ISSUE TEN

BIRCHGROVE

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Hepatitis C

WHAT IS HEPATITIS C?

Hepatitis C, (formerly called non-A, non-B hepatitis) is an infection of the liver caused by a recently identified bloodborne virus. The Hepatitis C virus was first isolated in 1989 and in 1991 a reliable test for Hepatitis C antibody detection became available in the UK. Since 1991 the test has been routinely used for screening all blood donations. The Hepatitis C virus infection is found in 0.5% to 8% of blood donors worldwide.

WHO GETS HEPATITIS C?

Hepatitis C occurs most often in people who have received blood transfusions, major pooled blood products or those who have shared needles.

People with chronic (persistent) Hepatitis C, are often only mildly symptomatic, the infection being slowly progressive, but up to 25% of patients may develop cirrhosis after at least 20 years of infection, and a number of those with cirrhosis will develop hepatocellular carcinoma (liver cancer).

Some people infected with the Hepatitis C virus will become sick with jaundice or have other symptoms. Up to eighty percent of these individuals may go on to develop chronic liver disease.

HOW CAN THE SPREAD BE PREVENTED?

Hepatitis C is spread by exposure to blood from an infected person, such as through a blood transfusion, the sharing of needles or unsterile tattooing. There is no evidence that it can be transmitted by casual contact, through foods or by coughing or sneezing.

The risk of sexual transmission of the Hepatitis C virus appears to be small. Sexual activity should be considered risky if infected blood is able to get into another person's bloodstream. Follow safe sex practices.

Pregnant women infected with Hepatitis C are believed to have only a small risk of transmitting the virus to their unborn child. People who have Hepatitis C should be aware that their blood, and possibly other body fluids, are potentially infective. Care should be taken to avoid the sharing of toothbrushes, razors, needles, etc. Infected people and their partners must not donate blood etc. and should inform their healthcare providers.

WHAT ARE THE SYMPTOMS?

Many people with Hepatitis C have no discernable symptoms. Although some people can experience appetite loss, fatigue, nausea and vomiting, vague stomach pain and jaundice.

Initial symptoms may occur from two weeks to six months after exposure to the virus. The disease may occur in the acute form and be followed by recovery, or it may become chronic and cause further symptoms over a prolonged period. People may continue to carry the virus in their bloodstream, and remain contagious.

WHAT IS THE TREATMENT?

There are no special medicines or antibiotics that can be used to cure people of Hepatitis C, but a drug called recombinant Interferon-α is often used for people with chronic Hepatitis C. Hepatitis C leading to liver failure, can be an indicator for liver transplantation in a limited number of people.

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Hepatitis C is an infection of the liver caused by a recently identified bloodborne virus.

WHAT IS HEPATITIS C?

Hepatitis C is an inflammation of the liver, caused by an infectious viral agent and it is characterised by jaundice, fever, liver enlargement, and abdominal pain. The Hepatitis C virus was first isolated in 1989 using genetic engineering techniques and in 1991 a reliable test for Hepatitis C antibody detection became available in the UK.

WHAT IS THE EVOLUTION OF THE DISEASE?

Although the exact natural evolution of Hepatitis C is unknown, it is thought that up to 80% of people infected with Hepatitis C will develop chronic hepatitis; and of those 20-30% may progress to cirrhosis and perhaps 50% of those with cirrhosis may develop hepatocellular carcinoma. Some people may develop chronic Hepatitis C infection without abnormal elevations of liver enzymes in the blood.

The initial Hepatitis C infection is infrequently identified, it is not usually severe, and does not require any specific treatment, it is necessary to wait six months to determine whether the infection has become chronic. It can take between 20-40 years for a percentage of those with chronic Hepatitis to develop liver cirrhosis. It should be born in mind that some haemophiliacs will already have had the infection for up to thirty years. This would depend on when they first received treatment with pooled blood products.

The risk of developing liver disease is significantly greater if the patient has HIV, and the rate of progression for either liver failure or the onset of an HIV related illness may be speeded up. This may be due to the significant role that an effective immune system plays in the control of viral infections.

WHAT ARE GENOTYPES?

Genotypes are the different strains or types of the Hepatitis C virus. Currently there are six known genotypes and most of these genotypes are known to have sub-strains. With the most common being type 1 with types 2 and 3 occurring less often.

The distribution of genotypes in haemophiliacs, many of whom were exposed to U.S. concentrate, was dissimilar to that in persons who acquired the infection after transfusion of local blood. Some haemophiliacs were infected with mixed genotypes, and with genotypes not found in the UK. Genotype 4 is common in the Middle East and Zaire; genotype 5 is predominant in South Africa although found rarely elsewhere. Tracing viral genotypes may question the sources of the plasma.

Progressive changes in the genotypes affecting individuals are thought to be associated with a poor response to treatment. This problem seems to particularly affect those people who are co-infected with HIV in addition to Hepatitis C. The identification of Hepatitis C genotypes is important as the response to treatment appears to depend on the strain of virus which is present. Also, it is believed that some genotypes are more likely to be associated with the development of cirrhosis.

HOW MANY HAEMOPHILIACS HAVE HCV?

There are approximately 3,000 haemophiliacs infected with Hepatitis C in the UK. Any haemophiliac, or person with a low clotting factor, who received freeze dried concentrate before 1986 is likely to have been infected with Hepatitis C. It is thought that over 90% of all UK haemophiliacs are Hepatitis C positive, 10% (mainly those who have not received freeze dried concentrate) are therefore Hepatitis C negative. Every time a haemophiliac injected a bottle of concentrate they are likely to have been re-infected with the virus. Hepatitis C tends to be more severe in haemophiliacs.

Hepatitis C is thought to be present in about 0.2% of the UK population (1 in 500 people), and is present in much higher frequencies in other parts of the world.

WHAT SCREENING IS DONE FOR HEPATITIS C?

Since 1991, blood donors have been routinely subjected to a blood donor screening test for Hepatitis C. Widespread use of this test has significantly reduced the number of post transfusion Hepatitis C cases. The risk is now thought to be one in 3,000 units of blood, or 0.12% for the typical recipient of a transfusion. Before screening tests were introduced, up to 20% of people who received blood transfusions risked developing Hepatitis C infection.

An experimental blood test that detects antibodies to Hepatitis C in donated blood identifies many, but not all, tainted units, two studies indicate. The data suggests that the test will reduce the number of transmission-associated cases of Hepatitis C. But the test's inability to flag all infectious units hints at the presence of an undiscovered causative agent underlying in some Hepatitis cases, and highlights the difficulties of eliminating liver disease.

Since 1985, all Factor VIII and IX concentrates have been heat treated and/or chemically processed to reduce the risk of viral transmission. Although cryoprecipitate which may be used in a small number of cases cannot be treated to inactivate viruses.

Screening for viral contamination can be carried out on pooled blood products, by using a PCR test (polymerase chain reaction), which magnifies the presence of viral particles in the blood. Unfortunately, it appears that this screening test is not currently used routinely on heat treated blood products.

Contaminated batches of Gammagard, a non-heat treated blood product, which is primarily used to boost a patient's immune system, caused many patients, mostly children, to contract the Hepatitis C virus.

HOW CAN I PREVENT TRANSMISSION?

Hepatitis C is not thought to be highly infectious. It cannot be transmitted by normal social contact, through the air, or by touching or kissing a person who is infected.

You should advise your healthcare workers, including dentists, of your status. If you are infected with Hepatitis C you and your partner should not donate blood, plasma, body organs, tissue or sperm. You and your partner should not share needles or injecting equipment, such as needles or syringes etc. Sharps or items used for intravenous injection should be disposed of carefully to avoid the risk of needlestick injury.

