



MASTERCLASS PLUS

EDUCATION UNIT 14

Hepatitis B Infection : Meeting the Challenge

PART A

DISTANCE LEARNING WORKBOOK

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This distance learning has been developed
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WELCOME AND INTRODUCTION

Welcome to Masterclass plus – a series of education units designed to help you meet your continuing professional development (CPD) needs as a health or social care professional, and have the opportunity to gain higher education credits.

Overview of education unit

'Hepatitis B Infection: Meeting the Challenge' has been developed for health or social care professionals who are currently seeing or in contact with people who have hepatitis B infection or are at risk of acquiring it. The education unit comprises:

- self-directed distance learning in three parts (A, B and C)
- tutor-led on-line learning including ongoing written work with individual feedback and assessment for credits.

You can choose to study the distance learning only and use the work as part of your continuing professional development (CPD). Alternatively, after completing the distance learning, you can opt to finish the education unit by doing the on-line learning activities. These provide opportunities for more CPD learning and if you pass the assessment at the end you'll be awarded 15 higher education credits at level 3. This education unit has been credit rated by the University of Greenwich.

Studying the whole education unit obviously gives you a more comprehensive educational experience and by doing the on-line written work you consolidate your learning and have the benefit of receiving individual feedback on how you're doing.

Let's take a closer look at what's involved in the self-directed distance learning and the on-line learning.



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Self-directed distance learning

The self-directed distance learning comprises text interspersed with a number of learning exercises. These are designed to help you make links with your practice, develop your knowledge and generally have your say, so that studying the distance learning is an active process. There are boxes in the text, and you can print these and use the space to write down your ideas related to the exercises. After some of the exercises we've included some discussion. We recommend that you don't read this until you've jotted down your own thoughts; that way you'll get more out of the exercises! Estimated timings are included to help you plan your study. Some exercises are designed to help you record some aspects of your CPD learning.

Note that in order to complete Part C of the distance learning, you need the free CDROM that accompanies this education unit. The CDROM will automatically be posted to you.

The Forum

As you have access to the Internet you can make use of 'The Forum'. This is an on-line peer support network for Masterclass plus participants. It consists of a bulletin board which enables you to chat about the content of the distance learning with other participants, exchanging ideas and discussing books and journal articles you've read. In order to join The Forum, access the Masterclass plus website www.masterclassplus.co.uk, click on 'The Forum' and follow the instructions.

Tutor-led learning activities (on-line)

Registration

If you want the opportunity to gain credits that you can use towards a higher education award you need to register for the on-line learning activities. In order to register you must have access to the Internet; have access to a library holding professional journals and books; and submit a self-verification statement confirming that you have completed Parts A, B and C of the distance learning.



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Tutorial support

During the on-line learning activities you are entitled to premium on-line support. This has two components:

- a bulletin board entitled 'The Forum plus'. This is used for discussions and tutorials that aren't private
- private communication between students and their tutor via a dedicated post box located in The Forum plus members' area. Emails are used to send written work to tutors and to receive it back with individual comments.

Written work and assessment

The on-line learning activities include some optional pieces of written work that have the sole purpose of helping your learning i.e. they're not graded as part of your final result. However, you do receive individual feedback on them and you're strongly recommended to complete them. At the end of the education unit comes the assessment that determines your final result. It comprises a practice-based written assignment, 2000 words in length. On successful completion of the whole education unit, you'll receive 15 higher education credits at level 3.

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Content of education unit

Table 1 shows the content of Parts A, B and C of the distance learning and the on-line learning, and the estimated study time required.

TABLE 1: CONTENT OF DISTANCE LEARNING AND ON-LINE LEARNING

COMPONENT	CONTENT	TIME
SELF-DIRECTED DISTANCE LEARNING: PART A	Liver anatomy, physiology and pathophysiology; general introduction to hepatitis B (HBV) infection: the hepatitis B virus and its characteristics; epidemiology and transmission; serological tests for HBV infection; prevention; introduction to management.	12 hours
SELF-DIRECTED DISTANCE LEARNING: PART B	Chronic HBV infection: natural history; further investigations; selecting patients for treatment; management.	3 hours
SELF-DIRECTED DISTANCE LEARNING: PART C	Consideration of five case studies related to HBV infection which will help you to consolidate and expand your knowledge. Case studies available on a free CDROM.	5 hours
TUTOR-LED ON-LINE LEARNING	Professional, ethical and cultural issues. Living with the hepatitis B virus. National policy and context of HBV infection; local provision related to testing, treatment and prevention of HBV infection and consideration of how local services could be improved.	70 hours (includes 30 hours for assessment)

Let's turn now to the aim and intended learning outcomes of Part A of the distance learning.





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AIM AND INTENDED LEARNING OUTCOMES

Aim

The aim of Part A of the distance learning is to enable you to develop fundamental knowledge about hepatitis B virus (HBV) infection.

Intended learning outcomes

- Develop understanding of aspects of liver anatomy, physiology and pathophysiology relevant to HBV infection.
- Describe the main characteristics of the hepatitis B virus.
- Discuss key epidemiological aspects of HBV infection.
- Demonstrate understanding of the significance of hepatitis B serological test results.
- Explain how HBV infection may be prevented.
- Be aware of some aspects of management related to HBV infection.

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HEPATITIS B INFECTION: INTRODUCTION

There are two possible outcomes following infection with the hepatitis B virus:

- complete recovery – the virus is no longer present in the body;
- progression to chronic (long-term) HBV infection – the virus persists in the body.

As you know, the title of this education unit is 'Hepatitis B Infection: Meeting the Challenge'. Hepatitis B infection is a challenge because people who have chronic HBV infection are at risk of developing liver damage. The liver carries out essential functions in the body, therefore damage to it can result in serious illness or death. So chronic HBV infection will be the main focus of this education unit.

As chronic HBV infection can result in liver damage, let's begin this distance learning by focusing on some general points about the liver: its basic anatomy and functions in the body. Then we'll consider some causes of liver damage and the impact of this on the patient's health.





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ANATOMY OF THE LIVER

Below are some brief notes that are principally intended for social care professionals with minimal knowledge of the subject. If you're a health professional you may wish to use a textbook to supplement these notes and refresh your memory of liver anatomy and physiology.

The liver: where it is

The liver lies in the right upper quadrant (hypochondrium) of the abdominal cavity, beneath the protective cover of the lower ribs (Clancy and McVicar, 2002).

For a picture of a healthy liver, see:

<http://www-medlib.med.utah.edu/WebPath/LIVEHTML/LIVER001.html>

Structure

The liver is mainly composed of tiny cylindrical lobules with a hexagonal cross section (see Figure 1).

Lobules are made up of sheets of hepatocytes (liver cells) that radiate from the centre like spokes of a wheel. Separating the sheets are channels (bile canaliculi) that collect bile produced by the hepatocytes, and also channels (blood sinusoids) that carry blood flowing through the lobule (Porth, 2002).

The liver lobules receive their blood supply from branches of the hepatic artery and branches of the portal vein. Blood enters a liver lobule at its outer aspect, flows inwards through the sinusoids and leaves via the central vein in the middle of the lobule. The central veins of the lobules unite to form the hepatic vein which carries the blood away from the liver towards the heart (Van De Graaff, 2002).

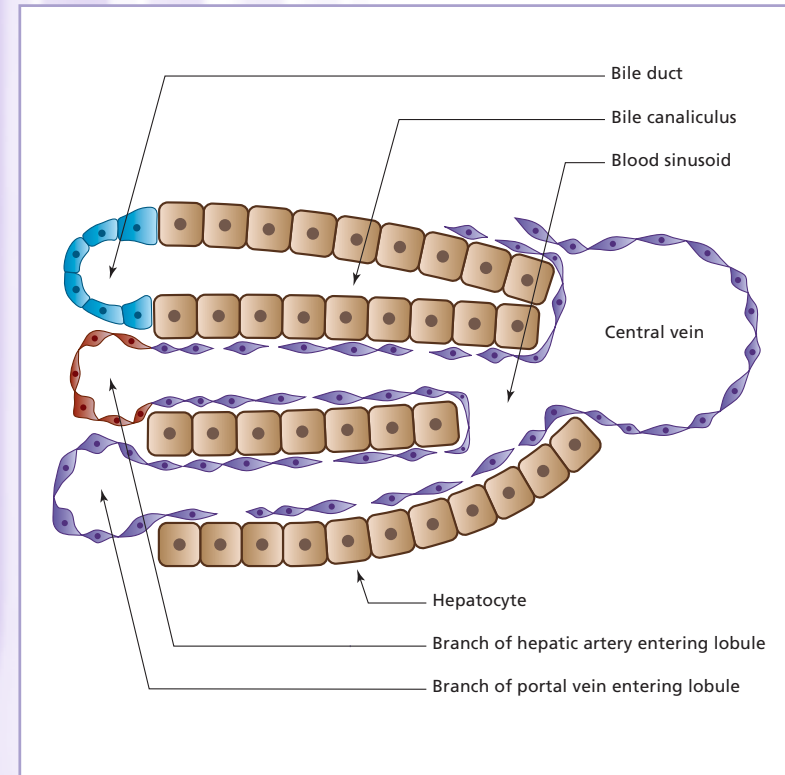
Bile flows in the bile canaliculi outwards into the bile ducts which in turn drain into progressively larger ducts. Eventually these form the common bile duct (Porth, 2002). The common bile duct carries the bile to empty into the duodenum.

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FIGURE 1 : DIAGRAM OF LIVER LOBULE





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FUNCTIONS OF THE LIVER

The liver has many essential functions and is vital to life.

Metabolism of carbohydrates, protein and fats

The liver is important in carbohydrate metabolism and has a central role in maintaining the correct level of glucose in the blood.

The liver is also important in the metabolism of protein and in the safe disposal of ammonia. Ammonia is a toxic by-product of protein metabolism. Two important enzymes involved in protein metabolism are produced in the liver. The enzymes are alanine aminotransferase (ALT) and aspartate aminotransferase (AST) (Brooker, 1998). The liver synthesises plasma proteins, including albumin, and other important proteins such as blood clotting factors (e.g. prothrombin) (Porth, 2002). These activities are part of the 'synthetic function' of the liver.

A considerable part of fat metabolism takes place in the liver e.g. the liver is involved in the storage of fat and its release, when required, to provide energy for the body (Brooker, 1998).

Production of bile

The hepatocytes secrete about 600-1200ml of bile every day. The production of bile is essential for the digestion of dietary fats and for the absorption of fats and fat-soluble vitamins from the gut (Porth, 2002).

Storage of vitamins and minerals

The liver stores some vitamins and minerals e.g. vitamin B₁₂, D, E and K as well as iron and copper (Huether, 2000a).

Detoxification

The liver alters (detoxifies) potentially toxic chemicals such as alcohol and so facilitates their excretion from the body. In the case of alcohol, however, the end-product of detoxification is also toxic. Excessive alcohol intake over a

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prolonged period causes these end-products to damage the hepatocytes (Huether, 2000a).

Metabolism of bilirubin

The liver is involved in breaking down old red blood cells and bilirubin is a by-product of this process. There are two types of bilirubin: fat soluble and water soluble (Huether, 2000a).

Fat soluble (unconjugated) bilirubin is toxic to cells (Brooker, 1998) and so the body needs to get rid of it. It is carried in the plasma bound to a protein. In the hepatocytes the unconjugated bilirubin is converted into a less toxic water soluble form known as conjugated bilirubin. This forms a component of bile and is excreted via the bile channels in the liver lobules. These small bile channels merge and form the hepatic duct. Some bile flows to the gall bladder for storage and release into the gut when required for digestion. The rest flows through the common bile duct into the gut (Huether, 2000a). In the gut, conjugated bilirubin is converted into urobilinogen. Some urobilinogen is reabsorbed into the circulation to be excreted in the urine, but most is excreted in the stools as stercobilin (Marshall, 2000). It is stercobilin that gives the stools their brown colour.

Let's move on now from the normal, healthy liver to the damaged liver and consider some causes and effects of damage.





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LIVER DAMAGE

Causes

Common causes of liver damage are excessive alcohol consumption and viral hepatitis. 'Hepatitis' simply means inflammation of the liver and two viruses that can result in chronic (i.e. long-lasting) inflammation are HBV and the hepatitis C virus (HCV).

Effects

Chronic liver inflammation and cirrhosis

Chronic inflammation results in death (necrosis) of liver cells and scarring (fibrosis). Extensive scarring is known as cirrhosis, the end result of which is liver failure and death. For a picture of liver cirrhosis, see: <http://www-medlib.med.utah.edu/WebPath/LIVEHTML/LIVER009.html>

Only approximately 10% of liver tissue is required for the liver to remain functional (Porth, 2002). So the liver is very effective in compensating for loss of tissue. The term compensated cirrhosis means that the liver has extensive scarring but is not failing in its vital functions.

The liver's ability to compensate for loss of functional tissue means that liver disease may be far advanced before the patient recognises any warning signs or symptoms. However, complications such as portal hypertension and oesophageal varices (see below) can occur in compensated cirrhosis.

If liver disease is progressive there comes a time when the liver has no functional reserve left i.e. it can no longer compensate for loss of liver tissue and starts failing to carry out its functions. The term decompensated cirrhosis means that liver failure is occurring. It is associated with certain serious clinical features. These include:

- development of ascites
- development of encephalopathy
- variceal bleeding which often leads to ascites and the development of encephalopathy.

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Let's consider these terms, starting with variceal bleeding. A common site for such bleeding is the oesophagus.

Oesophageal varices

Liver damage/disease (e.g. scarring or tumours) alters the internal architecture of the liver, distorting the normal symmetrical pattern of the hepatocytes and disrupting the normal flow of blood through the liver.

If normal blood flow through the liver is obstructed, pressure builds up in the portal vein. This is known as portal hypertension. It causes back pressure to build up in other veins that drain into the portal vein. For example, pressure increases in the gastric vein and then, in an attempt to cope with continuing back pressure in this vein, collateral channels open up between the gastric veins and the oesophageal veins (i.e. the veins that drain blood away from the oesophagus – the tube that carries food from mouth to stomach). The high pressure in the oesophageal veins causes them to become large and distorted. These abnormal veins are known as oesophageal varices (Gould, 2002). They may rupture and bleed.

Approximately 30% of people with cirrhosis have oesophageal varices at the time of diagnosis. About 30% of patients with oesophageal varices will bleed within the first year of diagnosis (Renner, 2003).

