedicated machines, in isolation) until they achieve better disease control (ungraded evidence).

**Ungraded suggestions for clinical care**

- We suggest that staff training should include education about maintaining and respecting patients’ privacy in the dialysis unit where possible, to protect confidentiality surrounding the diagnosis of a blood borne virus.
- We suggest that patients receive referral for counselling care where appropriate, particularly following a positive diagnosis with a blood borne virus.
- In order to help reduce fear/confusion and alleviate the stigmatisation associated with a blood borne virus, we suggest that education be provided to patients and their carers regarding the level of risk of BBVs, and importance of the practice of isolation and cohorting in the management of blood borne viruses in the dialysis unit.

There have been very few studies that have examined the psychosocial impact of the diagnosis and management of blood borne viruses within the haemodialysis setting. In the development of these guidelines, a workshop to identify patient and caregiver priorities was held in 2015. Nine patients and three caregivers attended and identified salient topics, which included: privacy and confidentiality of disease notification, psychosocial care during and after diagnosis, psychosocial care during isolation, and empowering patients to express concerns anonymously [74].

**Equipment**

**General – We recommend**

k. Single use items should be disposed of after use on one patient (1D).

l. Non-disposable items should be disinfected between patient use. If disinfection is not possible (for example, tourniquets and tape) then these devices should be dedicated for single patient use only (1D).

m. Physiological monitoring equipment such as thermometers and sphygmomanometers scales should be dedicated for use for each patient, when disinfection is not possible between uses (1D).

n. Medications and supplies should not be moved between patients. If multi-dose medications are to be used (multi-dose vials or requiring diluents dispensed from a multi-dose vial) then these should be prepared in a central designated area, and then dispensed to individual patients. No drugs or materials from the dialysis station should be returned to the preparation area (1C).

o. Needles should be dispensed into a sharps container. Containers should be designed to allow for non-touch technique (1D).

Single interventions and their impact on infection control have been difficult to evaluate as most of these interventions are bundled together. The reuse of priming receptacles without disinfection handling blood specimens adjacent to medications and clean supplies, the use of multi-dose vials, the
reuse of needles and using mobile carts to deliver injectable medications have been identified as important risks for HCV, HBV and HIV transmission in dialysis units [38].

Associated dialysis-related measures – We recommend

p. After each dialysis session all surfaces should be wiped clean. Disinfection of the surface of dialysis machines should be undertaken according to the manufacturers’ specifications (type of disinfectant, contact time and concentration) (1C).

q. External circuits, once removed, should be transported from the dialysis station in a leak proof bag to a designated clinical waste area. If components require reprocessing or the circuit needs to be drained, then this should be undertaken in a dedicated area separate to treatment areas or areas used for the preparation of medications (1C).

r. Dialysis machine should be fitted with an external transducer protector to the pressure lines of external circuitry. The fit to the pressure monitor should be tight to minimise risk of wetting. If wetting occurs then the transducer should be replaced (1D).

s. If fluid is evident on the machine side of the filter then the machine should be taken out of service, the internal filter changed and the internal housing disinfected (1D).

The contamination of environmental surfaces by HCV and HBV has been identified from environmental sampling [62]. Circuitry, including dialysate (inlet-outlet) connectors and moisture contaminated transducers and personal patient equipment such as blood pressure cuffs have been identified as potential sources of HCV transmission. [30, 40, 62] The use of multidose vials, preparation of medications in proximity to areas where blood products or blood contaminated equipment is handled, or the use of medication trolleys within a dialysis treatment area, have been identified as potential risk factors for BBV transmission [27, 38, 44, 75]

WHAT DO THE OTHER GUIDELINES SAY?

Kidney Disease Outcomes Quality Initiative: No recommendations.

UK Renal Association:
Blood Borne Virus Infection Guideline [63]
A) Surveillance:

i) Routine surveillance

- Recommended screening for all patients starting haemodialysis (including patients with acute kidney injury) or returning to haemodialysis after another modality of renal replacement therapy should be known to be HbsAg negative before having dialysis on the main dialysis unit. (1A)

- Patients should be dialysed in an area that is segregated from the main dialysis unit and the machine should not be used for another patient until the result is known to be negative. (1A)

- Patients on regular hospital haemodialysis who is immunized to hepatitis B (anti HBs antibody titre >10mIU/ml), annual testing for HBsAg is recommended. Non-responders should be tested at least every 3 months. (1C)