You and your partner should not share toothbrushes, razors, scissors or nail files. All these items may have come into contact with infected blood and could be responsible for transmitting the Hepatitis C virus.

In dealing with soiled items you should wear disposable gloves. Wipe up all blood spills with bleach and cover cuts and wounds with a clean waterproof dressing. Dispose of blood stained tissues, sanitary napkins and other dressings safely. Hepatitis C is a particularly hardy virus, and it may be capable of surviving in dried blood for prolonged periods of time. Some sources believe that this could be for up to eight weeks!

Follow safe sex practices. Even if Hepatitis C is not a sexually transmissible disease (STD), it is advisable to consider prevention of other STD's.

WHAT ARE THE RISKS OF SEXUAL TRANSMISSION?

The risk of sexual transmission of the Hepatitis C virus appears to be small. Several studies suggest that spread seldom occurs from people with chronic Hepatitis C disease to their steady sexual partners. Sexual activity should be considered risky if infected blood is able to get into another person's bloodstream. This would include, for example, anal intercourse and sex during menstruation. Follow safe sex practices.

The Japanese have done a study following couples with no risk factors other than sex. They found that there was a 15-25% chance of spread between an affected person and their partner. There still is no data about whether or not condoms are totally effective.

All sexual partners of those who are Hepatitis C positive should have access to regular clinical and virological monitoring. Monitoring of sexual partners for seroconversion, offers the prospect of early treatment with drugs such as Interferon-α, when it appears to be more effective.

WHAT ARE THE RISKS OF HEPATITIS C TRANSMISSION IN CHILDBIRTH?

Mother to baby transfer (vertical transmission) has been reported in a small number of pregnancies.

Mothers whose serum is Hepatitis C positive, can transmit Hepatitis C in 10% of cases of pregnancy. This can be as high as 25% if the mother is also HIV positive. Those mothers who have a high level of the Hepatitis C virus appear to transmit Hepatitis C in up to 40% of infants.

The virus has been found in breast milk, but there are no reported cases of babies being infected in this way. Currently doctors do not advise against breast feeding. You should tell your obstetrician or gynaecologist about your infection so that he can check and perhaps take further advice.

WHAT ABOUT ALCOHOL AND DRUG USE?

As a general principal, if you have Hepatitis C infection it is best to avoid taxing your liver. It is advisable to avoid alcohol, (which is probably the worst drug to use), and avoid the impurities involved in all street drugs. It may also be important to consider limiting your intake of tea, coffee and nicotine.

Alcohol consumption speeds up the progression of liver disease and in general the less alcohol consumed the better. Guidelines suggest that it may be possible to consume up to 21 units per week for men, and 14 units per week for women, although others believe that only an occasional drink is acceptable. A pint of beer contains the same amount of alcohol as a double measure of spirits or a large glass of wine. They all have the same effect on the liver, whether taken straight or diluted with water.

But, some people feel that they are more able to tolerate, (have less of a hangover), certain types of alcohol. Grain based spirits, seem particularly hard to cope with, while some feel that white wine is easier to tolerate than red wine. There is even a belief that favours the drinking of dark beers and stouts against more acidic alcohol, such as lager and cider. Choose your poison carefully!

As far as drug use is concerned, purer forms of drugs are advisable in all cases, for instance pharmaceutical heroin (methadone) is better than street heroin, pharmaceutical amphetamines are better than street amphetamines, but this is only a minor improvement.

Hepatitis C generally increases the chance of overdosing (especially on alcohol, and benzodiazepine tranquillisers such as: Valium, Mogadon, and Temazepam) because the liver cannot handle the doses of the drugs to which the user was formerly accustomed. It is possible to mistake the symptoms of Hepatitis C for the signs of hanging out. This can lead to overdosing, especially when the inclination to take more drugs presents itself, along with the livers decreased ability to remove the substances from the body.

We neither condemn or endorse alcohol or drug use. We do feel that it is essential that you make informed decisions about your health.

WHAT MEDICINES AFFECT MY LIVER?

Apart from alcohol, many drugs and toxins are broken down by the liver. People with significant liver disease metabolise and eliminate drugs and toxins more slowly than normal. This can lead to an increase in drug toxicity or an exaggeration of the therapeutic effects of a drug. Medications may be prescribed in reduced dosages to such individuals, these may include sedatives, pain killers, some diuretics, non-steroidal anti-inflammatory agents, steroids and many others.

Some drugs, even in normal doses, can worsen the condition of those suffering from liver disease. This can be as a result either, of a direct toxic effect, or through a drug allergy.

Anaesthetics can occasionally have an adverse effect on the liver. Before any surgical procedure is carried out, it is important that the surgeon and the anaesthetist are fully aware of your medical history including the condition of your liver.

Large doses of the painkilling drug, paracetamol can damage the liver and an overdose causes severe liver damage or death, the problem may not become obvious until several days after the overdose. Normal, recommended doses appear to be safe, but it may be advisable to discuss regular dosages with your doctor.

WHAT SYMPTOMS CAN HEPATITIS C CAUSE?

Although most people do not experience problems, the symptoms of Hepatitis C can be many and variable. Quite frequently, the patient has no noticeable symptoms until liver damage occurs after many years of infection. Symptoms may include: generalised tiredness, itching (generalised or localised), mood changes (irritability, depression etc.), low-light vision, heat intolerance, muscle pain and skin eruptions. It is not easy to attribute symptoms of ill-health directly or indirectly to Hepatitis C or liver related complications.

There seems to be a pattern to many people's reactions to Hepatitis C; for a while you may feel pretty good, then bad (maybe days or weeks for each period), then good again. It is a pattern that can be characterised as a cyclical asymmetrical. In this, it may be similar to Seasonal Affective Disorder, a condition which causes depression during the winter months. People can start to feel worse in August-September, with a low point usually around November-December, as spring approaches they start to feel better.

WHAT TESTS CAN BE USED TO ASSESS MY LIVER?

The liver is a complex organ and fulfils many functions so that it is difficult to have a single measure of its efficiency. Liver function tests, (LFT's) are usually performed two to three times over a six month period. Even if your LFT's remain normal, doctors may continue monitoring your LFT's over a longer period. If a person has intermittent or persistently abnormal LFT's further investigation may be warranted.

ALT (alanine aminotransferase) and AST (aspartine transaminase) are intracellular enzymes which are produced by the liver. When they are present in high levels, it may be an indication of liver cell damage. It is only regarded as significant when it is twice the level of the normal range. Liver cells are damaged, not only by virus particles, but also by alcohol and drugs. ALT and AST are not reliable indicators for chronic Hepatitis C, the condition may exist in the presence of a normal ALT/AST result.

The most sensitive method of detecting Hepatitis C, is the PCR (polymerase chain reaction) test, which can detect up to 250-500 genomes/ml. If AST/ALT levels are consistently normal, then, wherever possible, a PCR test should be performed to detect whether the virus is present, despite the normal enzyme levels.

Other tests include: Bilirubin, which is an enzyme produced by the liver and is thought to reflect hepatic protein synthesis in general, it increases in people who are jaundiced. Alpha Fetoprotein, which increases in people who are affected by liver cancer. GGT, which is more influenced by what you drink. Albumin, which is a blood protein that helps regulate fluid balance and can be reduced in a badly damaged liver. Prothrombin Time (PT) and Partial Thromboplastin Time (PTT), which assess the clotting time of the blood.

HOW CAN LIVER DAMAGE BE ASSESSED?