Ascites

Portal hypertension, along with other pathological changes, upsets the normal balance that exists between fluid in the body cells and fluid in the blood. As a result, fluid is shifted into the peritoneal cavity which lies between the membrane lining the abdominal wall and the membrane covering the abdominal organs. The accumulation of fluid in the peritoneal cavity is called ascites. It is a complication of cirrhosis (Gould, 2002).

Ascites is uncomfortable for the patient. It creates upwards pressure on the diaphragm, impairing breathing. It is also a potential site of infection (Gould, 2002).





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Hepatic encephalopathy

Remember that one of the liver's functions is the safe disposal of toxic ammonia. It is thought that increased levels of ammonia may be a key factor in the development of hepatic encephalopathy (Blei and Córdoba, 2001). This serious complication of severe liver disease may manifest itself in many ways e.g. confusion, drowsiness, deteriorating intellectual ability and coma (Tibbs and Smith, 2001).

Hepatocellular carcinoma

Hepatocellular carcinoma (HCC) is primary liver cancer. HCC develops in 15% of patients with cirrhosis followed up for a 10-year period. The main clinical features are ascites, weight loss, abdominal pain and asymmetrical enlargement of the liver. By the time HCC becomes clinically apparent the tumour may be too large to be treated effectively (Tibbs and Smith, 2001). For a picture of HCC, see:
<http://www-medlib.med.utah.edu/WebPath/LIVEHTML/LIVER026.html>

Blood clotting disorders

You'll recall that the liver synthesises clotting factors such as prothrombin. People with severe liver disease have increased clotting times and therefore tend to bleed excessively.

Weakness and fatigue

The liver plays a vital role in digestion and hence in nutrition. People with advanced liver disease experience weakness, fatigue, indigestion and weight loss.



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THE HEPATITIS B VIRUS (HBV)

Introduction

Chronic HBV infection can lead to chronic liver inflammation (chronic hepatitis). Chronic hepatitis causes liver damage. Advanced liver damage is cirrhosis. So now we need to take a closer look at this virus and its characteristics.

Family

HBV is a microorganism belonging to the hepadnavirus family and straight away that tells us a good deal about it. Let's consider the components of this family name: hepa-dna-virus:

- hepa – it attacks the liver ('hepa' is derived from the Greek word for liver)
- dna – the nucleic acid in its core is deoxyribonucleic acid (DNA)
- virus – it belongs to the wider family of viruses (as distinct from bacteria or fungi, for instance)

We'll start by looking at some of the characteristics of the wider family of viruses and then we'll focus specifically on HBV.

Viruses

Size

Viruses are smaller than other microorganisms. They vary in diameter from 10–300 nanometers (nm). Bacteria are much larger (about 1000 nm in diameter) (Timbury et al, 2002).

Replication

Unlike bacteria, viruses do not multiply by cell division. Instead, new viruses are assembled from component parts (nucleic acid and protein). Viruses are parasites that require living host cells for the manufacture of new virus components. They infect the host cells and use the replication machinery within the host cells to copy and build new viruses (Hardy, 2002).



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Wild-type virus

This term is generally used to denote the predominant form of a virus occurring naturally in a geographic region or a community (Fagan and Harrison, 2000).

Genetic variation: mutation

A mutant virus is one that has undergone genetic change and thereby developed a phenotype (physical characteristics) which makes it distinct from the wild-type (Fagan and Harrison, 2000).

Unlike other organisms, viruses only possess one type of nucleic acid: either DNA or RNA (ribonucleic acid), never both. Genetic variation, such as mutation, arises much more frequently during replication of RNA viruses (e.g. HCV and the human immunodeficiency virus – HIV) compared with DNA viruses (e.g. HBV) (Hardy, 2002).

Clinical implications of genetic variation

Viral genetic variation has important clinical implications. It's very difficult to develop effective vaccines against viruses that are constantly changing. Developing effective treatments is more problematic. Then there is the problem of drug resistance. The viral genome may mutate ('adapt') in response to antiviral drugs and thereby the virus may develop resistance to the drugs. These changing viruses can also repeatedly infect the host (Hardy, 2002), because although the host immune system mounts a response to the virus, this may not provide protection against any subsequent infection by a different strain of the virus.

HBV: genetic variation

Fortunately, a safe vaccine is available against HBV. However, mutations do occur in HBV and population surveillance to detect the emergence of these HBV mutants is crucial for a correct evaluation of the effectiveness of current vaccination strategies (World Health Organization, 2002). Moreover, the development of HBV resistance to antiviral drugs presents an ongoing challenge (see, for example, Lok and McMahon, 2004).



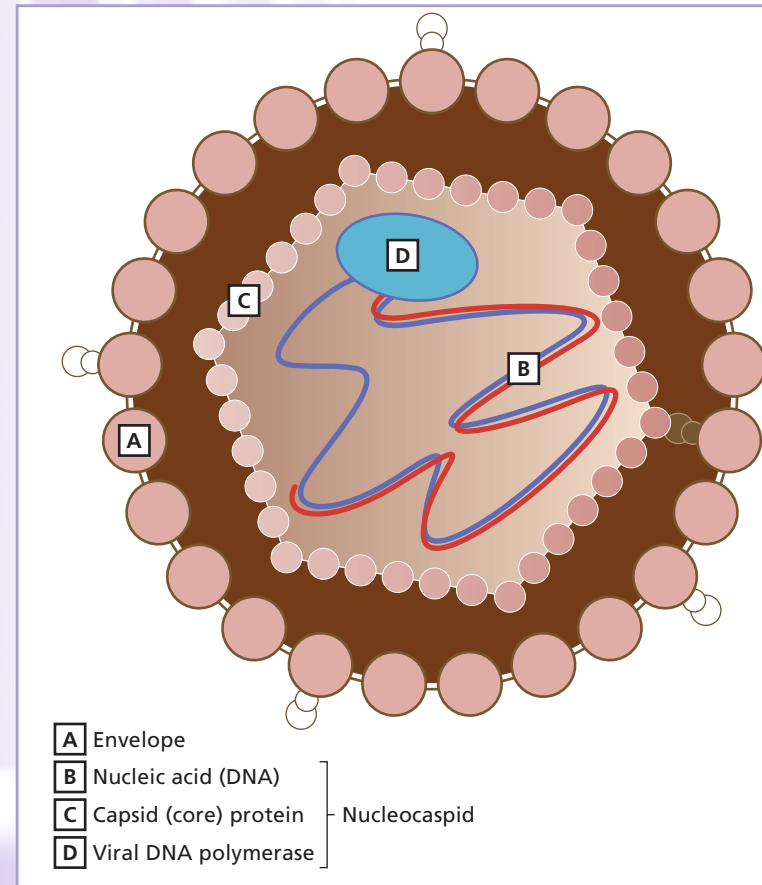
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Structure of HBV: virion (Dane particle)

A structurally complete virus is known as a virion, virus particle or Dane particle. HBV virions are infectious spherical particles 42nm in diameter (World Health Organization, 2002). The structure of HBV is shown in Figure 2.

FIGURE 2 : STRUCTURE OF HBV





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Structure of HBV: envelope

The envelope of the virion is an outer coat composed of lipid (fat) and proteins (Tibbs and Smith, 2001). Sometimes the envelope is extended as a tubular tail on one side of the virus particle (World Health Organization, 2002).

Structure of HBV: nucleocapsid

The nucleocapsid or core comprises three main components: the capsid (core) protein surrounding the nucleic acid (DNA) and the viral DNA polymerase.

The total genetic material (genome) of the virus is in the DNA. One of the main functions of the capsid is to protect the genome (Hardy, 2002; Tibbs and Smith, 2001; Timbury et al, 2002). The capsid also surrounds the viral DNA polymerase, an enzyme essential in the process of replicating the viral DNA needed to make new viruses (Timbury et al, 2002).

The nucleocapsid is spherical in shape and 27 nm in diameter (Tibbs and Smith, 2001).

Viral particles found in serum of HBV-infected people

Electron microscopy of HBV-infected serum shows the larger infectious Dane particles, as well as smaller empty spherical and tubular particles that are aggregates of the envelope protein. The tubular particles are identical to the tails of the virions. The smaller particles lack nucleic acid and so are non-infectious (Timbury et al, 2002; World Health Organization, 2002).

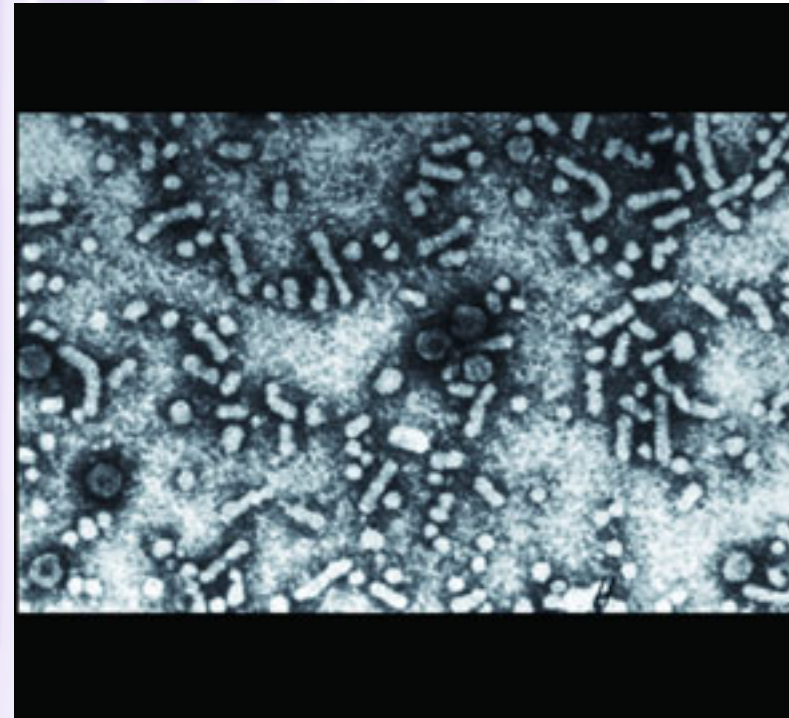
Figure 3 is an electron micrograph showing the Dane particles and the smaller spherical and tubular particles.

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FIGURE 3 : ELECTRON MICROGRAPH OF HBV



Reproduced courtesy of Centers for Disease Control and Prevention

HBV antigens

An antigen (Ag) is a substance that can elicit an immune response (e.g. formation of antibodies) in a host. The majority of antigens are protein molecules, such as those that comprise the structural proteins of a virus.

Components of HBV (envelope and nucleocapsid) are antigens. Three antigens (see Table 2) are used as indicators of HBV infectivity and disease progression.





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TABLE 2 : HBV ANTIGENS

<p>HBsAg Hepatitis B 's' or surface antigen (envelope protein of virion)</p> <p>NB The smaller spherical and tubular particles are also made up of HBsAg</p>
<p>HBcAg Hepatitis B 'c' or core antigen (nucleocapsid of virion)</p>
<p>HBeAg Hepatitis B 'e' antigen (water-soluble form of core protein – encoded by the virus DNA and secreted by infected cells)</p>

Sources: Tibbs and Smith (2001); Timbury et al (2002); World Health Organization (2002)

HBV: infectivity

Serum and other body fluids are infectious. According to World Health Organization (2002), HBV is approximately 100 times more infectious than HIV. However, it should be remembered that the infectivity of a fluid mainly depends on the concentration of the virus in the fluid and that this concentration varies from patient to patient and from time to time.

In common with all viruses, HBV can only multiply inside living cells (Timbury et al, 2002). However, it can survive outside the body (e.g. in blood stains, on surfaces such as razor blades) for about a week and may remain infectious during that time (World Health Organization, 2002).

HBV: carriers

People with chronic HBV infection carry the virus in their bodies. They are chronic carriers who are at risk of liver disease and can transmit the virus to others (World Health Organization, 2002).

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HBV: effects on the liver

Hepatitis simply means 'inflammation of the liver'. HBV multiplies in the cells of the liver (hepatocytes) and thereby interferes with the normal functions of the liver. The body's immune system is activated to attack infected hepatocytes and the liver becomes inflamed. Chronic hepatitis may result in cirrhosis and/or liver cancer (World Health Organization, 2002; Tibbs and Smith, 2001).





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EPIDEMIOLOGY: HBV ROUTES OF TRANSMISSION

HBV is transmitted by contact with the blood or body fluids of an infected person. The routes by which HBV enters a new host are via breaks in the skin (e.g. injections, abrasions) or via mucous membranes (World Health Organization, 2002).

You'll find some examples of transmission routes on the next few pages, but it's important to note that in about 35% of HBV infections the source cannot be identified (Tibbs and Smith, 2001; World Health Organization, 2002).

Transmission via mucous membranes

Here are some examples of transmission via mucous membranes.

Unprotected sexual contact

Vaginal and menstrual fluids and semen are sources of HBV infection. Transmission usually occurs through exposure of mucous membranes to infected blood or body fluids during sexual contact between heterosexual or homosexual people (World Health Organization, 2002).

Mother-to-baby contact at the time of birth (vertical transmission)

Pregnant women who are infected with HBV can transmit the virus to their babies at birth (perinatally). Usually transmission results from exposure of the baby's mucous membranes to the mother's infected blood or body fluids (World Health Organization, 2002).

Breast feeding

HBV has been found in breast milk but this is not thought to be a significant route of transmission (Tibbs and Smith, 2001). The Department of Health advises that breastfeeding should be encouraged and supported. There is no contraindication to breastfeeding when a baby born to a carrier mother begins immunisation at birth and proceeds with a complete course of vaccination. However, mothers should not donate their milk (Department of Health, 2000).

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Transmission via the skin (percutaneous)

Here are some examples of percutaneous transmission.

Sharing injecting equipment (injecting drug users)

An HBV infected drug user contaminates a needle with blood containing the virus and shares the needle with an uninfected drug user. The virus is transmitted from the needle into the second user via the injection site. HBV can also be transmitted by other shared drug equipment. For example, a tourniquet, spoon, filter or syringe may be contaminated with infected blood and if this comes into contact with even a small break in the skin, such as a minor graze, the virus can be transmitted.