- Patients on regular hospital haemodialysis should be tested for HCV antibody at least every 6 months. (1C)

- Antibody surveillance testing for HIV is not necessary for patients on regular hospital haemodialysis unless the patient is at high risk. (1C)

- Patients who do not consent to BBV surveillance should have dialysis in a segregated area unless they are known to be HBV immune. If patients who are known to be HBV immune do not consent to BBV surveillance then they should be managed in the same way as patients with HCV infection. (2C)

- Testing for HBV DNA and HCV RNA should be performed in haemodialysis patients with unexplained abnormal serum aminotransferase concentrations. (1B)

ii) Enhance surveillance

- Patients returning from dialysing abroad should have a risk assessment and where exposure is considered likely, enhanced surveillance testing for BBV should be instituted. Patients should have dialysis in a segregated area until the HbsAg is known to be negative unless they are known to be HBV immune (anti-HBs >100mIU/mL within the last 12 months). (1B). Enhanced surveillance in patients deemed to be at high risk after returning from abroad should consist of HCV RNA (or HCV core antibody) every 2 weeks for 3 months and, if not known to be HBV
immune (anti-HBs >100mIU/mL within the last 12 months), HbsAg (or plasma HBV DNA) every 2 weeks for 3 months. Nucleic acid testing (NAT) for HCV and HBV in the first 1-2 months virtually excludes acute infection. If HIV is a possibility screening with 4th generation (antigen/antibody combination) assays should be used. (1B)

- If a new BBV infection in a haemodialysis unit is identified testing for viral RNA or DNA should be performed in all patients who may have been exposed (1B)

iii) Infection control

- Universal precautions should include hygienic precautions that effectively prevent the transfer of blood or fluids contaminated with blood between patients either directly or via contaminated equipment or surfaces. (1A)
- Medicine vials should be discarded after single use or, if used for more than one patient, divided into multiple doses and distributed from a central area. (1B)
- Separate machines should be used for patients known to be infected with HBV (or at high risk of new HBV infection). A machine that has been used for HBV patients can be used again for non-infected patients only after it has been thoroughly decontaminated. (1A)
- Dedicated machines are not required for patients with HCV or HIV provided that disinfection processes are properly carried out between patients according to a local protocol that incorporates the manufacturer’s instructions. (1B)
- Dialysers for multiple use can be re-used provided there is implementation of, and adherence to, strict infection control procedures to avoid dialysers or blood port caps being switched between patients. (1C)
- External transducer protectors on the blood circuit pressure monitoring lines should be inspected by healthcare personnel during and after each dialysis session. If there is evidence of breach by blood or saline then the machine should be taken out of service and machine components that may have come in contact with blood should be replaced or decontaminated by qualified personnel according to a protocol that incorporates the manufacturers’ instructions. (2C)

Canadian Society of Nephrology:
The prevention of transmission of blood-borne pathogens in hemodialysis patients (2005) [76]

i) Routine surveillance

- BBV screening recommended between 3 to 6 months depending on individual unit incidence/prevalence rates. For HBV-susceptible patients who are returning from travel, HBV testing is recommended upon their return to the dialysis center.
- Patients who have received HBV vaccination should be tested for anti-HBsAb 1-2 months after the last primary vaccine dose. For HBV immunized patients serum antibody levels should be monitored at yearly.
- Hemodialysis patients with HBV infection should receive their dialysis in a dedicated room, separate from other patients in the unit, and with a dedicated machine, equipment, instruments, and supplies. For hemodialysis units where a separate room is not available for HBV positive patients, these patients should be separated from HBV-susceptible patients in an area removed from the mainstream of activity, and should undergo hemodialysis on dedicated machines.
- Isolation of patients who are HCV (+) or HIV positive in the hemodialysis unit is not necessary.
- Hemodialysis units to develop policies on frequency of liver function testing that are in keeping with the incidence and prevalence of HCV infection in their populations.

European Best Practice Guidelines: No recommendations.

International Guidelines:
KDIGO guideline for the prevention, diagnosis, evaluation and treatment of Hepatitis C in chronic kidney disease (2008) [77].