An Ultrasound Scan can be performed using a probe that is held against the abdomen. This test is not a precise diagnostic tool but may identify major liver abnormalities such as liver cancer.

An Endoscopy uses a fibre optic tube which is swallowed and fed into the stomach. The oesophagus can be examined for the presence of oesophageal varices which are an indicator of impaired liver function.

A Laparoscopy can be performed by inserting a telescopic instrument into an incision made in the abdominal wall. This test can determine whether the liver is functioning or whether it is inflamed. A small piece of liver tissue can be removed for further examination.

A Hepatic Angiogram is performed under a local anaesthetic. A tube is inserted into an artery in the groin and a dye is injected so that the blood vessels in the liver can be seen on an x-ray.

The gold standard for defining the state of the liver is a Liver Biopsy, but this is not without its problems. When a biopsy is performed a long needle is passed between the ribs into the liver and a small sample of liver tissue is withdrawn so that it can be studied under the microscope. Ultrasound may be used to guide the needle into the liver and to ensure that there is no abnormality in the way the liver is positioned

SHOULD I HAVE A LIVER BIOPSY?

There is currently a debate as to whether to routinely perform liver biopsies on haemophiliacs with Hepatitis C. Without biopsy, one risks treating a patient who who may have a normal histology, with toxic and expensive drugs such as Interferon-α. One also risks missing other causes of liver disease, frequent in HIV positive patients. However, biopsy is more costly in haemophilia because of the need for concentrate, and may be more risky. The main complication is potential bleeding into the peritoneum, which can be very serious.

Haemophiliac patients should be treated with appropriate amounts of blood product to ensure an acceptable clotting time, to cover the procedure and maintain good levels throughout the recovery period. Risk of complications is strongly correlated with amount of experience of the person doing the biopsy, many doctors in haemophilia centres have not seen excessive complications.

If you are uncomfortable or worried about pain, ask for a local anaesthetic or valium. Following the biopsy, you should stay very still. Some hospitals will ask you to lie on your back for several hours, others to curl up on your side as this can prevent further complications such as bleeding.

WHAT IF I AM HIV AND HEPATITIS C POSITIVE?

Studies suggest that the liver is an important site of HIV replication. Liver problems are frequent causes of illness and death in people with HIV infection. Despite the lack of therapy options for many HIV-related liver diseases, there are some treatable conditions that make proper monitoring and diagnosis important. An awareness of symptoms, methods of diagnosis, drug toxicities and interactions, and the available treatments will help patients lead longer, healthier lives.

Higher levels of the Hepatitis C virus are found in HIV positive than in HIV negative persons. The higher the serum level of the Hepatitis C virus, the less the chance of a response to Interferon-α. A higher rate of liver failure is seen in people with Hepatitis C who also are HIV positive. The majority of liver disease in patients with haemophilia and HIV is caused by Hepatitis C, but other opportunistic infections can go unrecognised.

Studies have found that 40 percent of the livers from deceased people with AIDS contain undiagnosed opportunistic infections. Some of these conditions are treatable, with prognosis directly tied to how early a diagnosis is made. Various unexpected non-viral pathogens may also be found in the liver following a diagnosis of Hepatitis C. Since these often respond to antibiotic treatment, doctors and patients must carefully watch for such infections. Due to the nature of these infections, tissue specimens may be necessary in order to make the diagnosis.

HOW DO HIV DRUGS AFFECT MY LIVER?

Drugs used in the treatment of HIV may affect liver function. These include: clarithromycin, dapsone, dilantin, fluconazole, fluctosine, isoniazid, ketoconazole, rifabutin, rifampin and septrin or bactrim. Protease Inhibitors: saquinavir, ritonavir, indinavir, viracept are also processed by the liver and may interact with other drug regimes.

Nucleoside Analogues: AZT, ddI and ddC are not processed directly by the liver. They do not seem to cause significant liver toxicity. Still, there is a concern that in some people with HIV and Hepatitis C, their use may cause additional liver damage.

A study followed thirteen persons with haemophilia who were co-infected with HIV and HCV. Amongst the five who developed liver disease, four were being treated with AZT. When some patients are treated with anti-HIV drugs metabolised by the liver, sub-clinical liver disease may become more apparent. The liver, which may have been progressively damaged by Hepatitis C, is exposed to an HIV treatment which then causes further liver complications. It is very much under discussion which multiple drug combinations are appropriate for HIV and Hepatitis C infected people with haemophilia.

Indicators of liver disease

Although most people do not experience problems, the symptoms of Hepatitis C are many and variable.

WHAT ARE THE FIRST SYMPTOMS?

The most common symptoms include: generalised fatigue, intermittent nausea, discomfort in the liver area, alternating diarrhoea and constipation, gastric reflux, general malaise and a lack of energy. Some people may also experience jaundice, appetite loss, nausea and vomiting and vague abdominal pain (pain which appears to move around).

The combined effects of these symptoms can be extremely debilitating and frustrating. Constant fatigue also makes people with Hepatitis C easy targets for stress and depression. Evidence exists that stress may have a negative effect on progression of the disease.

WHAT IS ENCEPHALOPATHY?

The liver is particularly critical to the brain and central nervous system. These tissues receive their energy supply only from sugar, and so are extremely vulnerable to liver failure. In its early stages, subtle mental changes such as poor concentration, a change in sleeping patterns, or an inability to construct simple objects can occur. In severe cases, hepatic encephalopathy can lead to stupor, coma, brain swelling and death.

WHAT IS GYNAECOMASTIA?

This is an enlargement of breasts in men. This may occur as a result of liver failure caused because the liver fails to break down the hormone oestrogen.

WHAT IS HEPATOMEGALY?

Hepatomegaly is an enlargement of the liver, occurring as a result of a liver disorder. The enlargement may cause tenderness or pain beneath the ribs, particularly on the right side of the body. A serious enlargement of the liver will normally be detected by a doctor during a physical examination.

WHAT IS JAUNDICE?

Jaundice is a yellowing of the skin and the whites of the eyes. It is caused by an accumulation of the yellow-brown bile pigment, bilirubin, in the blood. Bilirubin builds up in the body tissues because the liver becomes less capable of excreting the bile as a result of liver damage. Jaundice is the chief sign of a breakdown of the liver and biliary system.

WHAT IS OEDEMA?

This is an accumulation of fluid, commonly in the abdomen (where it is termed ascites), but also in the legs and ankles (peripheral oedema). In addition to abdominal swelling and discomfort, ascites may cause breathing or heart difficulties, due to the pressure of fluid build up. It is a symptom of the failure of the liver to produce the protein albumin, leading to salt retention and an increase of fluid in the body tissues. It may be helped by restricting salt in the diet, or by the use of diuretic drugs.

WHAT ARE OESOPHAGEAL VARICES?

Oesophageal varices are basically abnormally enlarged veins in the gullet. This happens when damage to the liver makes blood flow through the liver more difficult, so that the blood is forced to avoid the liver. These can be very common in the oesophagus, and if they rupture they can cause anaemia, blood in the motions or you may vomit blood. An endoscopy, a fibre optic tube which is fed into the stomach, can be used to look for varices. Bleeding oesophageal varices may be treated by intravenous sclerotherapy, or by use of an inflatable bladder temporarily inserted into the oesophagus.

WHAT ARE RED PALMS?

Some people can experience a reddening or hardening of the palms of the hand. This symptom is caused by a build up of the hormone oestrogen.

WHAT ARE SPIDER NEVI?