Sharps injuries (occupational exposure)

Health care workers may sustain injuries from needles or surgical instruments that are infected with HBV. They may also be directly exposed to infected blood or body fluids e.g. their gloves may tear when they are dressing the wound of an HBV-infected person and the virus can then enter via a cut or crack in their skin. The risk of HBV infection is two-way i.e. an infected health care worker may infect patients.

Transfusion with contaminated blood or blood products

All blood in the UK is screened for HBV but travellers to countries where screening is not routine are at risk if they receive a transfusion in these countries.

It's also worth bearing in mind that even where blood donor screening is carried out, donors in the early incubation stage of the infection are capable of transmitting the virus but cannot be identified with current techniques. The risk for a recipient of acquiring HBV by transfusion is about one in 50,000 (World Health Organization, 2002).

Haemodialysis

In the past, HBV has often been associated with outbreaks of infection among patients and staff in renal dialysis units and, in spite of preventative





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measures, HBV infections still occur as a result of inadequate infection control procedures (Department of Health, 2002a).

Other examples

HBV can be transmitted as a result of unhygienic tattooing, body piercing, acupuncture or dental treatment, and by sharing household items such as razors or toothbrushes with an infected person. Ritual circumcision and scarification are risk activities if hygiene is poor.



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EPIDEMIOLOGY: GEOGRAPHICAL DIFFERENCES IN AGE AND ROUTE OF TRANSMISSION

Developing countries

In African and Asian countries HBV infection is mainly transmitted perinatally from an infected mother to her baby (vertical transmission) or as a result of close childhood contact (e.g. grazes) (European Association for the Study of the Liver, 2003; World Health Organization, 2002).

Developed countries

In developed countries the situation is very different. Have a look at Tables 3 and 4 which show acute HBV infection reports for England and Wales in 2003 by age and risk group respectively.

TABLE 3 : ACUTE HBV INFECTION LABORATORY REPORTS: ENGLAND AND WALES BY AGE GROUP, 2003 (provisional figures)

AGE GROUP IN YEARS	<1	1-4	5-9	10-14	15-24	25-34	35-44	45-54	55-64	>=65	Not known	TOTAL
NUMBER OF REPORTS	0	2	4	4	120	232	170	77	44	28	14	695

Source: Health Protection Agency (2004)

TABLE 4 : ACUTE HBV INFECTION LABORATORY REPORTS: ENGLAND AND WALES BY RISK GROUP, 2003 (provisional figures)

RISK GROUPS	Intravenous drug users	Sex between men	Sex between men and women	Other Identified risk	No identified risk	TOTAL
NUMBER OF REPORTS	124	51	95	61	364	695

Source: Health Protection Agency (2004)



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Table 3 shows that most acute HBV notifications in England and Wales relate to adults.

At first sight Table 4 seems to show that intravenous drug use (124 reports) is the main route of HBV transmission in England and Wales. However, if you add the reports related to homosexual sex (51) and heterosexual sex (95), it becomes clear that sexual transmission is the principal identified route of HBV transmission i.e. 51+95 =146 reports. In fact, the figure for sexual transmission is probably higher, since it seems likely that many of the 364 'No identified risk' cases were acquired sexually. Intravenous drug use is relatively easy to pinpoint accurately as a risk factor, but the same does not apply to sex.

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EPIDEMIOLOGY: HBV PREVALENCE WORLDWIDE

HBV is one of the commonest and most serious infectious diseases in the world. It is estimated that more than a third of the world's population has been infected with the virus and that there are about 350 million people with chronic HBV infection. Approximately five per cent of the world's population are chronic carriers of the virus and nearly a quarter of all carriers develop serious liver diseases (World Health Organization, 2002). Every year there are 500,000 to 1.2 million HBV-related deaths caused by chronic hepatitis, cirrhosis, and hepatocellular carcinoma (Lavanchy, 2004).

HBV infection is prevalent to some degree (i.e. endemic) in populations throughout the world (World Health Organization, 2002). Areas of high, moderate and low prevalence are described. Prevalence data relate to chronic infection and the number of carriers in the population (see Table 5).

TABLE 5 : PREVALENCE OF CHRONIC HBV INFECTION

PREVALENCE	AREAS OF WORLD
High (more than 8% of general population)	<ul style="list-style-type: none"> • Sub-Saharan Africa • South-East Asia, including China, Indonesia, Democratic People's Republic of Korea and the Philippines • Eastern Mediterranean except Israel • South and Western Pacific islands • Interior Amazon Basin • Parts of Caribbean (Dominican Republic and Haiti)
Moderate (2% - 7% of general population)	<ul style="list-style-type: none"> • South Central and South-West Asia • Israel • Japan • Eastern and Southern Europe • Russian Federation • Most of Central and South America
Low (under 2% of general population)	<ul style="list-style-type: none"> • Northern and Western Europe • Australia • New Zealand • North America

Source: World Health Organization (2003)





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Table 5 provides a useful 'bird's eye view' of the prevalence of chronic HBV infection worldwide. However, in real life, regions of high, intermediate and low prevalence are not neatly separated into boxes! The world is a global village and there is constant movement of people between the different regions. In particular, there tends to be migration from poorer countries (with high HBV prevalence) to rich countries, such as the United Kingdom (UK), where HBV prevalence is low. So any consideration of chronic HBV infection in the UK needs to take account of the impact of migration.



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EPIDEMIOLOGY: CHRONIC HBV INFECTION IN THE UK

Importance of chronic HBV infection data

Having information about chronic HBV infection in the UK is important because it has implications for HBV vaccination policy. Moreover, as we mentioned before, it is chronic HBV infection that causes liver damage. So in order to provide the best possible care we need to be able to identify those people who have chronic HBV infection.

Estimated chronic HBV in England and Wales

Hahné et al (2004) estimated the annual number of new cases of chronic HBV infection in England and Wales. They considered chronic HBV infection in two different groups of people:

- a) chronic HBV infection arising from acute HBV infection in residents in England and Wales
- b) chronic HBV infection imported into England and Wales by people who acquired the infection prior to immigration (i.e. established HBV carriers).

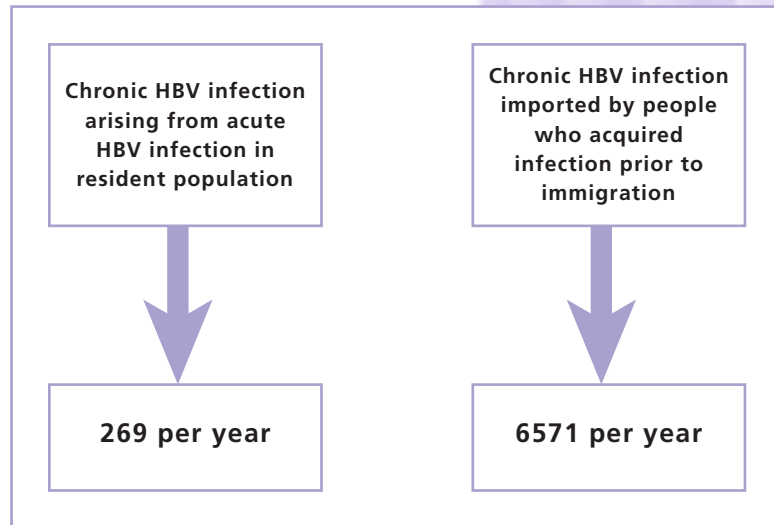
Figure 4 compares the estimated annual new cases of chronic HBV in the two groups (Hahné et al, 2004).



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FIGURE 4 : ESTIMATED ANNUAL NEW CHRONIC HBV INFECTIONS IN ENGLAND AND WALES



These figures show that most chronic HBV infection in England and Wales results from the immigration of HBV carriers. Chronic HBV infection arising as a result of infection in residents (269 per year) is estimated to account for only 3.9% of the total annual number of new cases of chronic HBV infection in England and Wales (Hahné et al, 2004).

Hahné et al (2004) also point out that immigrating HBV carriers are likely to have acquired the infection at an earlier age compared with carriers who are UK residents. This is significant because, in general, the outcomes of HBV infection acquired perinatally and in early childhood are much worse than HBV infection acquired in adulthood. This will become clear when we compare disease progression following HBV infection in the two groups: babies/young children and adults. First, though, we need to consider two very different conditions: acute HBV infection and chronic HBV infection.



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ACUTE HBV INFECTION

Table 6 summarises some key features of acute HBV infection.

TABLE 6 : SUMMARY OF KEY FEATURES OF ACUTE HBV INFECTION

When do people acquire it?	How do they acquire it?	How long does it last?	What are the clinical features?	What's the treatment?
Mainly in adulthood (Health Protection Agency, 2004)	Sexual transmission is main route (Health Protection Agency, 2004)	Up to six months (Health Protection Agency, 2004)	Approx. 70% have signs/symptoms e.g. <ul style="list-style-type: none"> • Jaundice • Fatigue • Loss of appetite, nausea, vomiting • Abdominal pain • Joint pain (NB: apart from jaundice, symptoms are non-specific, flu-like) Approx. 30% have no symptoms (Centers for Disease Control and Prevention, 2004a)	No specific treatment required (Tibbs and Smith, 2001)



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CHRONIC HBV INFECTION

Table 7 summarises some key features of chronic HBV infection.

TABLE 7 : SUMMARY OF KEY FEATURES OF CHRONIC HBV INFECTION

When do people acquire it?	How do they acquire it?	How long does it last?	What are the clinical features?	What's the treatment?
Mainly childhood – especially first year of life and in particular perinatally (at birth) (Poynard, 2004)	Mainly vertical transmission from mother to baby at birth or early childhood contact (Poynard, 2004)	Longer than six months (Hepatitis B Foundation, 2004)	<ul style="list-style-type: none"> • Most people have no symptoms. (Hepatitis B Foundation, 2004) • Some may experience malaise, anorexia and fatigue (World Health Organization, 2002) • Often by the time a person becomes aware of symptoms, he or she may have significant liver disease 	Specific treatment e.g. with antivirals may be indicated

Tables 6 and 7 show that acute and chronic HBV infections are different in their principal routes of transmission and age of initial infection, as well as the duration of infection and need for treatment. The two types of infection also differ in their possible outcomes. This brings us to a comparison of the natural history of HBV infection acquired in adulthood and childhood.



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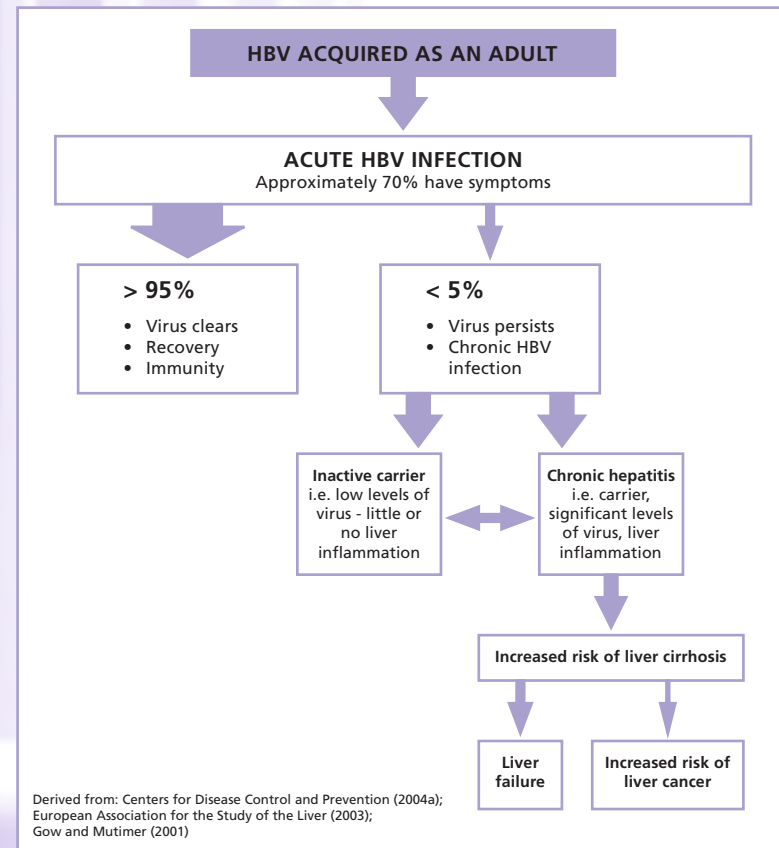
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NATURAL HISTORY OF HBV INFECTION

HBV infection acquired as an adult

Figure 5 shows the natural history (i.e. disease progression) of HBV infection acquired in adulthood.

FIGURE 5 : NATURAL HISTORY OF HBV INFECTION ACQUIRED AS AN ADULT





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EXERCISE ONE

Carefully study Figure 5. What does it tell you about the possible outcomes for a person who acquires HBV infection as an adult? Write your answers on a printed copy of Box 1. (20 minutes)

BOX 1 : OUTCOMES OF HBV INFECTION ACQUIRED AS AN ADULT

Notes:



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Figure 5 shows that most adults who are infected have acute HBV infection from which they make a full recovery and through which they develop immunity to the virus. In other words, their immune system swings swiftly into action resulting in short-term acute liver inflammation (i.e. acute hepatitis), clearance of the virus and no liver damage. (Remember when we discussed the hepatitis B virus, we noted that liver inflammation is caused when the body's immune system is activated to attack infected hepatocytes).

Adults vary in the strength of their immune response and hence in the degree of acute liver inflammation they experience. Some have only mild acute hepatitis and few, if any, symptoms while others have acute hepatitis with obvious symptoms. The majority (70%) of adults have symptoms (Centers for Disease Control and Prevention, 2004a), while 30% have no symptoms. Approximately 30% of adults have acute hepatitis associated with jaundice (icterus) (European Association for the Study of the Liver, 2003). This is known as acute icteric hepatitis. This results in abnormal clinical signs, such as dark-coloured urine and yellow discolouration of the whites of the eyes. A tiny proportion (0.1-0.5%) of patients with acute icteric hepatitis develop fulminant hepatitis (European Association for the Study of the Liver, 2003). 'Fulminant hepatitis' means that the liver has failed. This is a very serious life-threatening illness.

Interestingly, but not surprisingly, those people whose immune system launches a strong attack on the virus (and who therefore have acute symptoms, such as jaundice) are more likely to clear the virus-infected hepatocytes than people who have a weak immune response (Fagan and Harrison, 2000).