Guideline 1 – Detection and evaluation of HCV in CKD
A) Surveillance:

- Patients on hemodialysis should be tested for HCV when they first start hemodialysis or when they transfer from another hemodialysis facility. (Strong)
- For patients on hemodialysis who test negative for HCV, retesting every 6–12 months (Moderate)
- Testing for HCV should be performed for hemodialysis patients with unexplained abnormal
aminotransferase(s) levels. (Strong)

B) Infection control:

- If a new HCV infection in a hemodialysis unit is suspected to be nosocomial, testing with should be performed in all patients who may have been exposed. (Strong)
  - Repeat testing is suggested within 2–12 weeks in initially HCV negative patients. (Weak)
- Hemodialysis units should ensure implementation of, and adherence to, strict infection-control procedures designed to prevent transmission of HCV. (Strong)
- Isolation of HCV-infected patients is not recommended as an alternative to strict infection-control procedures. (Weak)
- The use of dedicated dialysis machines for HCV infected patients is not recommended. (Moderate)
- Where dialyser reuse is unavoidable, the dialysers of HCV-infected patients can be reused provided there is implementation of, and adherence to, strict infection-control procedures. (Weak)
- Infection-control procedures should include hygienic precautions that effectively prevent the transfer of blood or fluids contaminated with blood between patients, either directly or via contaminated equipment or surfaces. (Strong)

US Center for Disease Control
Recommendations for preventing transmission of infections among chronic hemodialysis patients (2001) [78].

i) Routine surveillance:

- Routinely test all chronic hemodialysis patients for HBV and HCV infection, promptly review results, and ensure that patients are managed appropriately. Communicate test results (positive and negative) to other units or hospitals when patients are transferred for care.
- For patients transferred from another unit, test results should be obtained before the patients’ transfer. If a patient’s HBV serologic status is not known at the time of admission, testing should be completed within 7 days.
- Monthly ALT testing will facilitate timely detection of new infections and provide a pattern from which to determine when exposure or infection might have occurred. In the absence of unexplained ALT elevations, testing for anti-HCV every 6 months should be sufficient to monitor the occurrence of new HCV infections. If unexplained ALT elevations are observed in patients who are anti-HCV negative, repeat anti-HCV testing is warranted.

ii) Infection control

- Isolation of HBsAg positive patients in a separate room. Dialysers should not be reused on HBsAg-positive patients.
- Isolation is not recommended for patients who are anti-HCV positive (or HCV RNA positive). They can participate in dialyser reuse programs.
- Assignment of staff members to HBsAg-positive patients and not to HBV-susceptible patients during the same shift
- Assignment of a supply tray to each patient (regardless of serologic status), cleaning and disinfection of non-disposable items (e.g., clamps, scissors) before use on another patient;
- Glove use whenever any patient or hemodialysis equipment is touched and glove changes between each patient (and station)
- Routine cleaning and disinfection of equipment and environmental surfaces.

Local guidelines:

A) Queensland Health Recommended Practices – Guideline for the prevention and control of infections in dialysis settings (2013) [79].

- All patients must be tested with informed consent, for HBsAg, HBsAb (or anti-HBs), anti-HBc, HCV and HIV before admission or transfer to/from the dialysis service. If a patient’s BBV serological status is not known at the time of admission, testing should be completed within 7 days12
- Recommend testing six-monthly depending on patient’s serological status and the prevalence of BBV infection in the unit.
- Recommend vaccination for HBsAg-negative HD patients. Non-responders should be referred to an Infectious Diseases Physician or Infection Control Practitioner if patients’ HBV serological marker is anti-HBc in the absence of acute HBV infection, and for assessment for assessment for intradermal vaccination.
- Guidelines recommend use of standard precaution including hand hygiene, appropriate personal protective equipment (PPE), immunization and training of healthcare workers, aseptic technique, routine environmental cleaning, and management of sharps, blood spills, linen and waste to maintain a safe environment.

B) South Australia Statewide Renal Clinical Network – Blood Borne Virus working group
Management of haemodialysis patients with a blood borne virus (August 2011) [80]

ii) Infection control
- Isolation of patients with a BBV in a separate room is strongly recommended for units with a high prevalence of BBV infection (>30%) and / or evidence of new seroconversion associated with dialysis.
- Patients, who are HBsAg and HBV DNA positive, should be dialysed in a separate room due to their high level of infectivity.
- Patients with different BBV should be managed separately and not cohorted.
- If isolation is not available, BBV positive patients should be separated from susceptible patients (negative for HBsAg, anti-HBs, anti-HBc, anti-HCV) and undergo dialysis on dedicated machines. The use of physical barriers between all patients’ chairs is recommended i.e. Perspex screen. Anti-HBs positive patients (anti-HBs >10 mIU/mL) may undergo dialysis in the same area as HBsAg positive patients or they may serve as a geographical buffer between HBsAg positive and susceptible patients (negative for HBsAg, anti HBs, anti-HBc).