Spider nevi are small capillaries that are seen on the surface of the skin. Branches form from a single capillary and it can either look like a small red spider or a splat (like a squashed spider). They are also referred to as spider angiomas. If you have less than 10, that can be considered normal, more than that and it can be an indication of chronic liver disease. They can be found above the waist, usually on the chest, upper arms, shoulders, face, and upper back.

Treatments of Hepatitis C

It is important to remember that all currently available treatments for Hepatitis C are experimental.

WHAT IS ALPHA INTERFERON?

Alpha Interferon is a genetically engineered copy of a protein, found naturally in low levels in the human body. Interferon-α is the only licensed form of treatment for Hepatitis C. Interferon-α is usually given by subcutaneous injection in the leg or stomach. This can be done by the patient themselves.

In multi-centre studies, 166 patients were given injections of Interferon-α for six months. About half of the group treated with high doses showed improvement and, of those, half maintained the response for up to six months.

According to the manufacturer's literature for using Interferon-α in the treatment of Hepatitis C: 3 million units per dose a week for three months. Treatment may be continued for up to fifteen months. Regular monitoring of a patients blood is advisable during Interferon-α treatment. A minority (10-25%) of those treated with Interferon-α may experience a long term response, some report increased well being and some are symptomatically worse off. Undergoing treatment with Interferon-α is an involved and difficult decision and should not be represented in any other way.

WHAT CAN BE INTERFERON'S SIDE EFFECTS?

Some people feel fine during treatment, however adverse reactions reported with the use of Interferon-α include: headaches, fever, and other mild, flu-like symptoms and generalised pains. The side effects appear to lessen during continued therapy. Less frequently, side effects may include stuffiness of the nose, hair loss, itchiness and psoriasis.

It is not uncommon for a course of treatment to result in some kind of physical or emotional strain. Interferon-α, in a few cases, is capable of creating severe depression and can cause extreme lethargy, irritability and a tendency to weep. Past and present emotional well being, or a history of psychiatric illness must be taken into account.

WHAT HAPPENS WHEN YOU STOP THE TREATMENT?

About half of patients treated with Interferon-α respond, with improved blood tests and/or improved liver biopsy results. Half the patients who respond relapse once Interferon-α treatment is stopped.

For a very few individuals, Interferon-α appears to offer a total clearance of the Hepatitis C virus. In others, Interferon-α has no effect, or the virus starts to multiply again when the treatment is stopped. Sustained remission can be achieved in approximately 25% of people treated with Interferon-α.

WHEN IS INTERFERON-α MOST EFFECTIVE?

Not everyone with Hepatitis C is suitable for treatment and not everyone responds to Interferon-α. Conditions associated with a favourable response include: a short duration of infection, an absence of liver cirrhosis, low levels of serum Hepatitis C, and infection with Hepatitis C genotypes 2 or 3, with 2b being the most favourable. However, genotype 1a accounts for 37% of Hepatitis C infection and 1b for 35%. It is thought that in people with ascites and, or cirrhosis, Interferon-α is of little value and may be hazardous.

French researchers have found that large doses of Interferon-α can help long-term Hepatitis C sufferers, but smaller doses are less effective. A study evaluated 303 patients who had received six months of treatment with three-times-per-week injections of Interferon-α. They found that among 103 volunteers who continued the treatment for a further 12 months, 45 showed significant improvement by the end of the study. In 101 patients who received one-third the dose, the success rate was only 28%. It was noted that even in the group that fared best, only 22% seemed to remain free of the disease when this portion of the study ended. Treatment should only be considered for those with a high likelihood of progressive disease and for those most likely to have a response to treatment.

A Japanese research team reports that heavy drinking reduces the efficacy of Interferon-α therapy and that this effect can be reversed by abstinence. The rate of response to Interferon-α therapy was 36% in infrequent drinkers, 33% in moderate drinkers, 26% in heavy drinkers who had stopped drinking and 6% in heavy drinkers who continued to drink. The adverse effects of habitual heavy drinking might be reversed by abstinence for more than 6 months before the start of therapy."

WHAT IS AMANTADINE?

Amantadine hydrochloride is an antiviral agent that has been used to prevent and in some people to treat, symptoms caused by the influenza A virus. A open-label study was conducted to test the safety and efficacy of amantidine-HCl, in patients with Hepatitis C who had previously failed therapy with Interferon-α.

Twenty of the twenty-two patients completed therapy with 30% not responding to amantadine-HCl. Responders had lower ALT values, and Hepatitis C RNA values decreased. Hepatitis C RNA levels were undetectable in 6 patients at completion, while RNA levels fell by >50% in eleven patients. Chronic Hepatitis C infection may be successfully treated in some patients with a six-month course of amantadine-HCl, whereas in others, amantadine treatment effectively lowers Hepatitis C RNA and Hepatic transaminases.

WHAT IS HYPERICIN?

A program has been launched to develop Hypericin, an antiviral/antiretroviral compound which may inactivate viruses in blood. This broadens its antiviral profile to potentially include Hepatitis C as well as HIV. The results of recent Hypericin studies raise the possibility that it may be useful as a therapeutic for treating people who are infected with Hepatitis C. The investigators used a virus known as bovine viral diarrhoea virus as a surrogate of Hepatitis C. The two viruses are closely related and thus hoped to respond in a similar way to inactivation processes. The results indicate that the procedures developed for the use of Hypericin may be effective in the inactivation of the Hepatitis C virus.

WHAT IS IRON REDUCTION THERAPY?

The theory behind Iron Reduction Therapy is that viruses need iron to replicate, and by reducing the hepatic iron in the liver you might prevent them from replicating. It should be noted that this new procedure is not yet approved and is in early trial stages.

A new study suggests that using "Iron Reduction Therapy" along with Interferon-α can result in an effective cure rate in the area of 75-80% and that adding cytokins and antivirals, such as Ribavirin, can improve its effectiveness even further.

WHAT DOES A LIVER TRANSPLANT OFFER?

A liver transplant may be considered for haemophiliacs who have liver failure as a result of Hepatitis C. It may also be a possibility for people with cancer that has not spread beyond the liver. Liver transplantation, not only provides a new liver with an improved function, but also offers the additional advantage of 'curing' the patient's haemophilia.

Liver transplant centres have similar criteria for offering transplant, usually the presence of advanced liver failure and a life expectancy of less than a year. In general, only patients younger than 65 and those who can demonstrate a minimal alcohol intake would be considered. In haemophilia, patients should not have an inhibitor or HIV infection. Liver transplant patients have to take immunosuppressive drugs permanently to prevent rejection and this would be problematic in HIV patients who are already immunosuppressed. Although, some transplant centres have considered offering HIV patients, who meet specific criteria, a liver transplant. Currently, there have been a limited number of haemophilia patients who have been transplanted (less than 10) in the UK.

The Hepatitis C virus is able to persist in other parts of the body and recurrence is almost universal after liver transplantation. Cirrhosis may occur in up to 10% of cases after transplant. The one-year graft-survival rate is thought to be 60% for Hepatitis C infected patients, 72% for others; 3-year patient survival is 60% for those with Hepatitis C and 78% for others.

WHAT IS N-ACETYL CYSTEINE?

A small study in Spain reports that N-Acetyl Cysteine may enhance the effectiveness of interferon-α in people with chronic Hepatitis C. Fourteen patients with chronic Hepatitis C who had failed interferon-α were given N-Acetyl Cysteine. Six patients had a normalisation of liver tests and eight had a marked reduction in Hepatitis C virus levels. N-Acetyl Cysteine had no effect without Interferon-α in these patients.

WHAT IS RIBAVIRIN?