As those who develop chronic HBV infection still have the virus in their bodies, they are carriers and most carriers are infectious (World Health Organization, 2002). 'Silent carriers' are people who carry the virus but are unaware that they are infected. Notice in Figure 5 the inactive carriers – they have low levels of the virus and so their livers are not being damaged. However, the small double-headed horizontal arrow indicates that their viral



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levels may rise, increasing their risk of developing chronic liver inflammation and liver damage. The arrow also indicates that levels of the virus can fall in people with chronic liver inflammation and these people can become inactive carriers. This illustrates an important point: that there is a difference between chronic HBV infection and chronic hepatitis.

- Chronic HBV infection means the virus persists in the body at varying levels e.g. high or low.
- Chronic hepatitis means there is a sufficient level of the virus to cause chronic liver inflammation and liver damage.
- Chronic HBV infection is therefore not necessarily associated with chronic hepatitis.



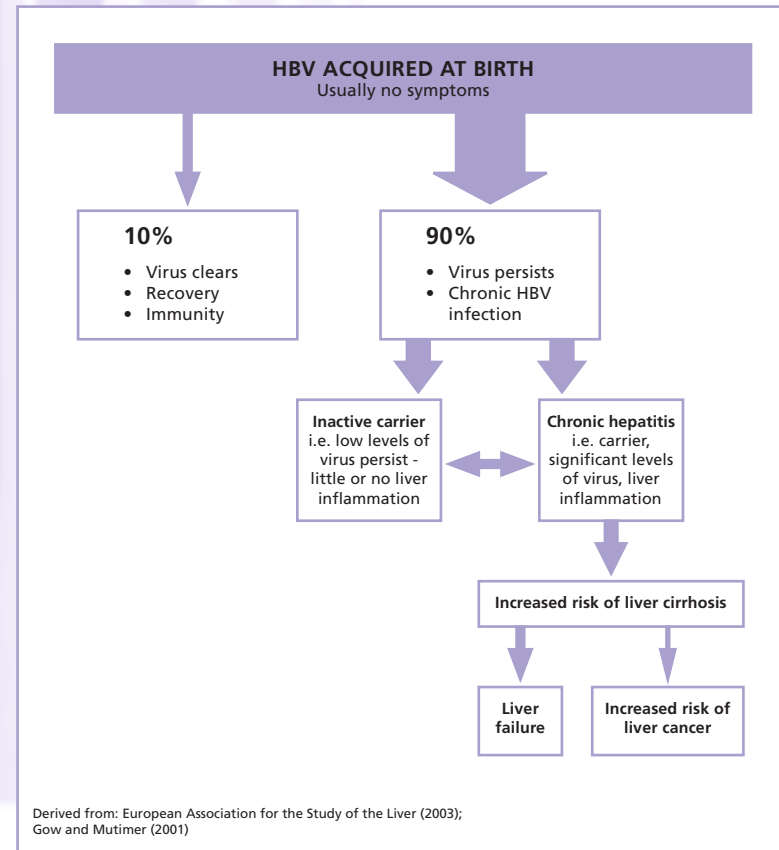
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HBV infection acquired at birth (vertical transmission)

Figure 6 shows the natural history (i.e. disease progression) of HBV infection acquired at birth.

FIGURE 6 : NATURAL HISTORY OF HBV INFECTION ACQUIRED AT BIRTH





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EXERCISE TWO

Carefully study Figure 6. What does it tell you about the possible outcomes for a person who acquires HBV infection at birth? Write your answers on a printed copy of Box 2. (20 minutes)

BOX 2 : OUTCOMES OF HBV INFECTION ACQUIRED AT BIRTH

Notes:



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Figure 6 represents a completely different picture from adult-acquired HBV infection. It shows that most babies infected with HBV at birth will develop chronic HBV infection. Their immune system doesn't respond to the infection – it 'tolerates' the virus. This immune tolerance phase is prolonged, and moderate to severe chronic hepatitis only develops after 10-30 years when at last the immune system becomes active (European Association for the Study of the Liver, 2003). So most babies infected at birth with HBV are not acutely infected i.e. they do not have acute hepatitis. Instead they enter the chronic HBV pathway.

Figure 6 applies to HBV infection at birth. However, HBV infection in early childhood also carries a significant risk of chronicity. In those who are not vaccinated against HBV, chronic HBV infection occurs in 30% of children infected at ages 1-5 years (Centers for Disease Control and Prevention, 2004a).

Summary: acute and chronic HBV infection

Let's pull all this together with a brief summary of some important points.

- Most acute HBV infection is acquired by adults (sexual transmission). Most infected adults spontaneously clear the virus and develop immunity.
- Most chronic HBV is acquired by babies at birth (vertical transmission) or in early childhood. Most fail to clear the virus spontaneously and develop chronic HBV infection.

So far we have only referred to clinical features of HBV infection, such as jaundice, abdominal pain and nausea. However, these could be related to a variety of illnesses; they aren't specific to HBV infection. In order to make a specific diagnosis of HBV infection, it's necessary to examine the patient's serum. In the next section, we'll consider serological tests and what they can tell us about a patient's HBV status.



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SEROLOGICAL TESTS FOR HBV

HBV antigens and antibodies

Table 2 of this distance learning shows three antigens to HBV. Remember that an antigen (Ag) is a substance that can elicit an immune response (e.g. formation of antibodies) in a host. Antibodies are proteins known as immunoglobulins (Ig) which are designed to recognise and bind to antigens (Eales, 2003). Both antigens and antibodies are important in HBV serological tests so have a look at Table 8 which shows the three HBV antigens together with their corresponding antibodies.

TABLE 8 : HBV ANTIGENS AND ANTIBODIES

Antigens	Antibodies
HBsAg – hepatitis B ‘s’ or surface antigen (envelope protein of virion) NB The smaller spherical and tubular particles are also made up of HBsAg	Anti-HBs (also known as HBsAb or ‘surface antibody’) – antibody to HBsAg
HBcAg – hepatitis B ‘c’ or core antigen (nucleocapsid of virion)	Anti-HBc (also known as HBcAb or ‘core antibody’) – antibody to HBcAg Two classes of Anti-HBc: • Anti-HBc IgM • Anti-HBc IgG
HBeAg – hepatitis B ‘e’ antigen (water-soluble form of core protein – secreted by HBV-infected cells)	Anti-HBe (also known as HBeAb or ‘e antibody’) – antibody to HBeAg

Sources: Tibbs and Smith (2001); Timbury et al (2002); World Health Organization (2002)



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Serological markers in acute and chronic HBV infection

Let’s consider now the serological markers associated with acute HBV infection and chronic HBV infection (see Table 9). You’ll see that with one exception, all the serological markers (indicators) for HBV are HBV antigens or their corresponding antibodies. The one exception is HBV viral DNA.

If the topic of serological markers is new to you, don’t worry if Table 9 seems very complicated and you feel the shutters coming down over your eyes! When you’ve read through the markers we’ll have a look at some practical examples which will help to make things clearer and, most importantly, will help you if patients/clients ask you about HBV test results.

TABLE 9 : SEROLOGICAL MARKERS IN ACUTE AND CHRONIC HBV INFECTION

SEROLOGICAL MARKERS	ACUTE HBV INFECTION	CHRONIC HBV INFECTION	GENERAL NOTES
HBsAg (surface antigen)	<ul style="list-style-type: none"> Can be detected for several weeks before symptoms of acute infection. Present during acute infection. 	<ul style="list-style-type: none"> It is always present in chronic infection. 	<ul style="list-style-type: none"> Indicates person is potentially infectious. Useful for diagnosis of HBV infection. Used in vaccines to elicit a protective antibody response.
HBeAg (e antigen)	<ul style="list-style-type: none"> Detectable in early phase of HBV infection, shortly after surface antigen appears. At this early stage it indicates an active acute infection, at its most infectious period. 	<ul style="list-style-type: none"> Positivity in chronic infection is always associated with high levels of virus. 	



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SEROLOGICAL MARKERS	ACUTE HBV INFECTION	CHRONIC HBV INFECTION	GENERAL NOTES
Anti-HBs (surface antibody)	<ul style="list-style-type: none"> Appearance 1-4 months after start of symptoms indicates recovery and subsequent immunity to HBV. In people who are recovering from acute HBV infection, surface antibody usually appears after surface antigen has disappeared. 	<ul style="list-style-type: none"> Is never detectable in chronic infection. 	<ul style="list-style-type: none"> Can neutralise HBV. Protects against reinfection. Marker of immunity against HBV (used to assess response to vaccination).
Anti-HBc (core antibody) (anti-HBc IgM and anti-HBc IgG)	<ul style="list-style-type: none"> Usually anti-HBc IgM indicates recent infection. Appears soon after surface antigen and may be only marker of infection in 'window period' after surface antigen disappears and before surface antibody appears. 	<ul style="list-style-type: none"> Anti-HBc IgG is always present in chronic infection. Anti-HBc IgM is not present. 	<ul style="list-style-type: none"> Core antigen (HBcAg) is not detectable in serum so is detected indirectly via presence of core antibody. Anti-HBc indicates past or present infection i.e. the person has been in contact with the virus. Anti-HBc testing identifies all previously infected people but does not differentiate between carriers and non-carriers.

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SEROLOGICAL MARKERS	ACUTE HBV INFECTION	CHRONIC HBV INFECTION	GENERAL NOTES
Anti-HBe (e antibody)	<ul style="list-style-type: none"> Indicates infection is likely to resolve spontaneously. 	<ul style="list-style-type: none"> In chronic infection its presence usually (but not always) indicates that the level of virus is likely to be low. 	<ul style="list-style-type: none"> Transition from e antigen to e antibody positivity usually indicates that virus production has decreased significantly. But e antibody may be associated with low or high viral DNA levels (usually low).
HBV DNA	<ul style="list-style-type: none"> Detectable as soon as 1 week after initial infection (but not routinely measured in acute HBV infection). 	<ul style="list-style-type: none"> An important indicator of the level of viral replication. Used to identify patients who may need treatment. Used for monitoring patient's response to antiviral treatment. 	<ul style="list-style-type: none"> Indicates the presence of circulating complete viruses (always infectious) (World Health Organization, 2002). High levels do not necessarily equate with liver damage, but significant ongoing damage will not be observed in the context of low levels.

Sources: Tibbs and Smith (2001); World Health Organization (2002); Hepatitis B Foundation (2003b); Lok and McMahon, 2003)



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Laboratory detection of serological markers

Detection of HBV antigens and antibodies

Laboratory detection of antibodies is usually based on enzyme-linked immunosorbent assay (abbreviated to ELISA or EIA). ELISA is also adapted to detect antigens (Timbury et al, 2002).

Tests for HBV antigens and antibodies are simple, automated, inexpensive and readily available. Results can be quick e.g. it is possible to obtain an HBsAg result in a day.

Detection of HBV viral DNA

The polymerase chain reaction (PCR) is used to detect viral DNA. PCR can be adapted to quantify viral DNA (i.e. to measure the level of circulating viruses). The branched DNA (bDNA) is another test used to quantify viral DNA (Timbury et al, 2002).

Testing for HBV DNA is not routine and is expensive. It takes at least a week to get the results. The test is only performed by very specialised laboratories.

Coming up now is a learning exercise to help you get to grips with some of these serological markers. It requires some detective work on your part!

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EXERCISE THREE

Cheng is Chinese. He is 35 years old and his uncle has just died of liver cancer. In Box 3 you'll see Cheng's HBV test results. What do/might the results indicate? (Use Table 9 to help you). Write your answers on a printed copy of Box 3. (30 minutes)

BOX 3 : CHENG'S HBV TEST RESULTS

CHENG'S RESULTS	WHAT RESULTS INDICATE/ MIGHT INDICATE
<p>Cheng's results show that he is:</p> <ul style="list-style-type: none"> • HBsAg negative (i.e. he has no HBsAg) • Anti HBs positive (i.e. he has anti-HBs) • Anti-HBc positive (i.e. he has anti-HBc) 	





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Discussion: Cheng's HBV test results

- HBsAg negative – this test result, **taken on its own**, indicates that Cheng:
 - a) does not have HBV infection, or
 - b) has HBV infection very recently acquired and has not yet developed HBsAg.
- Anti-HBs positive – indicates that Cheng has developed antibodies against HBsAg and so has acquired immunity to HBV infection. So he's either:
 - a) had HBV infection and acquired natural immunity to it, or
 - b) he's been immunised against HBV and acquired immunity to it.
- Anti-HBc positive – taken on its own is most likely to indicate that Cheng has been infected with HBV in the past.

Taking all three results into account it appears that Cheng was infected with HBV in the past. His immune response included the development of antibodies against HBsAg (anti-HBs) and HBcAg (anti-HBc). The development of anti-HBs conferred on him natural immunity to HBV. So he no longer has the infection and can't catch it again.

Let's try another one of these exercises!



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EXERCISE FOUR

Sophie is 19 years old. She has recently returned from a gap year in Africa. She is jaundiced and feeling ill and tired. In Box 4 you'll see Sophie's test results. What do/might the results indicate? (Use Table 9 to help you). Write your answers on a printed copy of Box 4. (30 minutes)

BOX 4 : SOPHIE'S HBV TEST RESULTS

SOPHIE'S RESULTS	WHAT RESULTS INDICATE/ MIGHT INDICATE
Sophie's results show that she is: <ul style="list-style-type: none"> • HBsAg positive • Anti-HBs negative • Total anti-HBc positive • Anti-HBc IgM positive 	



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Discussion: Sophie's HBV test results

- HBsAg positive – taken on its own this result indicates that Sophie has HBV infection.
- Anti-HBs negative – taken with the fact that Sophie is HBsAg positive, this indicates that Sophie:
 - a) is in the early stages of an acute HBV infection and hasn't yet developed anti-HBs, or
 - b) has failed to develop anti-HBs in response to HBsAg and has chronic HBV infection.
- Total anti-HBc positive – indicates that Sophie has current or past HBV infection.
- Anti-HBc IgM positive – indicates that Sophie has recently acquired HBV infection (remember that anti-HBc IgM usually disappears within six months and is a marker of acute HBV infection).

Taking all Sophie's results into account it appears that she has acute HBV infection.

Let's have a look at Mohammed's test results.