C) State of Victoria, Department of Health and Human Services
Hepatitis B infection control in haemodialysis centres – Victorian Renal Clinical Network consensus document [81]

General policy statements
- All units must have, and be familiar with, a written HBV policy (which may be this HBV consensus document).
- Standard precautions must be practised by all staff for all patients regardless of viral status.
- Machine cleaning in accordance with the manufacturer’s guidelines must occur between patient sessions of dialysis and must be to the required standard. This includes standard heat disinfection and a full manual clean after every dialysis, which includes a full wipe down of all external surfaces.
- All blood spills must be dealt with promptly in accordance with local policy, and personal protective equipment (PPE) standards must be adhered to (1).
- The serial number of every machine should be noted (usually on the dialysis run chart) for every patient on every dialysis session so that contact tracing can occur should problems arise.
- All HBVsAg positive or HBV DNA positive haemodialysis patients should have been offered an opinion from an infectious diseases physician and or a hepatologist.

Staff
- The Australian national guidelines (3) state that ‘HCWs are expected to protect the health and safety of their patients. This obligation includes preventing transmission of … BBVs from themselves to their patients’.
- Of equal importance is the need to prevent transmission from patients to HCW. Haemodialysis HCW have a greater chance of contact with blood and/or body substances from haemodialysis patients than most other HCW.
- All staff must take personal responsibility for their own safety by knowing their vaccination history and HBsAb status.
- Anyone working on a dialysis unit should be offered vaccination against hepatitis B if they do not have prior immunity.
- Pre-employment screening and assessment of immunisation requirements should be undertaken when staff commence employment, and the employer should maintain a record of these results (1).
- Staff should maintain a personal immunisation record (1).
- Once a staff member has achieved an HBVsAb level > 10 IU/mL no further vaccination or testing is needed (unless there is concern over immune-competence) (1).
- If staff fail to seroconvert after two full vaccination courses, they should be counselled about the risks of HBV transmission and/or offered alternative vaccination strategies such as subcutaneous or novel adjuvant intradermal vaccination if available (11).
- Staff who have never attained an HBVsAb level > 10 IU/mL should not knowingly look after patients on dialysis known to have circulating HBV DNA.
- Staff must take individual responsibility for informing their renal unit if they do not have protective immunity against hepatitis B (they have never had an HBVsAb level ≥ 10). Where a staff member without immunity informs a unit of this fact, it is the responsibility of the renal unit to ensure that such a staff member does not knowingly look after a patient who is known to be viraemic (viral load detectable by HBV DNA polymerase chain reaction) on dialysis. This must not prejudice the working opportunities of such a staff member, and compliance with equal employment opportunity legislation is paramount.
- Staff looking after patients with detectable HBV DNA should not simultaneously look after haemodialysis patients who have no demonstrable immunity to HBV (any patient with HBVsAb level < 10) during the same dialysis shift. If resources are unavailable locally to avoid this, then equipment and PPE must be provided at each dialysis space and must not be taken from one patient to the next.
- Staff without protective immunity should be advised of the importance of post-exposure prophylaxis with hepatitis B immunoglobulin (HBIg) within 72 hours of an exposure event (13).
- Staff should be aware of the viral status of their patient after the last routine screening, and this information should be readily available at each dialysis session if needed.

**HBV transmission prevention**

- A high level of compliance with serological testing and reporting for patients is mandatory (see revised testing path schedule at Appendix 1).
- All dialysis patients should be tested yearly for HBVsAg.
- If a patient is found to be HBVsAg positive, the patient will need viral load studies HBV DNA (at least six-monthly).
- Yearly screening testing for HBVcAb should be performed unless previously positive.
- If a patient has a previously confirmed HBVcAb-positive result then no further testing of HBVcAb is needed. These patients have been infected and are at risk of reactivating the virus if they are, or become, immunosuppressed.
- All dialysis patients should be tested yearly for evidence of HBV immunity with HBVsAb titre.
- Patients should undergo three-monthly liver function testing to detect any hepaticillitits.
- If a potential exposure or a reactivation event has occurred, such testing may need to be more frequent.
- A viral status (within one year) should be determined on all patients prior to starting dialysis but definitely within seven days of starting dialysis.
- The results of a patient’s viral status including HBVcAb, HBVsAg, HBVsAb, HCVAb, HIV Ab (and HBV DNA if applicable) should be available locally.
- Patients who are positive for HBCAb, HBVsAg or HBV DNA should have HBV DNA viral load testing at least six-monthly.
- A rising HBVsAg titre or HBV DNA copy number should prompt a review of the patient by an infectious disease physician or hepatologist.