Ribavirin is an anti-viral drug that is believed to be effective against Hepatitis C. Trials have been taking place with it being used in combination with Interferon-α.

In an Italian, study 5 of 10 patients with chronic Hepatitis C had their liver function tests return to normal with a combined Ribavirin/Interferon-α.-2b therapy. ALT tests remained normal six months after treatment was stopped. The virus was "not detectable" in the blood of these five patients who responded favourably to the combined therapy.

Researchers in Maryland investigated the therapeutic effects of Ribavirin, a broad-spectrum antiviral agent, in a 48-week randomised placebo-controlled trial involving 58 patients with chronic Hepatitis C infection. ALT levels decreased rapidly during the first 2 months and remained stable thereafter in the treatment group, but they reverted to pre-treatment levels within 2 to 3 months after the therapy was discontinued. Researchers concluded that Ribavirin is of limited value as a single short-term therapy.

WHAT IS THYMOSIN ALPHA 1?

Thymosin Alpha 1 is a protein produced by the human body. It is associated with the thymus gland, which has an important role in immunity. There is also a synthetic "Thymosin alpha 1" being produced and available only in trials. It is currently being studied for use in treating Hepatitis C. In Hepatitis B the results have been promising, and it is now being studied in combination with Interferon-α.

Results from a randomised, placebo-controlled, double-blind phase III study in chronic Hepatitis C patients receiving a combination therapy of Thymosin alpha 1 and Interferon-α -2B showed almost 50% of the 65 patients had complete normalisation of ALT in the Thymosin combination treated group and in less than 20% of the Interferon-α only treated group. A 15-patient, open label Italian study used combination therapy with Thymosin alpha 1 and Interferon-α to treat chronic Hepatitis C patients. This showed reduction in ALT and RNA levels and an improvement in histology.

THE PROSPECT FOR A HEPATITIS C VACCINE

Five years after the discovery of Hepatitis C, a vaccine against the virus still seems a long way off. Chronic carriers of Hepatitis C make antibodies to a variety of virus-specified proteins. However, individuals with persistent Hepatitis C infection may also be seropositive for antibodies against the surface glycoproteins of the virion.

Without an efficient and reliable cell-culture system for Hepatitis C, an inactivated, whole-virus vaccine is not yet possible. Similarly, the scarcity of suitable primate hosts and lack of markers of virulence and attenuation limit the prospects for a live, attenuated vaccine. The most straightforward approach is to develop a vaccine based on Hepatitis C proteins expressed by recombinant DNA technology.

WHO MIGHT RECEIVE AN HEPATITIS C VACCINE?

Possibly, haemophiliacs, dialysis patients, and the spouses of infectious individuals. But the targeting of these high-risk groups has notoriously failed to reduce the incidence of acute Hepatitis B in countries such as the USA. The risk of Hepatitis C infection to the recipients of blood, and blood products is now small. Until a vaccine is available that is not only safe and effective, but also cheap enough for widespread application, precautions for preventing transmission are likely to be the only way of limiting Hepatitis C.

WHAT FUTURE HOPES EXIST?

New drug combinations, such as Ribavirin with Interferon-α, may have a synergistic effect in eliminating Hepatitis C infection. Multi-drug therapies are currently the most hopeful method of slowing the replication, or reducing the level of, HIV within the body. This may become a possibility for attempting to manage the Hepatitis C virus.

Several agents have been experimented with in addition with Interferon-α. Future ancillary treatments may include; ursodeoxycholic acid, N-acetyl cysteine, Interferon-α and thymosin, the use of non-steroidal anti-inflammatory drugs to prevent formation of immuno-suppressive agents and Iron reduction by phlebotomy may enhance the effect of Interferon-α. Though improvements in ALT levels can result with these combination treatments, any long term benefits of these protocols is, as yet, unknown.

Researchers have succeeded in growing liver cells in the laboratory. Growing liver tissue in vitro, (in a test tube with nutrients), enables researchers to subject the cells to a much wider range of tests. Methods are being developed to grow large quantities of normal liver cells for testing drugs used in treating liver disease. It also offers the chance that liver tissue could be 'manufactured' for use in transplant surgery.

A technique has been experimentally developed to deep freeze human organs, enabling them to be stored and used for transplantation many years after they have been removed from the donor. This raises the possibility of establishing organ banks of frozen donor organs for emergency operations. It may also offer the opportunity for potential recipients to be prepared for transplant by 'seeding' their bodies with cells from the new organ, thus reducing the risk of organ rejection.

Research teams are developing an 'artificial' liver which could save lives. The artificial liver could be used as an alternative to transplantation or as a way of keeping patients alive while waiting for donor organs. It would be used in the same way as a dialysis machine is employed in cleaning the blood of patients with kidney disease. Currently, it is expected to be a short term external support, but eventually it may be adapted for internal use as a more permanent solution for liver failure.

Information and opinion in this issue has been gathered from a variety of sources. We have done our best to confirm the statistics and data contained within. Please remember that Hepatitis C is a rapidly developing area of knowledge and that any information may be subject to amendment.

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DAVE'S STORY...

I'm 27 years old – I live just outside Manchester, England and have done so for most of my life. On my first birthday, I was diagnosed as having Christmas Disease – a rare form of haemophilia; as you can imagine that wasn't much of a birthday present for my Mum and Dad.

In the mid-eighties, there was a sudden panic. All these gay guys had started dying in the States of some strange disease, and the theory was that it could be transmitted through blood? As more information came out, haemophiliacs started to get really nervous – and then really ill. I was scared for quite a while – but then I found that because I had a rare form of haemophilia, the UK was self-sufficient in my treatment. I was very, very lucky, but an awful lot of friends with haemophilia were very unlucky. I felt like I'd had a death sentence reprieved –

I made sure that that I treated myself when I needed it, and apart from some early damage to my ankles, I didn't really have any problems. Well....actually..... there was this one little thing called "non-A, non-b hepatitis", but the doctors had known about that for years and I was fine. Wasn't I? I thought so, until 18 months or so ago the Clinic started to get a bit more inquisitive about how much I drank, what size my liver was, what my liver function tests looked like. "That's nice", I thought, "they're really looking after me". All of a sudden, it stopped being nice, trusty, non-a, non-b and became nasty, liver crunching C.

"....medical profession is only just realising the long term problems associated with hep C..... appears to develop over a 25 to 30 year period.....probably had it since your first injection..... your liver functions are pretty abnormal.....the response rate to treatment is only about 20% at best.....a good chance that you'll develop cirrhosis leading to liver cancer.....". Not generally the kind of thing you want to hear just before Christmas, really. And worst of all – no big drinking parties over Christmas and New Year

Actually, the worst thing isn't not being able to go for a drink – it's telling parents, friends, family and a girlfriend that I worship. How do you make friends understand that you're not being a party pooper, you just don't really need a drink to kill your liver off? How do you talk about death with the woman that you want to make a life with? How do you deal with it on daily basis? I just have to accept what's happened and move on – but they have to stand by and watch. I wouldn't swap places with them for a golden pig!

As usual, the comparisons with HIV are ever present – and just as most people have come to see that AIDS respects no boundaries of class, race, sexuality, background, so, too, Hepatitis does not discriminate. Viruses are equal opportunity microbes for our politically correct times. Protect yourself and those around you. Look after yourself. Make a noise. Fight.

SARA'S STORY...

As close as I can tell, I injected this virus into my veins in about 1972 or 1973. For a period of about 1½ years I partied hard and indulged in various forms of high-risk behaviours with no thought of how it would be when I got older. I was in my mid-20s and I thought I was immortal, invincible.