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EXERCISE FIVE

Mohammed is 20 years old. He was born in Pakistan but came to the UK with his parents 15 years ago. He went with his work mates to give blood but on routine screening was found to be HBV positive. He was referred for further serological tests. In Box 5 you'll see Mohammed's test results. What do/might the results indicate? Write your answers on a printed copy of Box 5. (30 minutes)

BOX 5 : MOHAMMED'S HBV TEST RESULTS

MOHAMMED'S RESULTS	WHAT RESULTS INDICATE/ MIGHT INDICATE
Mohammed's results show that he is: <ul style="list-style-type: none"> • HBsAg positive • Total anti-HBc positive • Anti-HBc IgM negative • HBeAg positive 	



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Discussion: Mohammed's test results

- HBsAg positive – taken on its own this indicates that Mohammed has HBV infection.
- Total anti-HBc positive – indicates that Mohammed has current or past HBV infection.
- Anti-HBc IgM negative – indicates that Mohammed has not been recently infected.
- HBeAg positive – indicates that Mohammed has high levels of HBV in his blood.

Taking all Mohammed's results into account we can say that he has chronic HBV infection with high levels of the virus.



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Summary of some commonly used HBV tests

Table 10 summarises some common HBV tests.

TABLE 10 : INTERPRETATION OF SOME COMMON HBV TESTS

TESTS	RESULTS	INTERPRETATION
HBsAg Anti-HBs Anti-HBc	Negative Negative Negative	Has no natural or acquired immunity against HBV and is susceptible to HBV infection.
HBsAg Anti-HBs Anti-HBc	Negative Positive Positive	Has had HBV and acquired immunity.
HBsAg Anti-HBs Anti-HBc	Negative Positive Negative	Is immune as a result of hepatitis B vaccination.
HBsAg Anti-HBs Anti-HBc Anti-HBc IgM	Positive Negative Positive Positive	Has acute HBV infection.
HBsAg Anti-HBs Anti-HBc Anti-HBc IgM	Positive Negative Positive Negative	Has chronic HBV infection.

Source: Adapted from Centers for Disease Control and Prevention (2004b)

Serological tests in context

It's important to remember that serological tests always need to be interpreted in context: for example, the reason for the HBV tests, the patient's age and state of health and whether he or she has had any other investigations, such as liver function tests. If you've had experience of looking at HBV test results you'll also know that concentrations (titres) of serological markers vary at different stages of HBV infection. All of these factors need to be taken into account when making clinical decisions.

In the next section we'll mention serological tests again in relation to possible HBV disease progression.



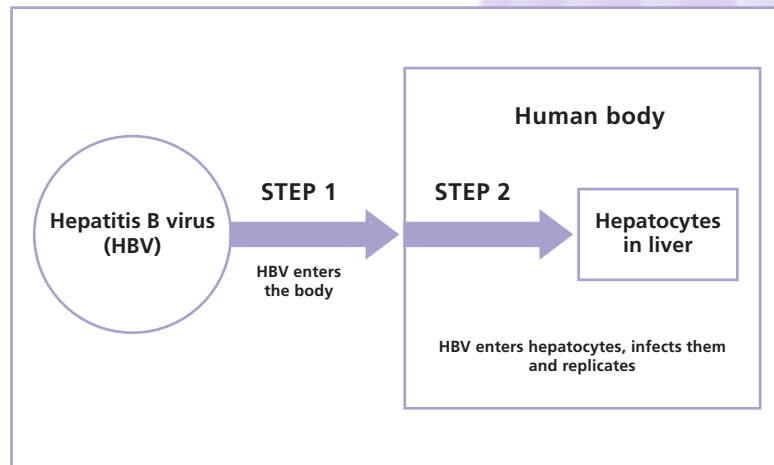
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PREVENTION OF HBV INFECTION

In considering prevention of HBV infection, we need to remind ourselves of the basic process by which HBV infection occurs and identify those steps where the process can be blocked (see Figure 7).

FIGURE 7 : REPRESENTATION OF STEPS IN HBV INFECTION



Prevention of HBV infection involves actions to block steps 1 and 2.

Step 1

Actions taken to prevent HBV entering the body.

Step 2

Actions taken to ensure that if HBV does enter the body, antibodies are available to neutralise it.

Education is important in preventing HBV infection. People need to understand how the virus is transmitted and what they can do to minimise risks to themselves and others.



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EXERCISE SIX

On your printed copy of Box 6 write down how you think HBV infection may be blocked at stages 1 and 2. (1 hour)

BOX 6 : PREVENTING HBV INFECTION

Notes:



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continued...

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Discussion: Step 1 – actions to prevent HBV entering the body

You probably included some or all of the following:

Injecting drug users

Encourage them to give up injecting but if they can't, give information about harm minimisation (ways of reducing the risk of acquiring HBV) e.g. avoid sharing needles, syringes and other equipment such as tourniquets, use of needle exchange service.

Safer sex practices

Use of condoms.

Hygienic practices

Hygiene in relation to skin piercing, such as tattooing and acupuncture. Avoid sharing domestic items e.g. razors and toothbrushes (Tibbs and Smith, 2001).

Use of universal precautions by health care workers.

Remember that 'universal precautions' means that all blood, tissues and some body fluids (e.g. vaginal secretions, semen, blood-stained fluids and amniotic fluid – fluid surrounding baby in the uterus) are regarded as potentially infectious. Measures designed to minimise the risk of occupational exposure to blood borne viruses include exercising care in handling and disposing of sharps (e.g. needles and blades), correct use of gloves, and covering all breaks in the skin with waterproof dressings (UK Health Departments, 1998).

Blood donor screening

This is carried out in the UK but is not worldwide (World Health Organization, 2002).





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Discussion: Step 2 – actions taken to ensure that antibodies are available to neutralise HBV

There are two courses of action available to neutralise HBV:

- vaccination – people are stimulated to produce their own antibodies (anti-HBs) (active immunity)
- administration of hepatitis B immunoglobulin (HBIG) – people are given antibodies (anti-HBs) (passive immunity) (Tibbs and Smith, 2001). This can give immediate but temporary protection (Department of Health, 1996).

Vaccination

HBV is a sexually transmitted disease that can be prevented by vaccination. Vaccination is the most effective method of preventing HBV infection.

Hepatitis B vaccine contains HBsAg which stimulates the production of anti-HBs. The basic vaccination regimen consists of three doses of vaccine normally given by intramuscular injection. The second dose is given one month after the first dose; the third dose is given six months after the first dose. Antibody titres (levels) are checked to ensure they are sufficient to provide protection. Poor responders should be given a booster dose. A repeat course of vaccination should be considered for non-responders (Department of Health, 1996).

In many countries of the world universal vaccination is carried out. In others, including the UK, HBV vaccination is recommended for high risk groups. The following risks groups are those specified in the Department of Health's *Immunisation against Infectious Diseases* (the Green Book) (Department of Health, 1996).

Babies born to infected mothers

Babies born to mothers who are chronic HBV carriers or who have had acute hepatitis B during pregnancy should be vaccinated. Those providing



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antenatal care need to identify infected mothers during pregnancy and ensure that babies born to these mothers are given a complete course of vaccination. This is best done by screening women early in pregnancy. If this has not been done it should be possible to detect carrier mothers at delivery and vaccinate their babies within 24 hours of birth.

In some cases babies should also be given HBIG (see Table11).

TABLE 11 : PREVENTING NEONATAL HBV INFECTION

Mother's history/test results	What newborn baby should be given
Is HBsAg positive and HBeAg positive	Hepatitis B vaccine and HBIG
Is HBsAg positive without e markers (or where they have not been determined)	Hepatitis B vaccine and HBIG
Had acute hepatitis B in pregnancy	Hepatitis B vaccine and HBIG
Is HBsAg positive and anti-HBe positive	Hepatitis B vaccine

Source: Department of Health (1996)



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Note that the Department of Health has recommended that all pregnant women should be offered antenatal screening for HBV and has provided advice to midwives about offering testing to women. The Department of Health has also emphasised the vital importance of ensuring that all babies of infected mothers complete a full course of vaccination as follows:

- first dose as soon as possible after birth and always within 24 hours of birth
- second dose at one month of age
- third dose at two months of age
- booster at one year at which time follow-up testing should be carried out.

(Department of Health, 2000)

Injecting drug users

These are an important target group for vaccination.

Individuals who change sexual partners frequently

This particularly applies to homosexual and bisexual men, and also men and women who work in the sex trade (prostitutes). The Department of Health's *Strategy for Combating Infectious Diseases* stated that by the end of 2003, all gay and bisexual men attending genitourinary clinics should be offered vaccination against HBV (Department of Health, 2002b).

Close family contacts of a case or carrier

These include close household contacts and sexual partners. Contacts should be tested to see if they are already infected. Those who are HBsAg, anti-HBs or anti-HBc positive do not require vaccination but in the case of sexual partners it may be unwise to wait for the test results before giving the first dose of vaccine. Advice should be given about the use of condoms until immunity is established. Sexual contacts of patients with acute hepatitis B infection should also be given HBIG.

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Families adopting children from countries with high prevalence of HBV infection

The adopted children could be chronic carriers. Families should be counselled about the risks and offered vaccination. Consideration should be given to testing the adopted children too, as infected children could benefit from referral and further management.

Haemophiliacs

Those receiving regular blood transfusions or blood products, or carers who administer them, should be vaccinated. (This is because of the potential risk of contact with blood from a donor who has an early undetected infection).

Patients with chronic renal failure

Patients on renal dialysis should be vaccinated against HBV. However, only 60% of patients on dialysis develop anti-HBs following vaccination. For this reason it is recommended that all patients with chronic renal failure should be vaccinated as soon as it appears they may require dialysis or kidney transplantation. (Note that people who are immunocompromised respond poorly to HBV vaccine because their immune system doesn't function effectively in producing anti-HBs. Patients having kidney transplantation are immunocompromised because they require drugs to suppress their immune system and prevent rejection of the grafted kidney).

Occupational risk groups

People whose work involves direct contact with blood or other infected fluids or tissues should be vaccinated e.g. health care workers and morticians.

Prisoners

All prisoners should be offered vaccination against HBV.

Staff and residents in accommodation for those with severe learning disabilities

A higher prevalence of HBV carriage has been found among some groups of people with learning disabilities, than in the general population. Children





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and staff in day care settings and special schools for those with severe learning disability may also be at increased risk of HBV infection.

Travellers

Vaccination against HBV is recommended for people who travel to areas of high HBV prevalence to seek employment as health care workers, as well as for those who plan to stay for lengthy periods and who may be at increased risk if they require medical or dental procedures. Some short stay travellers may put themselves at risk by their sexual behaviour.

Hepatitis B immunoglobulin (HBIG)

The administration of HBIG is known as post-exposure prophylaxis. According to the Department of Health's *Immunisation against Infectious Diseases* (the Green Book) (Department of Health, 1996) groups requiring HBIG are:

- newborn babies indicated in Table 11 above.
- people who are accidentally inoculated (e.g. needlestick injury), or who become contaminated (e.g. eye, mouth, fresh cuts or abrasions of the skin) with blood from a known HBsAg positive person. People who sustain such accidents should wash the affected area well with soap and warm water and seek medical advice.
- sexual partners (and in some circumstances a family contact judged to be at high risk) of individuals suffering from acute hepatitis B infection, who are seen within one week of onset of jaundice in the contact.

HBIG should be given to newborns as soon as possible after birth. For other groups, HBIG should be given preferably within 48 hours and not later than a week after exposure.

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If infection has already occurred at the time of giving HBIG, viral multiplication may not be completely inhibited, but severe illness and the development of the carrier state may be prevented (Department of Health, 1996).

For guidance on post exposure prophylaxis for health care workers, see UK Health Departments (1998).

Summary of key measures to prevent HBV infection

Hygiene

Education

Post-exposure prophylaxis

Blood donor screening

Vaccination

Injecting drug users – harm minimisation

Routine antenatal screening

Universal precautions

Safer sex practices





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ACUTE HBV INFECTION: MANAGEMENT

No specific treatment is necessary for acute viral hepatitis, although some patients may need symptom control measures, such as anti-emetics for nausea and vomiting (Tibbs and Smith, 2001). 'Safer sex' practices as well as vaccination of close household members should be advised (Hepatitis B Foundation, 2003a).

CHRONIC HBV INFECTION: MANAGEMENT

Preventing transmission to others

Patients should be advised about the risk of transmitting HBV to household, sexual and professional contacts and given information about how they can prevent transmission (European Association for the Study of the Liver, 2003).

Contacts

Household and sexual contacts should be vaccinated against HBV (European Association for the Study of the Liver, 2003).

Lifestyle

Patients should be advised to minimise the danger from other factors that might exacerbate liver damage e.g. excessive alcohol consumption and obesity. If they are not immune to hepatitis A they should be vaccinated against it (European Association for the Study of the Liver, 2003).

Monitoring of patients

Monitoring of patients with chronic hepatitis is used to assess:

- progression of liver disease
- need for treatment
- response to therapy.

(European Association for the Study of the Liver, 2003)

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A key issue is deciding which patients will benefit from treatment. This will be discussed in Part B of this distance learning.

Antiviral drugs

There are three main drugs: interferon alpha, lamivudine and adefovir dipivoxil. They will be discussed in Part B of this distance learning.

Liver transplantation

Some patients should be considered for liver transplantation e.g. those with decompensated liver cirrhosis (i.e. liver failure) and some people with liver cancer. Antivirals can be used to prevent recurrent HBV infection.





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CONSOLIDATING YOUR LEARNING



EXERCISE SEVEN

Spend some time reading to consolidate your knowledge of the content of Part A. (You may like to visit the websites listed at the end of Part A).
Make notes on your printed copy of Box 7. (1 hour)

BOX 7 : SELF-DIRECTED READING

What I read	What I learnt

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What I read	What I learnt
continued...	continued...



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REFLECTING ON YOUR LEARNING



EXERCISE EIGHT

On your printed copy of Box 8 give a personal view (reflection) of how Part A has informed and influenced your work. What effect has it had on the way in which you work or intend to work in the future? Do you have ideas or plans for any follow-up learning? (1 hour)

BOX 8 : OUTCOME OF PART A

Please begin by completing this sentence:

"The way in which this learning has influenced my work is....."

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continued...

Large empty rectangular box for writing the reflection.





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END OF PART A

We've come to the end of Part A of this distance learning. In Part B we'll examine in more detail the management of patients with chronic HBV infection.