**Patient vaccination**

- All patients with CKD 4 or 5 and those on dialysis who have no serological evidence of a previous HBV infection or immunity should be encouraged to undergo a full vaccination course.
- Patients should be vaccinated at the earliest opportunity and levels of protective antibodies assessed after a vaccination course.
- Vaccination for CKD 4 and 5 patients consists of 40 mcg of hep B vaccination (H-B-Vax II dialysis formulation) at zero, one and six months (14).
- Patients recently vaccinated for HBV may have false positive HBsAg, and this test should not be performed for at least three months after vaccination (14).
- Patients who fail to develop adequate HBVsAb after the first course should be offered a second vaccination course at the same intervals (14).
If patients fail to seroconvert after two full courses of vaccine (six injections) then this should be noted in the patient history, but it is not necessary to offer further vaccination. However, consider subcutaneous or other vaccination strategies in some circumstances such as where a unit may be considering listing a patient for a kidney transplant and would consider a HBVcAb-positive kidney (15).

Dialysis patients and any patient on the transplant waiting list should be given a booster vaccination if HBVsAb titres drop below 10 IU/mL (14).

Post-exposure prophylaxis (PEP)
- Exposure is contact of patient secretions or blood with mucous membranes, non-intact skin or via percutaneous means (for example, needlestick).
- PEP is not required for patients or staff with detectable immunity after an exposure.
- Non-vaccine responders (HBsAb < 10) should receive two doses of hepatitis B immunoglobulin – the first within 72 hours of an exposure (12).

Machines and environment
- Patients who are positive for HBVsAg or HBV DNA or patients where the viral status is unknown should use a dialysis machine that is dedicated for their use only, until such time as the viral status is known or they are known to be negative.
- Where facilities exist, haemodialysis patients with detectable HBV DNA should be treated in an isolation bay, provided that isolation is not considered detrimental to the patient’s wellbeing.
- All haemodialysis patients with detectable HBV DNA should be allocated a dedicated machine and associated equipment (such as a blood pressure cuff) solely for their own use while HBV DNA remains detectable. These machines and equipment should not be used for other patients at other times until the patient no longer has detectable circulating HBV DNA. These machines and equipment should undergo a major decontamination protocol clean before being put back into the general pool.
- If dialysing an HBV DNA-positive patient in a non-isolated area (because isolation facilities do not exist), patients dialysing in adjacent dialysis chairs should have detectable HBVsAb > 10 (and ideally > 100 IU/mL) when last tested.

SUGGESTIONS FOR FUTURE RESEARCH
1. We recommend further qualitative and quantitative research into long term psychosocial effects and potential harms that a diagnosis and treatment of a BBV has on patients and their carers undergoing renal replacement therapy.
2. Research into interventions aimed at reducing the stigmatisation associated with the diagnosis of BBV, and the isolate required for patients positive for HBsAg.
3. We recommend dialysis centre and health services undertake regular point-prevalence surveys on BBV in Australia and New Zealand to monitor the prevalence and incidence and trends in BBV epidemiology locally and regionally.
4. Well-designed clinical trials are needed on the route and dose of vaccination for HBV non-responders.
5. Research into the efficacy and safety of direct acting antivirals therapies for hepatitis C virus in patients with end-stage renal disease on haemodialysis is needed.
6. Research is needed into the epidemiology and dynamics of occult HBV infection in patients with ESRF on haemodialysis.
7. Cohort and/or case-control studies in Australia and New Zealand are needed to identify risk factors for the acquisition of BBV in the setting of haemodialysis.
8. The application of molecular epidemiology to investigate future institutional outbreak or transmission events of BBV in Australian and New Zealand hemodialysis units will identify where breaches in standard and enhanced infection control precautions have occurred, and will inform quality improvements in the delivery of haemodialysis.
9. Surveys of Australian and New Zealand dialysis centres are needed to assess current practices, knowledge, human and materiel support for the control of BBV infections in the haemodialysis setting.

CONFLICT OF INTEREST
The authors have no relevant financial affiliations that would cause a conflict of interest according to the conflict of interest statement set down by KHA-CARI.
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