In 1973 I got very sick and got a diagnosis of hepatitis, non-A non-B. I dropped about 15 pounds, which I couldn't afford to do. I was exhausted most of the time. This went on for about a month. I didn't eat much, but I was smoking cigarettes and drinking cheap wine. Great way to live. Eventually I got over this phase and I thought I was cured. Little did I know! I spent the next few years living clean, occasionally smoking pot but no more hitting up, no more drinking. It was not a conscious effort, but it happened. I gave up all drugs except caffeine, which I still indulge in (shame on me!). I was still smoking cigarettes though, and having the occasional glass of wine, maybe one a month or so.

Through the 1980's I continued my pattern of clean living. I felt really healthy and energised almost all the time. Except for two bouts with kidney stones, once in 1985 and once in 1988, I was fine! I could eat anything. I still was taking the occasional glass of wine – maybe two or three a year.

In 1991 I started getting what I thought was severe heartburn. I couldn't figure it out. The pain was concentrated on my right side, under my rib cage, and it would shoot up my side all the way into my throat. I thought I was on fire inside. My throat was always a little bit sore. I gave up cigarettes and that helped some, but the pain did not go away. It would lie dormant for a period of time and then it would return full-force. I also suffered from itching that I couldn't put a cause to. The tops of my feet, and my ankles, itched so much at times that I couldn't wait to get home and tear off my socks. And my head would itch. And I got itchy skin on my sides and stomach. I got real familiar with the pink stuff – Gaviscon, but it seemed to help, kind of.

I changed doctor and had a complete medical. I told my new doctor about the pain in my gut and we thought it might be my gall bladder. I did mention to him that I had had Hepatitis way back when, and so unbeknownst to me he ordered Hepatitis testing of my blood. My best friend received a diagnosis of HCV+ a few years ago, neither of us knew what it was, all we knew was that it was a malfunction of the liver. So when I got my diagnosis, we both had a laugh over it. Then we got serious. As of today, I have had no treatment other than having my enzyme levels checked. By the end of next week I will know what my test results are, get a referral to a gastroenterologist, and begin seriously treating this nasty-ass little opportunistic virus.

For me the worst things about this disease are the sudden bursts of anger that make me want to be violent; the fire in my gut; and the knowledge that I am a poisonous being. I cannot donate blood or organs. My blood is poison. My tears are poison. My sweat could be poison. My saliva could be poison. My heart is poison. And that hurts!

JOHN'S STORY...

I was driving home in June of 1977 after working late when my car was struck head on by a drunken driver. We were both lucky to be alive and were rushed to the nearest hospital, we both needed surgery and I received a blood transfusion. My broken bones healed and my head injury was nothing permanent. Life soon returned to normal and I was glad to be alive.

Besides an occasional bout of bronchitis, I really didn't need to see our local doctor over the years. But in 1991, intestinal problems that wouldn't let up forced me to seek help. I told the doctor that I had felt a strange weariness coming on for the last year along with the stomach and bowel problems, that I lacked energy and felt like I had some flu bug that wouldn't go away because I felt achy all over. I was sent home with some medicines.

But nothing worked, and the cramping and diarrhoea forced me to stay at home for days at a time, and I couldn't stop losing weight. There had to be something that could be done. Back to the doctor, a few different medicines and advice to change my diet and to exercise. I had no appetite and everything that I ate came out as fluid. I was too wasted at this point to exercise or work.

So on to the hospital, I was there all day, blood was taken and two doctors asked me a string of questions. However, while the doctors fussed around with their tests and medicines, I got worse. From that first trip to the hospital, my liver enzymes were high, but that was never mentioned to us at the time. An ultrasound test was done and we were told that I had gallbladder problems. A month later, my gallbladder was removed. Recovery from that surgery was tough because I still didn't feel right. Besides the aching and fatigue, I had been feeling sick, weak and had trouble sleeping with itching and night sweats.

Two months later, I was tested for hepatitis and that's when we discovered that I had hepatitis C. The gastroenterologist told us, "Well, you've got hepatitis C, but it's nothing out of the ordinary. It's a mild hepatitis that shouldn't bother you much over the years." And the way he said it, sounded like what I had already gone through wasn't bad or connected to the Hep C.

Any improvement was slow to come over the weeks and then the months that followed. Eight months later, I was told that a liver biopsy might be a good idea so that was done. Then we were told that I had chronic active Hepatitis. My wife did some research on Hep C and had a lot of questions to ask the doctor, but he waved his hand and told her, "Your husband doesn't need answers to those questions, he needs to get better on his own." We still don't know what he meant.

Outside of the medical picture, we've lost a few friends and our life has changed. Finances are bad and now I've been diagnosed with diabetes. We still feel anger towards a few doctors, but we also feel sorry for them for not knowing what they needed to know in the first place. Read as much as you can about the disease yourself. It is something you can take control of in your life. It makes a difference.

Other approaches

There are a variety of unproven therapies that may be of some use in treating the effects of Hepatitis C.

ACUPUNCTURE

Acupuncture is a form of complementary therapy that involves inserting thin, solid needles into selective sites on the surface of the body. It offers a range of techniques for dealing with liver stress or disfunction.

ASTRAGALUS

A herb used in China for boosting the immune system and preventing chemotherapy-related bone marrow suppression and nausea. There are some reports that astragalus helps protect the liver against toxicities.

DIETARY MODIFICATION

Foods to avoid include: Animal fats, Refined Carbohydrates (white flour, white sugar), processed foods containing additives, vinegar, pickles and highly spiced foods, chocolate and dairy products.

Foods to take in moderation include: Vegetable oils or fats (sunflower, soya, peanut or olive oil), Protein - preferably vegetarian protein, nuts, pulses etc. Dairy products should be avoided on a strict diet, but milk in tea, a small portion of cheese, 2 to 3 eggs and a yogurt per week may be taken.

Foods to take in abundance include: All fresh salads, All fresh vegetables, All fresh fruit, raw or cooked and sweetened with honey if necessary.

Foods which may be beneficial include: Artichoke, Beetroot, Carrot, Cucumber, Grapefruit, Grapes, Honey, Horseradish, Lemon and Radish. Juices may include Apple, Carrot, Grapefruit and Lemon.

Dieticians may recommend a low protein (meat, fish, eggs, etc.) and a low sodium (salt) diet in severe cases of liver disease.

ESSIAC TEA

Essiac Tea is traditionally very healing for the liver it is an immune system stimulator and a blood cleanser. Essiac is a powerful and effective natural herbal medicine. It is made of up four herbs; Burdock Root, Sheep Sorrel, Slippery Elm and Turkey Rhubarb.

GARLIC

Garlic is a natural antibiotic. Detoxifying and protecting the body from infection and lowering blood pressure. Garlic contains a natural antibiotic, and antifungicidal, and has many antiviral properties.

HOMEOPATHY

Homeopathy offers several remedies for the treatment of Hepatitis C. These may include Mercury and Natrum Sulfuricum. Natrum Sulfuricum has clinically been found a valuable remedy for spinal meningitis, and has also been found to be useful as a liver tonic.

KOMBUCHA TEA

The Kombucha organism is a symbiotic colony of yeasts and bacteria that form a strong membrane that covers the liquid/air interface of the vessel it grows in. To grow it, you take a batch of weak to moderately-strong black tea, sweetened with white sugar, that has been cooled to room temperature, and float the membrane in it. Within a week to 10 days, the Kombucha organism converts the tea into a fluid that is drunk several times daily by the patient.