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SOME USEFUL WEBSITES

The Hepatitis B Foundation
<http://www.hepb.org>

Centers for Disease Control and Prevention
<http://www.cdc.gov/page.do>

HepNet. The Hepatitis Information Network
<http://www.hepnet.com/hepb.html>

GLOSSARY

The World Health Organization has a useful glossary on its website:
<http://www.who.int/emcdocuments/hepatitis/docs/whocdscsrlyo20022/glossary.html>



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MASTERCLASS PLUS

EDUCATION UNIT 14

Hepatitis B Infection : Meeting the Challenge

PART B

DISTANCE LEARNING WORKBOOK



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INTRODUCTION

Welcome to Part B of the distance learning which will take about three hours to complete. Here are the aim and intended learning outcomes.

AIM AND INTENDED LEARNING OUTCOMES

Aim

The aim of Part B of the distance learning is to enable you to develop a deeper understanding of the management of chronic hepatitis B (HBV) infection.

Intended learning outcomes

- Deepen your understanding of the natural history of chronic HBV infection.
- Summarise further investigations that patients with chronic hepatitis B infection may require.
- Discuss how patients are selected for treatment.
- Discuss the management of patients with chronic HBV infection.



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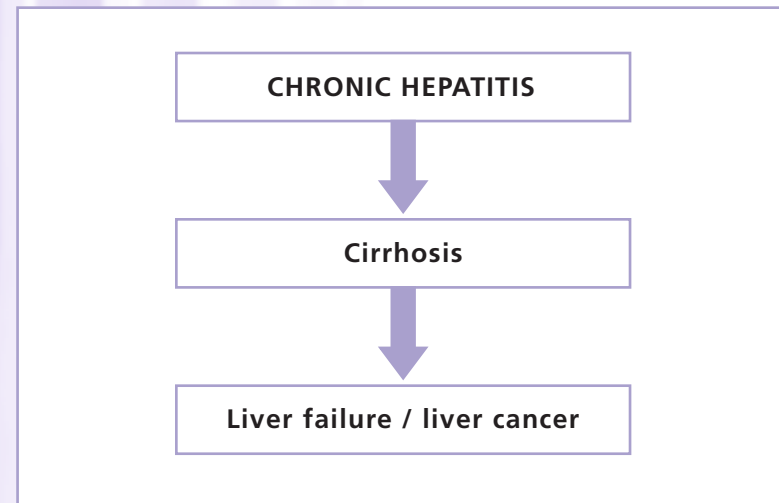
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NATURAL HISTORY OF CHRONIC HBV INFECTION

In Part A of this distance learning we considered the natural history of HBV infection acquired as an adult and at birth or as a young child. You may wish to refresh your memory of Figures 5 and 6 in Part A. It will also help you to revisit the serological markers of chronic HBV infection (Table 9) in Part A.

Remember that chronic HBV infection is the cause of liver disease because it can result in chronic liver inflammation (chronic hepatitis) and liver damage (see Figure 8 for a brief summary of possible disease progression).

FIGURE 8 : NATURAL HISTORY OF CHRONIC HEPATITIS



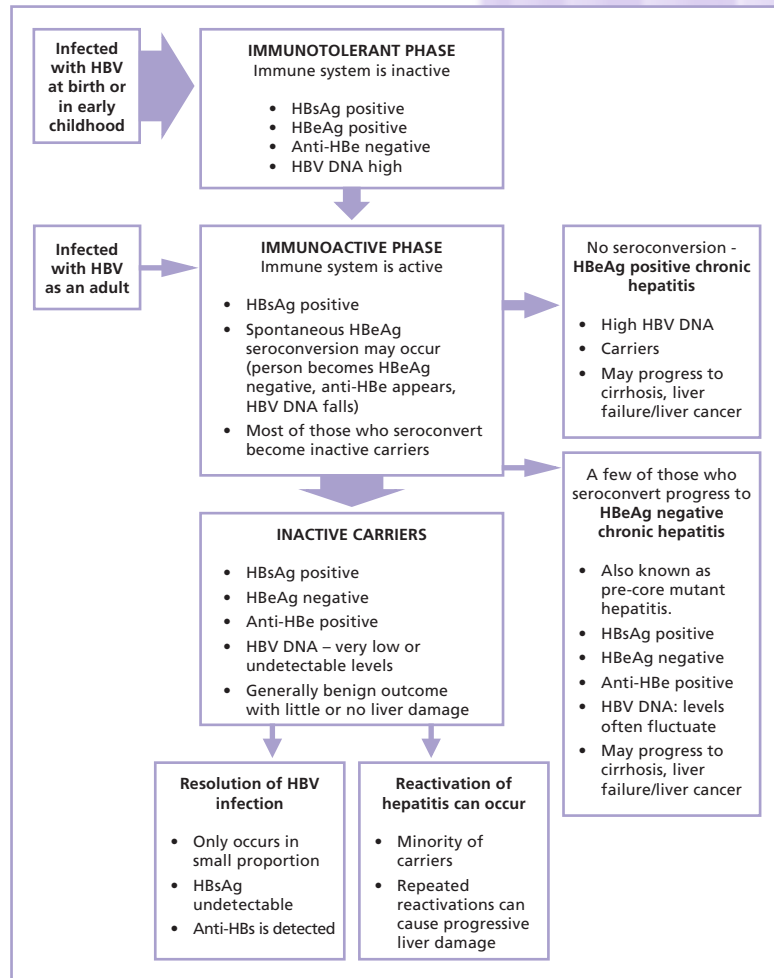
We now need to focus on chronic HBV infection and consider its natural history in more detail, including discussion of the serological profiles apparent in different phases of chronic HBV infection (see Figure 9). Understanding the natural history and serology of chronic HBV infection is essential when selecting patients for treatment.



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FIGURE 9 : OUTLINE OF POSSIBLE PHASES IN CHRONIC HBV INFECTION WITH SEROLOGICAL MARKERS



Derived from European Association for the Study of the Liver (2003); Lok and McMahon (2003)

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People who acquire chronic HBV infection

Let's have a closer look at Figure 9. The top left hand box with the large arrow indicates that most chronic HBV infection arises from initial infection acquired at birth or in early childhood. These individuals enter the immunotolerant phase i.e. their immune system tolerates the virus rather than attacking it.

In contrast, only a small proportion of chronic HBV infection arises from initial infection acquired as an adult. This is indicated by the small arrow in the left hand box. Most often, these adults do not enter the immunotolerant phase i.e. their immune systems don't tolerate the virus, they attack the virus. So most adults enter straight into the immunoactive phase.

Now let's consider the different phases of chronic HBV infection, starting with the immunotolerant phase.

Immunotolerant phase

Figure 9 shows the serological profile in this phase. HBV surface antigen is present and so is HBV e antigen but there are no antibodies because the immune system is inactive. High levels of HBV DNA are present indicating that levels of the virus are high. However, liver damage is not occurring because there is no immune response to cause liver inflammation and damage.

Immunoactive phase

This is when the immune system fights the infection and so it is a phase in which chronic liver inflammation occurs and with it, liver damage. (You'll recall that it is the body's immune response that causes inflammation). Although some people experience symptoms of chronic HBV infection (e.g. anorexia, malaise and fatigue), most do not have symptoms. So the disease can progress without the person being aware that anything is wrong.

Notice that HBeAg is still positive; this is always associated with high levels of the virus i.e. high HBV DNA. However, HBeAg seroconversion is a possibility in this phase.





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HBeAg seroconversion

You'll see from Figure 9 that in some people HBeAg seroconversion occurs. In other words, as a result of the immune response, the e antigen spontaneously disappears, is replaced by the e antibody and HBV DNA levels fall. This seroconversion marks the transition to the inactive carrier state (see below).

There are certain factors that make HBeAg seroconversion more likely to occur. These factors are older age, female gender and a strong immune response (resulting in inflammatory activity in the liver – detected by a biochemical test). HBeAg seroconversion may be followed by resolution of biochemical and histological signs of inflammatory activity. Spontaneous seroconversion occurs in 50% to 70% of patients within five to 10 years of diagnosis (European Association for the Study of the Liver, 2003).

HBeAg positive chronic hepatitis

People in whom HBeAg seroconversion hasn't occurred have HBeAg positive chronic hepatitis (liver inflammation).

The course of HBeAg positive hepatitis depends on the age of infection. Those infected at birth or early childhood progress through the immunotolerant phase, and may then develop moderate to severe HBeAg hepatitis during adult life. In contrast, those infected as adults usually present with moderate or severe liver disease after a shorter period of infection (European Association for the Study of the Liver, 2003).

In some people with HBeAg positive hepatitis, liver damage may result in cirrhosis, in particular in those who have recurrent flares of hepatitis. In HBeAg positive people, progression to cirrhosis occurs at an annual rate of 2.0% to 5.5% (European Association for the Study of the Liver, 2003).

HBeAg negative chronic hepatitis

In most people, HBeAg seroconversion marks the transition to the inactive carrier state. However, in a proportion of patients HBV DNA levels remain high or fluctuate – falling but then rising again. High levels of HBV DNA are

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associated with inflammatory activity in the liver. The condition in which hepatitis is associated with high viral levels and HBeAg negativity is called HBeAg negative chronic hepatitis or sometimes pre-core mutant hepatitis.

Patients with HBeAg negative chronic hepatitis tend to be older and male and to present with severe necro-inflammation (inflammation leading to death of hepatocytes) and cirrhosis. Progression to cirrhosis occurs at an annual rate of 8% to 10% in HBeAg negative patients with chronic hepatitis (European Association for the Study of the Liver, 2003).

Inactive carrier state

Following HBeAg seroconversion, most people enter the inactive carrier state. In this phase HBV replication continues but at very low levels because of suppression by the person's immune response. The outcome is generally benign (European Association for the Study of the Liver, 2003). Indeed, following spontaneous HBeAg seroconversion, 67% to 80% of carriers remain HBeAg negative and anti-HBe positive with minimal or no liver inflammation (Lok and McMahon, 2003).

Resolution of HBV infection

You'll see from Figure 9 that in a small proportion of inactive carriers, resolution of HBV infection occurs (European Association for the Study of the Liver, 2003).

Reactivation of hepatitis

Reactivation of hepatitis may occur in 20% to 30% of inactive carriers. Acute flares of hepatitis are usually the result of HBV replication but can occur in patients who also have another hepatitis virus or other causes of acute liver disease e.g. alcohol abuse or drug toxicity (European Association for the Study of the Liver, 2003). (An example of drug toxicity is paracetamol overdose).

Repeated reactivations or exacerbations of hepatitis can result in progressive liver damage (Lok and McMahon, 2003). Some patients may develop liver cancer (European Association for the Study of the Liver, 2003).





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Factors affecting likelihood of progression to cirrhosis in chronic HBV infection

- Infection acquired at an older age
- Male gender
- High levels of HBV DNA
- Infection with hepatitis C virus (HCV), hepatitis D virus (HDV) or human immunodeficiency virus (HIV) (see below)
- Alcohol abuse
- Recurrent bouts of severe acute exacerbation
- If extensive fibrosis is already present when chronic HBV infection is diagnosed

Hepatocellular carcinoma (HCC)

Some people with chronic HBV infection and chronic hepatitis will develop primary liver cancer i.e. hepatocellular carcinoma (HCC) (World Health Organization, 2002). In patients with cirrhosis the overall risk is over 2% per year (European Association for the Study of the Liver, 2003). The risk of developing HCC is much lower in patients who do not have cirrhosis.

HBV carriers at high risk of developing HCC include not only those with cirrhosis, but also males over the age of 45 and people with a family history of HCC (Lok and McMahon, 2003).

HCC is fairly uncommon in most Western countries but it is among the top three causes of cancer deaths in many Asian and some African countries. Chronic HBV infection arising from initial infection at birth or early childhood causes 80% of HCC cases (Asian Liver Center, 2003).

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HBV: interaction with other viruses

HBV and HCV

Co-infection (simultaneous transmission of both viruses) is common, especially among injecting drug users, and is reported to be associated with more severe liver damage than that occurring in HCV infection alone (Tibbs and Smith, 2001).

HBV and HIV

Co-infection is common in injecting drug users and is also seen in men who have sex with men. Co-infected people tend to have higher levels of HBV DNA, lower rates of spontaneous HBeAg seroconversion and more severe liver disease (Lok and McMahon, 2003).

HBV and HDV

HDV is rare worldwide and very uncommon in the UK.

HDV has an envelope of HBsAg so it can only establish itself in people who have HBV infection – it needs HBV as a ‘helper’ virus. HDV shares the same transmission routes as HBV. People who are immune to HBV are also protected from HDV infection.

HBV and HDV can be transmitted simultaneously or HBV carriers can subsequently be infected with HDV (superinfection) (Tibbs and Smith, 2001).

A higher proportion of people with chronic HBV/HDV infection develops cirrhosis, decompensated liver disease and HCC compared with those who have chronic HBV infection only (Lok and McMahon, 2003).





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FURTHER INVESTIGATIONS IN CHRONIC HEPATITIS B INFECTION

Serological tests

HBV DNA

As you know from Part A, HBV DNA is not a routine serological test in HBV infection. However, it is a very important investigation in the management of chronic HBV infection because it indicates levels of viral replication and there is a correlation between viral replication and liver damage.

Tests for other viruses

Since viruses such as HCV and HIV influence the course of chronic HBV infection it's important to carry out serological tests to detect these other viruses.

Liver enzymes

Alanine aminotransferase (ALT) and aspartate aminotransferase (AST)

Raised ALT and AST levels are associated with inflammation and cell death in the liver. ALT is a more specific and more sensitive indicator of hepatic inflammation in viral hepatitis than AST which is also present in heart muscle and other tissues. Generally, patients with active and progressive hepatitis have raised liver enzymes but some patients with liver fibrosis or even cirrhosis have normal liver enzymes (Tibbs and Smith, 2001).

Tests of liver synthetic function

The commonest tests are prothrombin time and serum albumin (Tibbs and Smith, 2001). Deterioration of these indicators of liver function means that the patient has advanced liver disease.

Serum bilirubin

Most patients with chronic HBV infection have normal bilirubin levels.

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Other investigations

In chronic hepatitis, a full blood count may reveal a low platelet count. This is often associated with impaired blood flow through a cirrhotic liver and consequent diversion of blood to the spleen, which becomes enlarged (Tibbs and Smith, 2001).