SCHIZANDRA – (SCHISANDRA CHINESIS)

Said to promote healing of the liver, in Hepatitis C and other inflammatory conditions. Schizandra is also considered an adaptogen, and similar to ginseng, it is believed to increase stamina and fight against fatigue.

VITAMINS AND MINERALS

In general, the recommended daily allowance of vitamins and minerals is sufficient for healthy adults. But, it is thought that people who are stressed or suffering from illness processes may not absorb sufficient amounts of vitamins and minerals from food alone. They may also be producing large amounts of toxins (free radicals), as a result of cell death, which certain vitamins and minerals may help to eliminate.

Care needs to be exercised in taking vitamins and minerals either in supplemental or therapeutic dosages. Some vitamins in high doses may possibly be harmful to a damaged liver (eg Vitamin A), others are particularly relevant in liver failure (Vitamin K).

Vitamins and minerals which may be beneficial: Vitamin A (in normal doses), B Complex, Vitamins C, E and K, Choline, Iron, Methionine and Zinc. Be sure to seek further professional advice!

Liver Tonics

There has been a long history of herbal hepatic and biliary treatments throughout western medical history.

Most have been tonic, bitter herb medications which help promote the flow of bile and relieve jaundiced conditions. Some of these treatments were Chicory, Dandelion, Wahoo, Centaury, Mandrake and Celandine. Modern pharmaceutical medicine does not provide liver tonics or supportives, and people have turned to alternative sources to handle their liver stress. Thioctic acid, Milk Thistle (Silybum Marianum), and Glycyrrhizin, are newer sources of treatment which have an efficacy in handling liver abnormalities, these treatments are supportive in nature, and affect the metabolism of the liver.

GLYCYRRHIZIN – LICORICE ROOT

Glycyrrhizin is a sulphated polysaccharide made from licorice roots, it has been isolated and prepared by Japanese pharmaceuticals for 40 years as a treatment for chronic liver disease, and stomach ulcer treatment. It is available both as tablets and intravenous forms. More recently, Japanese researchers have been focusing attention on glycyrrhizin in HIV therapy. Glycyrrhizin is a multifactorial medication, i.e. it acts upon several different systems in improving health. It is a lectin, and has many binding properties which uniquely protect and support liver cells, negating the destructive affects of toxins. These binding properties have recently been shown to clear fat-coated micro-organisms, where they are scavenged by macrophages and killed. It inhibits inflammatory processes of all sorts, including Hepatitis C and allergies, all of which produce destructive oxidants in the blood. Thus, glycyrrhizin prevents formation of oxidants and free radicals. Glycyrrhizin acts as an antiviral, an anti-inflammatory and prophylactic medication. The reduction of free radical oxidants in the blood stream relieves the depletion of hepatic gluthione, especially in the liver. Glycyrrhizin acts as a major antioxidant and aids in relieving liver stress.

MILK THISTLE – SILYBUM MARIANUM

Milk Thistle (Silybum Marianum) is a plant used for centuries as a medicinal agent, known for its abilities to cure jaundice, cleanse the blood and 'open up' the liver and gall bladder to proper functioning. Milk Thistle is a common plant, found in temperate climates, originating in western and central Europe. It is available in tincture form, or in tablets where the active agent, silymarin, has been concentrated. It has numerous modes of action on the liver, causing cell regeneration, increasing glutathione (a vital cellular antioxidant), increasing tolerance for processing toxins like alcohol, and normalising ALT and AST levels. Side effects have yet to be discovered, but since this medicine has been used for hundreds of years without reported untoward effects, therapeutic doses are believed to be quite safe.

THIOCTIC ACID – LIPOIC ACID

Thioctic acid, also know as lipoic acid or alpha-lipoic acid, is a liver protectant nutrient comprised of lipoic acid and fat soluble thiamin. An essential micro nutrient in liver cell metabolic pathways, lipoic acid is rapidly depleted during stress. Patients diagnosed with liver cirrhosis, diabetes militus, atherosclerosis and polynueritis have been found to contain a reduced level of endogenous lipoic acid. Lipoic acid works in catabolic and anabolic pathways with other co-enzymes. As the liver processes a high toxic load, indicated by elevated liver enzymes in the blood, thioctic acid appears to render these toxins harmless and opens pathways to accommodate the toxins. Thus, liver enzyme levels ALT and AST are lowered which reduces stress on the liver that jeopardises its function. The fat-soluble vitamin thiamin tetrahydroturturyl disulphide must be present in complementary amounts to work with and enable lipoic acid.

Thioctic acid has been used in treatment of alcoholics as a liver protectant. Physicians are using it as a therapeutic agent for virally or drug induced liver damage. Additionally, laboratory studies on HIV infected T-cells treated with thioctic acid showed inhibition of HIV by reducing the replication rates of active virus.

The recommended daily dosage to achieve a reduction in liver enzymes is 200-250 mgs. It could be damaging to exceed this dosage as toxicity has been documented in animals (although they were fed thioctic acid ⅓ of their body weight!) Thioctic acid needs to be formulated with fat-soluble thiamin to be effective so check this out.

There are other liver therapies, but these three have significant research and history, as well as anecdotal successes reported. Additionally, they contribute to immune modulation and are antiretroviral, particularly glycyrrhizin.

Glycyrrhizin, Milk Thistle and Thioctic acid are natural compounds and are available from various health food outlets, although they can be expensive.
Seek out further advice.

Liver Cirrhosis

Liver cirrhosis is characterised anatomically by widespread nodules in the liver combined with fibrosis.

The fibrosis and nodule formation causes distortion of the normal liver architecture which interferes with blood flow through the liver. Cirrhosis can also lead to an inability of the liver to perform its biochemical functions. To understand the pathophysiology of cirrhosis, the normal anatomy and physiology of the liver must first be briefly reviewed.

LIVER BLOOD FLOW

Oxygenated blood that has returned from the lungs to the left ventricle of the heart is pumped to all of the tissues of the body. This is called the systemic circulation. After reaching the tissues, blood is returned to the right side of the heart, from where it is pumped to the lungs and then returned to the left side of the heart after taking up oxygen and giving off carbon dioxide. This is called the pulmonary circulation. Blood from the gut and spleen flow to and through the liver before returning to the right side of the heart. This is called the portal circulation and the large vein through which blood is brought to the liver is called the portal vein. After passing through the liver, blood flows into the hepatic vein, which leads into the inferior vena cava to the right side of the heart. The liver also receives some blood directly from the heart via the hepatic artery. In the esophagus, stomach, small intestine and rectum, the portal circulation and veins of the systemic circulation are connected. Under normal conditions, there is little to no back flow from the portal circulation into the systemic circulation.

BILIRUBIN SECRETION

The liver is the site of bile formation. Bile contains bile salts, fatty acids, cholesterol, bilirubin and other compounds. The components of bile are synthesised and modified in hepatocytes (the predominant cell type in the liver) and secreted into small bile ducts within the liver itself. These small bile ducts form a branching network of progressively larger ducts that ultimately become the common bile duct that takes bile to the small intestine. Bilirubin is a yellow pigment that derives primarily from old red blood cells. Bilirubin is taken up by hepatocytes from the blood, modified in the hepatocytes to a water soluble form and secreted into the bile.

BIOCHEMICAL FUNCTIONS

The liver performs many biochemical functions. Blood clotting factors are synthesised in the liver. Albumin, the major protein in the blood, is also synthesised in and secreted from the liver. The modification and/or synthesis of bile components also takes place in the liver. Many of the body's metabolic functions occur primarily in the liver including the metabolism of cholesterol and the conversion of proteins and fats into glucose. The liver is also where most drugs and toxins, including alcohol, are metabolised.