An abnormally high level of alpha-fetoprotein (AFP) or a progressive rise in AFP may indicate HCC and the need for further investigations; for example, using ultrasound or computed tomography (CT) scanning. Magnetic resonance imaging (MRI) may also be used (Tibbs and Smith, 2001).

Liver biopsy

The purpose of liver biopsy is to assess the degree of liver damage and exclude other causes of liver disease. Key information includes:

- the identification of additional causes of the liver disease
- amount of inflammation (often referred to as 'grade')
- amount of scarring (fibrosis) (often referred to as 'stage')

The histological findings of liver biopsy will improve if viral replication goes down and will deteriorate if it goes back up.





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SELECTING PATIENTS FOR TREATMENT

Aims of treatment

In order to understand the aims of treatment you need to remember an important fact about chronic HBV infection:

**If people have low levels of the virus
their livers don't get damaged**

So the aims of treatment of chronic hepatitis are to achieve:

- sustained suppression of HBV replication which leads to
- remission of liver disease, including improvement in histological findings of liver biopsy (e.g. reduction in amount of scarring).

(Lok and McMahon, 2003)

Selecting patients for treatment

Most HBV carriers don't need treating because they have low levels of the virus and no significant liver damage; they will not die of HBV.

It is only a minority of people with chronic HBV infection who need treatment. People who should be considered for treatment are those who have high viral titres (i.e. evidence of viral replication), regardless of whether they are HBeAg positive or negative. So patients with high viral titres need further investigations (liver function tests, liver biopsy, ultrasound) to find out whether they have liver damage/disease.



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Treatment decisions will be influenced not only by the viral levels and severity of the liver disease, but also by the:

- patient's age
- likelihood of response to treatment
- possibility of adverse effects and complications.

(European Association for the Study of the Liver, 2003)

Gender is also important e.g. spontaneous HBeAg seroconversion is more likely to occur in females and this seroconversion usually results in a spontaneous fall in viral levels. Thus, it may be more appropriate to observe some patients without giving antiviral treatment, in anticipation of a spontaneous decline in the level of viral replication (i.e. HBeAg seroconversion).



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MANAGING CHRONIC HBV INFECTION

Importance of monitoring

Let's return to Figure 9 and the accompanying discussion and pull out three simple but very important facts about chronic HBV infection:

- In some people, levels of the virus fall spontaneously
- In some people, levels of the virus remain high
- In some people levels of the virus fall, then rise again

So viral levels can rise and fall and, of course, it's important to know when they rise because that indicates the virus is replicating. In patients with HBeAg negative or positive chronic hepatitis, if viral replication reaches a certain level, then liver damage occurs. This highlights the need for careful monitoring of patients e.g. checking for HBeAg seroconversion, monitoring HBV DNA levels (titres) and monitoring for signs of liver damage (by liver function tests and possibly liver biopsy) and early HCC (e.g. by regular ultrasound of patients who have cirrhosis).

Remember that:

- people who are HBeAg positive always have high levels of circulating virus i.e. high HBV DNA
- people who are HBeAg negative may have high or low levels of circulating virus (HBV DNA) e.g. they may be inactive carriers with very low or undetectable levels of the virus OR they may have HBeAg negative chronic hepatitis with high or fluctuating levels of the virus.

Monitoring is also necessary in order to assess the response of patients selected for treatment.



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Viral levels can *fall* spontaneously or as a result of treatment with antiviral drugs. Viral levels can *rise* spontaneously or because, in a patient having antiviral treatment, the virus develops resistance to the drug.

Antiviral drugs

The purpose of using antiviral drugs is to lower the levels of the virus in people who have high levels.

Interferon alpha

This has been shown to be effective in suppressing HBV replication and inducing remission of liver disease. Its efficacy, however, is limited to a small percentage of highly selected patients. The drug is administered as subcutaneous injections, daily or thrice weekly for adults; thrice weekly for children. Duration of treatment is from four months to one year, depending on the type of chronic hepatitis (i.e. HBeAg negative or HBeAg positive) (Lok and McMahon, 2003).

Interferon alpha is associated with many adverse effects, the most common being flu-like symptoms, fatigue, depression and lowered white cell count (Lok and McMahon, 2003). (White blood cells are part of the body's defence against infection). The flu-like symptoms usually improve as treatment progresses but fatigue, anorexia, hair loss and mood swings (including depression, anxiety and irritability) may persist throughout the course of treatment and for a few weeks after the therapy is discontinued (Lok and McMahon, 2003).

In March 2005 a modified form of interferon alpha was licensed for the treatment of chronic hepatitis B: pegylated interferon alpha 2a. This form of interferon alpha has been chemically modified so that it has an extended duration in the body and therefore only requires administration once a week (subcutaneous injection). It is expected that pegylated interferon alpha 2a will now replace unmodified interferon alpha for the treatment of chronic hepatitis B.

Lamivudine

This works by specifically inhibiting synthesis of HBV DNA (i.e. it stops replication of viral genetic material and so more virus particles can't be made). It is given orally every day for a year or more (Lok and McMahon, 2003).



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In general lamivudine is very well tolerated and most people don't have any side effects. However, during prolonged therapy the virus can become resistant to lamivudine. If resistance occurs, levels of virus go up and inflammation resumes.

Adefovir dipivoxil

This works in the same way as lamivudine. It is given orally, usually every day for a year or longer. It is not currently approved for children (Lok and McMahon, 2003). It has also been shown to be effective in suppressing both wild-type HBV and lamivudine-resistant HBV mutants (Lok and McMahon, 2003). Adefovir dipivoxil is well tolerated. Some impairment of kidney function has been reported, but this is a rare problem at the recommended treatment dose for hepatitis B (Lok and McMahon, 2003).

Resistance to adefovir can develop but is much less than that associated with lamivudine.

Duration of treatment

Table 12 shows the duration of treatment of interferon alpha, lamivudine and adefovir.

TABLE 12 : DURATION OF THREE APPROVED TREATMENTS OF CHRONIC HEPATITIS B

Types of chronic hepatitis B	Interferon alpha	Lamivudine	Adefovir
HBeAg positive chronic hepatitis	4-6 months	1 year or more	1 year or more
HBeAg negative chronic hepatitis	1 year	More than 1 year	More than 1 year

Source: Lok and McMahon (2003)



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Liver transplantation

Some people will require liver transplantation. Patients with decompensated cirrhosis should be considered for transplantation, as should selected individuals with liver cancer.

In order to prevent rejection of the transplanted liver, patients require powerful immunosuppressant drugs. Suppression of the immune system increases the risk that chronic HBV infection will recur. Antivirals and hepatitis B immunoglobulin are used to prevent recurrence of the infection following transplantation (Foundation for Liver Research, 2004).



EXERCISE 9

In Box 9 you'll see the clinical profiles of two patients. In broad terms how do you think they should be managed? Make notes on your printed copy of Box 9 and include the reasons for your answers. (30 minutes)

BOX 9 : CHRONIC HBV INFECTION – MANAGEMENT DECISIONS

PROFILES OF PATIENTS	MANAGEMENT DECISIONS
Mr Li's parents came to the UK from China. Mr Li was born in the UK. He now has chronic HBV infection. His liver function tests are normal and HBV DNA levels are undetectable. His ultrasound liver scan is normal.	
Mr Kaur's parents came to the UK from Asia. Mr Kaur was born in the UK. He is now 45 years old and he has chronic HBV infection. He presents with high HBV DNA levels and his liver function tests are abnormal (high ALT). His ultrasound liver scan is abnormal. Liver biopsy shows a severely damaged liver.	



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With their family histories both Mr Li and Mr Kaur are very likely to have acquired chronic HBV as a result of infection at birth or early childhood.

Mr Li has undetectable levels of the virus and no signs of liver damage so he doesn't need treatment. However, he should be monitored for evidence of viral replication (rising HBV DNA levels) and liver damage (e.g. raised ALT).

Mr Kaur has a very different clinical picture. He has evidence of viral replication (high HBV DNA) and liver damage (high ALT and findings of liver biopsy). It is not surprising that he has cirrhosis. He definitely needs to be considered for antiviral treatment. He is at risk for the development of liver cancer and should have regular ultrasound examination during follow-up.

In Part C of this distance learning there'll be an opportunity for you to consider some more detailed case studies of patients.

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CONCLUSION

To conclude this part of the distance learning here are 10 important facts about chronic HBV infection (see Table 13).

TABLE 13 : TEN IMPORTANT FACTS ABOUT CHRONIC HEPATITIS B INFECTION

1. Most chronic HBV infection arises from initial infection at birth or early childhood.
2. Chronic HBV infection can result in chronic hepatitis.
3. Chronic hepatitis causes liver damage that can progress to cirrhosis and liver failure/liver cancer.
4. Regardless of whether patients have HBeAg positive or negative chronic hepatitis, viral replication with high levels of HBV DNA causes liver damage.
5. People who need treating are those who have evidence of viral replication with high levels of HBV DNA and liver damage.
6. Antivirals reduce viral replication, and sustained suppression of replication protects the liver from further damage and improves its condition.
7. Some patients will need liver transplantation.
8. Most people with chronic HBV infection do not need treating.
9. Monitoring of disease progression is essential.
10. Most carriers are infectious and the best way of preventing HBV transmission is vaccination.





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CONSOLIDATING YOUR LEARNING



EXERCISE TEN

Spend some time reading to consolidate your knowledge of the content of Part B. (You may like to visit the websites listed at the end of Part B). Make notes on your printed copy of Box 10. (1 hour)

BOX 10 : SELF-DIRECTED READING

What I read	What I learnt

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What I read	What I learnt
continued...	continued...



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REFLECTING ON YOUR LEARNING



EXERCISE 11

On your printed copy of Box 11 give a personal view (reflection) of how Part B has informed and influenced your work. What effect has it had on the way in which you work or intend to work in the future? Do you have ideas or plans for any follow-up learning? (30 minutes)

BOX 11 : OUTCOME OF PART B

Please begin by completing this sentence:

"The way in which this learning has influenced my work is.....

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continued...

Large empty rectangular box for writing the reflection.





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END OF PART B

We've come to the end of Part B of this distance learning. Part C comprises five case studies on your free CDROM, with accompanying discussion in the next part of this PDF.

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REFERENCES

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FURTHER READING

For detailed information about pegylated interferon alpha 2a, please see the Summary of Product Characteristics for this drug.





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SOME USEFUL WEBSITES

The Hepatitis B Foundation
<http://www.hepb.org>

Centers for Disease Control and Prevention
<http://www.cdc.gov/page.do>

HepNet. The Hepatitis Information Network
<http://www.hepnet.com/hepb.html>

Asian Liver Center:
<http://liver.stanford.edu/index2.asp?lang=eng&page=livercancer>

GLOSSARY

The World Health Organization has a useful glossary on its website:
<http://www.who.int/emcdocuments/hepatitis/docs/whocdscsrlyo20022/glossry.html>

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NOTES



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MASTERCLASS PLUS

EDUCATION UNIT 14

Hepatitis B Infection : Meeting the Challenge

PART C

DISTANCE LEARNING WORKBOOK



WORKBOOK : PART C

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INTRODUCTION

Welcome to Part C of the distance learning which will take about five hours to complete. You'll need to have your free CDROM at hand.

The CDROM presents you with five case studies and you should study them in conjunction with this distance learning text. You should watch each case study and then answer the questions posed in this text. Don't be surprised if you need to revisit Parts A and B of the distance learning in order to answer some of the questions! When you've completed each set of questions, move on and read the discussion in this text.



You'll see that estimated timings are included for each case study and, in addition, this clock symbol is used to help you find the relevant parts of the CDROM quickly. The numbers relate to a clock that runs in the corner of the screen.

Here are the aim and intended learning outcomes of Part C.



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AIM AND INTENDED LEARNING OUTCOMES

Aim

The aim of Part C of the distance learning is to enable you to deepen your understanding of the management of people with chronic hepatitis B (HBV) infection.

Intended learning outcomes

- Develop increased understanding of the natural history of chronic HBV infection.
- Become more skilled in interpreting HBV test results.
- Apply the principles of HBV prevention to specific patients and their contacts.
- Develop awareness of the role of nurses in acting as an advocate for patients with chronic HBV infection.
- Develop increased understanding of the management of people with chronic HBV who have co-morbidities.
- Discuss issues involved in the management of a person with chronic HBV infection who is a drug user receiving methadone.
- Discuss issues involved in the management of pregnant women diagnosed with chronic HBV.



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TAO'S CASE STUDY – FIRST SECTION

Tao's case study is presented by Mark, her Specialist Nurse. There are two sections.



EXERCISE TWELVE

Watch the first section of Mark's presentation. Then answer these questions (include the reasons for your answers):

- Is Tao's place of birth relevant to her medical history?
- How might Tao's two sets of blood tests be interpreted?
- What is Tao's prognosis?

Make notes on your printed copy of Box 12. (30 minutes)

BOX 12: TAO'S CASE STUDY – FIRST SECTION

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continued...



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Discussion about Exercise 12

Is Tao's place of birth relevant to her medical history?

Vietnam is in South-East Asia – an area of high chronic HBV prevalence. Therefore Tao is more likely to have been exposed in the country of her birth than in the UK.

How might Tao's two sets of blood tests be interpreted?

Initially, Tao's results are suggestive of chronic HBeAg negative infection with minimal activity (though there are no liver biopsy results), but her latter results are suggestive of increased inflammatory activity (HBeAg negative hepatitis).

What is Tao's prognosis?

Tao's history suggests that she has been infected for most of her life. However, she is unlikely to have serious liver disease at the age of 26 and it is quite likely that she will never develop significant liver disease.



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TAO'S CASE STUDY – SECOND SECTION



EXERCISE THIRTEEN

Watch the second section of Mark's presentation. Then answer these questions (include the reasons for your answers):

- Should Simon be tested?
- What would you say to this couple about the test interpretations and the ultrasound scan result?
- Should they be concerned about transmitting the infection?
- Should they continue to try for a baby?

Make notes on your printed copy of Box 13. (30 minutes)

BOX 13: TAO'S CASE STUDY – SECOND SECTION

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Discussion about Exercise 13

Should Simon be tested?

Simon should be offered testing as he has been a sexual partner for at least two years. He needs counselling i.e. he may have caught the virus and be a carrier or, more likely, he is immune to the infection (because he will have acquired infection as an adult, and the majority of adult-acquired infections resolve completely).

What would you say to this couple about the test interpretations and the ultrasound scan result?

Tao has the virus and there is evidence of some viral replication. But her scan is normal - no evidence of liver damage. The chance of serious liver disease in the future is unlikely.

Should they be concerned about transmitting the infection?

Tao should consider discussing this with her family, who may wish to seek testing too. Any partners, family members or co-habitees will need to consider vaccination for hepatitis B if they are not already infected. Tao must not donate blood or organs. Healthcare workers providing care for Tao should already be practising universal precautions.

Should they continue to try for a baby?

Yes. Tao's liver is not damaged and so she doesn't need antiviral drugs. (Antivirals have not been shown to be safe for a developing fetus). They should ensure their baby is vaccinated at birth and completes the full course.





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JAZ'S CASE STUDY

Jaz's case study is presented by Marion, his Practice Nurse.



EXERCISE FOURTEEN

Watch Marion's presentation. Then answer these questions:

- What do these test results indicate?
- How could you act as Jaz's advocate with regard to subsequent management?
- What can Jaz be told about his prognosis and the fact he is not going to be offered treatment?

Make notes on your printed copy of Box 14. (45 minutes)

BOX 14: JAZ'S CASE STUDY

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Discussion about Exercise 14

What do these test results indicate?

The tests are highly suggestive that Jaz has chronic hepatitis B. The abnormal ALT suggests inflammatory activity in the liver. One test is not conclusive, but further investigation into liver disease progression is warranted.

How could you act as Jaz's advocate with regard to subsequent management?

Jaz requires consideration for further investigation (liver biopsy) and management. This would involve controlling any alcohol consumption, and could include antiviral therapy.

Some consultants would offer investigations such as liver biopsy to stable methadone users and would then treat them if required. However, one of the key objections to offering treatment is perceived non-adherence and that is probably why the consultant in this case has decided against a liver biopsy.

But that's not necessarily the end of the story for Jaz! You could act as his advocate, providing information and assessing adherence (compliance). Then, if it seems likely that he will adhere to treatment, you would be able to write to the consultant with a glowing report.

So a key question is this: is it probable that Jaz will adhere to his treatment? One way of answering this is by testing Jaz's adherence i.e. take some blood and ask him to come back for the results of the blood tests and also to have an ultrasound scan. If he doesn't attend for the results of the investigations, there's no point in his being booked for a liver biopsy.

What can Jaz be told about his prognosis and the fact he is not going to be offered treatment?

If Jaz is not being offered treatment at present, he needs to ensure he leads as healthy lifestyle as possible, with adequate nutrition and low consumption of alcohol. He should be given advice about safe sex and must be encouraged to avoid needle use.

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Jaz needs further assessment and he may or may not need treatment. (He is only 21 and so there is likely to be plenty of time before he may develop liver disease).

If Jaz adheres to the lifestyle advice, you his nurse could write to his consultant encouraging him to reconsider his original decision not to investigate Jaz further.





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LEONARD'S CASE STUDY

Leonard's case study is presented by Annie, his Practice Nurse and John Perriman, his Consultant.



EXERCISE FIFTEEN

Watch the presentations of Leonard's case study. Then answer these questions:

- What are the signs of an acute hepatitis B infection?
- What do the first set of test results mean?
- What do the second set of test results mean?
- Would you judge Leonard to be alcoholic? (Give reasons for your answer)
- What are the consequences of drinking with a chronic hepatitis B infection?
- What can be offered in primary care to support/help a person in Leonard's situation?

Make notes on your printed copy of Box 15. (1 hour 15 minutes)

BOX 15: LEONARD'S CASE STUDY

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Discussion about Exercise 15

What are the signs of an acute hepatitis B infection?

About 30% of people with acute HBV have no signs or symptoms (Centers for Disease Control and Prevention, 2003). Some experience flu-like illness including a sore throat, tiredness, joint pains, and a loss of appetite. Other symptoms may include nausea and vomiting. Acute infection can be severe resulting in abdominal discomfort and jaundice (Health Protection Agency, 2003).

Some patients have fatty, white stools, weight loss, upper right quadrant pain and, as well as gastrointestinal disturbances, they may experience food aversions (e.g. coffee and tea, fatty foods).

These symptoms may persist for up to three months but then wane. However, symptoms such as lethargy and malaise can persist for longer following recovery.

What do the first set of test results mean?

These are indicative of an acute hepatitis B. As the results show a positive anti-HBc IgM, this is evidence of acute, rather than chronic, infection.

What do the second set of test results mean?

He is still HBeAg positive which means he has high levels of the virus. The ALT result shows that his immune system is still attacking the virus with resultant liver damage. (Alcohol may be contributing to his liver damage). Remember, as we discussed in Parts A and B, the natural history of HBV infection is very different when the infection is acquired as an adult (Leonard's situation) rather than at birth or early childhood.

Would you judge Leonard to be alcoholic?

There are various definitions of alcoholism, but Leonard is drinking considerable amounts of alcohol – this may be continuous or in binges, but either will result in liver damage.





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A simple test is this: ask a patient how long it is after awakening in the morning before he or she has the first craving for a drink (the shorter the time the more concern there is a problem).

What are the consequences of drinking with a chronic hepatitis B infection?
If Leonard has chronic hepatitis B, and continues to drink alcohol at the same level, or greater than the level he admits to, he is probably in the highest risk group of patients who will progress to cirrhosis in a shorter time period of years, rather than decades.

What can be offered in primary care to support/help a person in Leonard's situation?

The critical factor in ensuring Leonard's survival is addressing his alcohol consumption, irrespective of his chronic hepatitis B.

From Leonard's current history it is evident that he recognises the need to stop, but cannot do so on his own. A structured detoxification and rehabilitation programme in an appropriate setting, whether community or as an in-patient, is probably the better alternative, but this will need to incorporate longer term coping strategies within Leonard's lifestyle, which is possibly quite stressful owing to the nature of his occupation.

He may wish to consider his future options once he has undergone a successful detoxification and rehabilitation. He may also be in a position to seek private healthcare support for this, or he may require NHS funding, which will need to be negotiated, but he is possibly a priority case because of concern over his liver.

Primary care staff can also help Leonard by encouraging him to adhere to his antiviral treatment.



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ADEOLA'S CASE STUDY

Adeola's case study is presented by Toni, her Practice Nurse.



EXERCISE SIXTEEN

Watch Toni's presentation of Adeola's case study. Then answer these questions:

- What sort of emotional support should be offered to Adeola?
- What facts would be given about the vaccination of the baby?
- How can you explain how Adeola became infected?
- How would you advise her against spreading the infection to her partner and close family?
- What is the relationship between ethnicity and hepatitis B?
- Should she be persuaded to have an HIV test? (Give reasons for your answer)
- What is her prognosis and should she be offered treatment? (Give reasons for your answer)
- Her records showed HBsAg positive, HBeAg negative and anti-HBe positive. How would you explain these results to her?
- What is the baby's prognosis? (Give reasons for your answer)
- What information would you give Adeola about breastfeeding?

Make notes on your printed copy of Box 16. (1 hour 15 minutes)



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BOX 16: ADEOLA'S CASE STUDY

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Discussion about Exercise 16

What sort of emotional support should be offered to Adeola?

She will require time, information and assistance with medical and social issues (partner, family), but she will need to still feel in control of her own health, maternal care, and her baby as much as possible. A multi-disciplinary team approach will be necessary to support Adeola fully with these issues.

What facts would be given about the vaccination of the baby?

Immediately after delivery the baby will receive the first of three vaccine injections. In order for her baby to be protected from the virus, it is essential that the whole course of vaccinations is completed.

How can you explain how Adeola became infected?

It is possible that she was infected from her current or previous partner, or more likely from her own mother and has grown up with it.

How would you advise Adeola against spreading the infection to her partner and close family?

Adeola needs to ensure that all blood and body fluid spillages are cleaned up by herself if possible, or by someone else wearing gloves. She should not share toothbrushes, razors, nail scissors and all other similar items. Adeola must not donate blood or organs.

It would be preferable for Adeola's close family to receive vaccination if they are not infected with HBV themselves.

As this is a long-standing infection, Adeola's partner has almost certainly either caught the infection and is a carrier, or he is immune. His blood should be checked to see if he is a carrier of hepatitis or is immune.

Healthcare workers providing care for Adeola should already be practising universal precautions.

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What is the relationship between ethnicity and hepatitis B?

Nigeria is part of Sub-Saharan Africa – an area of high chronic HBV prevalence. Adeola is most likely to have been infected in Africa, either at birth or in childhood. However, it is possible that she may have been infected in the UK by a partner or by some other route e.g. tribal markings that involve drawing blood. HBV serology can establish whether the HBV infection was acquired in childhood or more recently.

Should Adeola be persuaded to have an HIV test?

As a general point, Adeola's experience highlights the importance of health care professionals taking time to provide pre-test counselling for routine as well as non-routine antenatal blood tests and ensuring informed consent (a legal requirement).

On the question of whether Adeola should be persuaded to have an HIV test there are several factors that need to be weighed up:

- Most HBV-positive women are not HIV-positive.
- Adeola is already distressed and further discussion about HIV testing might be counterproductive.
- On the other hand, even though the risk of Adeola having HIV is low, if she were HIV-positive her baby would be at risk of HIV. Moreover, being co-infected would have implications for Adeola's treatment.

These risks could be discussed with Adeola at a suitable time i.e. the discussion need not necessarily be immediately after she has been told she has HBV infection. Ultimately it is up to Adeola to give informed consent to HIV testing or to withhold her consent.

What is her prognosis and should she be offered treatment?

Most women with chronic hepatitis B don't have a problem in their lifetime. The antiHBe positivity and normal ALT suggest that she has low levels of HBV.





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Anyway treatment should rarely be given in pregnancy because of the risk of damaging the unborn baby.

Her records showed HBsAg positive, HBeAg negative and anti-HBe positive. How would you explain these results to her?

It is likely that she has been infected from birth or early childhood. With long-term infection the infection evolves, often into the form she has, which is known as 'HBeAg negative' chronic hepatitis B.

More tests are required, in particular her viral levels (HBV DNA) to ascertain if she has detectable, replicating virus. It is likely to be low, but it will give some indication as to her infectivity and possibly her risk for disease progression.

What is the baby's prognosis?

Generally the baby's prognosis is very good. If her baby receives all three vaccine injections, then it is very likely that the baby will not acquire hepatitis B. Her baby would not be at risk of disease later in life, neither would the baby be an infection risk to others.

What information would you give Adeola about breastfeeding?

If the baby receives the vaccination, then she should not be concerned about breastfeeding her baby.



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MARTIN'S CASE STUDY

Martin's case study is presented by Brian, his Specialist Nurse.



EXERCISE SEVENTEEN

Watch Brian's presentation of Martin's case study. Then answer these questions:

- What do Martin's HBV tests indicate?
- What is the likely impact of having HIV infection and chronic HBV infection and how would you explain this to Martin?
- How could this HBV infection have been prevented?

Make notes on your printed copy of Box 17. (45 minutes)

BOX 17: MARTIN'S CASE STUDY

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Discussion about Exercise 17

What do Martin's HBV tests indicate?

The fact that he's anti-HBc IgM negative indicates that the HBV infection was not recently acquired – he's probably been at risk of chronic HBV-related liver damage for many years.

Being HBeAg positive is always associated with high viral levels (high HBV DNA) and therefore, in chronic infection, with the potential for liver damage.

What is the likely impact of having HIV infection and chronic HBV infection and how would you explain this to Martin?

There is little evidence that chronic HBV infection will accelerate HIV disease. But in patients with chronic HBV or HCV, co-infection with HIV can make the liver damage more aggressive. The hepatologist and HIV specialist will need to collaborate and make joint decisions about antiviral therapy.

How could this HBV infection have been prevented?

The most common route of acquiring HBV infection as an adult is sexual. Martin suggests that he practises safer sex, but further discussion is probably warranted.

HBV is a sexually transmitted infection that is preventable by vaccination. Other preventive measures include correct use of the right type of condoms during sex, not sharing toothbrushes, razors, nail scissors and other such items.





WORKBOOK : PART C

Education Unit 14
Hepatitis B Infection : Meeting the Challenge

REFLECTING ON YOUR LEARNING



EXERCISE 18

On your printed copy of Box 18 give a personal view (reflection) of how Part C has informed and influenced your work. What effect has it had on the way in which you work or intend to work in the future? Do you have ideas or plans for any follow-up learning? (30 minutes)

BOX 18: OUTCOME OF PART C

Please begin by completing this sentence:

"The way in which this learning has influenced my work is....."

WORKBOOK : PART C

Education Unit 14
Hepatitis B Infection : Meeting the Challenge

continued...

Large empty rectangular box for writing the reflection.





WORKBOOK : PART C

Education Unit 14

Hepatitis B Infection : Meeting the Challenge

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WORKBOOK : PART C

Education Unit 14

Hepatitis B Infection : Meeting the Challenge

CONTINUING YOUR MASTERCLASS STUDIES

Now that you've finished Parts A, B and C of the distance learning you may wish to study the final component of this education unit: the tutor-led on-line learning. This builds on the distance learning, enabling you to develop further your knowledge of the prevention and management of hepatitis B infection.

The tutor-led on-line learning activities include some optional pieces of written work that have the sole purpose of helping your learning i.e. they're not graded as part of your final result. However, you do receive individual feedback on them and you're strongly recommended to complete them.

Participants studying the final component of the education unit are entitled to join 'The Forum plus'. The bulletin board for this is used for peer support and tutorials. Students can also communicate privately with their tutor via a dedicated post box. Emails co-ordinated by the Masterclass plus Administrator are used to send written work to tutors and to receive it back with individual comments.

At the end of the education unit comes the assessment that determines the final result. Candidates will be required to use the knowledge developed during the education unit to write a reflective analysis of care, 2000 words in length. Those who do not have access to an appropriate patient will be given a patient profile as the focus of their assessment.

On successful completion of the whole education unit, participants will receive 15 higher education credits at level 3. The tutor-led on-line learning and assessment take about 70 hours to complete.

For further details about the tutor-led on-line learning and the fee payable, please visit the Masterclass plus website: www.masterclassplus.co.uk



Well, that's all for now.

We hope you've found Parts A, B and C of the distance learning useful and that you'll want to participate in the final component of this education unit and, who knows, in another education unit.

Keep an eye on the Masterclass plus website for details of new developments!

ACKNOWLEDGEMENTS

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