WHAT GOES WRONG?

Cirrhosis results from damage to liver cells from various toxins, inflammation, metabolic derangements and other causes. Damaged and dead liver cells are replaced by fibrous tissue which leads to fibrosis (scarring). Liver cells regenerate in an abnormal pattern primarily forming nodules that are surrounded by fibrous tissue. Grossly abnormal liver architecture eventually ensues that can lead to decreased blood flow to and through the liver.

Decreased blood flow to the liver and blood back up in the portal vein and portal circulation leads to some of the serious complications of cirrhosis. Blood can back up in the spleen causing it to enlarge and sequester blood cells. Most often, the platelet count falls because of splenic sequestration leading to abnormal bleeding. If the pressure in the portal circulation increases because of cirrhosis and blood back up (note: this can also sometimes occur in severe cases of acute Hepatitis and liver damage), blood can flow backwards from the portal circulation to the systemic circulation where they are connected. This can lead to varicose veins in the stomach and esophagus (gastric and oesophageal varices) and rectum (haemorrhoids). Gastric and oesophageal varices can rupture, bleed massively and even cause death. Hypertension in the portal circulation, along with other hormonal, metabolic and kidney abnormalities in cirrhosis, can also lead to fluid accumulation in the abdomen (ascites), around the ankles and the peripheral tissue (peripheral oedema).

Decreased bilirubin secretion from hepatocytes in cirrhosis leads to the back up of bilirubin in the blood. This leads to jaundice, the yellow discolouration of the skin and eyes. As the water-soluble form of bilirubin also backs up in the blood, bilirubin can also spill into the urine giving it a bright yellow to dark brown colour.

Abnormal biochemical function of the liver in cirrhosis can lead to several complications. The serum albumin concentration falls which can lead to aggravation of ascites and oedema. The metabolism of drugs can change requiring

dose adjustments. In men, breast enlargement (gynecomastia) sometimes occurs because metabolism of oestrogen in the liver is decreased. Decreased production of blood clotting factors (Factors II, VII, IX and X), can lead to bleeding complications. Derangements in the metabolism of triglycerides, cholesterol and sugar can occur. In earlier stages, cirrhosis frequently can cause insulin resistance and diabetes mellitus. In later stages or in severe liver failure, blood glucose may be low because it cannot be synthesised from fats or proteins.

Cirrhosis, especially in advanced cases, can cause profound abnormalities in the brain. In cirrhosis, some blood leaving the gut bypasses the liver as blood flow through the liver is decreased. Metabolism of components absorbed in the gut can also be decreased as liver cell function deteriorates. Both of these derangements can lead to hepatic encephalopathy as toxic metabolites, normally removed from the blood by the liver, can reach the brain. In its early stages, subtle mental changes such as poor concentration, a change in sleeping patterns, or an inability to construct simple objects can occur. In severe cases, hepatic encephalopathy can lead to stupor, coma, brain swelling and death.

Cirrhosis of the liver can also cause abnormalities in other organ systems. Cirrhosis can lead to immune system dysfunction causing an increased risk of infection. Ascites fluid in the abdomen often becomes infected with bacteria normally present in the gut (spontaneous bacterial peritonitis). Cirrhosis can also lead to kidney dysfunction and failure. In end-stage cirrhosis, a type of kidney dysfunction called hepatorenal syndrome can occur. Hepatorenal syndrome is almost always fatal unless liver transplantation is performed.

SYMPTOMS AND DIAGNOSIS OF CIRRHOSIS

Cirrhosis is usually diagnosed by liver biopsy when any or all of the above abnormalities and complications may be present. This is especially true when the underlying liver disease can be identified. The underlying liver disease is identified in most patients, however, sometimes it will not be discovered. Such cases are called "cryptogenic" cirrhosis. Sometimes, other conditions such as metastatic cancer, hepatic or portal vein thrombosis, severe acute Hepatitis or acute bile duct obstruction can cause some of the abnormalities seen in cirrhosis. A careful history combined with special diagnostic tests will usually identify these conditions.

Some patients with cirrhosis, especially early in the course of the disease, will have no overt clinical signs or symptoms. Some may have only subtle physical changes such as red palms, red spots that blanch on their upper body (spider angiomata), hypertrophy of the parotid glands, gynecomastia or fibrosis of tendons in the palms. Some patients may only have subtle abnormalities on blood tests, and in some cases, all blood tests may be normal. Radiological and nuclear medicine tests may give clues as to the presence of cirrhosis, but the diagnosis of cirrhosis must often be made by liver biopsy.

CAUSES OF CIRRHOSIS

Individuals suffering from liver cirrhosis can survive for many years. Almost any chronic liver disease can lead to cirrhosis. Cirrhosis of the liver can result from many causes. This list gives some of the many causes; Alcoholic liver disease (the most common cause), Chronic viral Hepatitis B, C and D; Chronic autoimmune hepatitis, Inherited metabolic diseases, Chronic bile duct diseases, Chronic congestive heart failure, Parasitic infections, Drug Hepatitis and Toxins.

THE TREATMENT OF LIVER CIRRHOSIS

Cirrhosis of the liver is irreversible but treatment of the underlying liver disease may slow or stop the progression. Such treatment depends upon the underlying etiology. Termination of alcohol intake will stop the progression in alcoholic cirrhosis and for this reason, it is important to make the diagnosis early in a chronic alcohol abuser. Similarly, discontinuation of a hepatotoxic drug or removal of an environmental toxin will stop progression. Treatment of metabolic diseases, such as treatment of iron overload in haemochromatosis or copper overload in Wilson disease, are also effective therapies. Chronic viral Hepatitis B and C may respond to treatment with interferon and autoimmune Hepatitis may improve with prednisone and azathioprine. Drugs such as ursodiol may slow the progression of primary biliary cirrhosis and possibly sclerosing cholangitis.

In patients with cirrhosis of the liver, treatment must also be directed at the complications. Bleeding oesophageal varices can be treated with endoscopic sclerotherapy or rubber band ligation. Ascites and edema are often responsive to a low sodium diet and such a diet must be emphasised in patients with these symptoms. More advanced ascites and oedema can respond to diuretic therapy. A low protein diet and agents such as lactulose may help hepatic encephalopathy. Infections such as spontaneous bacterial peritonitis must be rapidly treated with appropriate antibiotics. Drugs metabolised in the liver must be given with caution. Coagulation disorders will sometimes respond to vitamin K.

Liver transplantation is highly effective for the treatment of end-stage cirrhosis. Transplantation is usually needed when complications such as encephalopathy, ascites or bleeding varices are uncontrollable or when biochemical function is severely depressed. In patients with primary biliary cirrhosis, a rising bilirubin indicates a poor prognosis and such patients should be considered for transplantation as the serum bilirubin concentration begins to rise. Active drug or alcohol abuse are contraindications to liver transplantation. However, alcoholics who have abstained from drinking for an extended period of time (usually more than six months), and have participated in rehabilitation programs and support groups such as Alcoholics Anonymous, can be considered as candidates and will often have a good prognosis. Liver cancer is usually a contraindication to transplantation, except in experimental protocols. Liver transplantation is usually not performed in patients more than 70 years old.

Liver Cancer

Liver cancer remains one of the most challenging tumours faced by the oncologist.

Ninety-four percent of people who are diagnosed with primary liver cancer die as a result of it. The majority of patients with hepatocellular cancer, the most common type of liver tumour, live less than a year after their diagnosis. There are two problems behind these discouraging statistics: first, because the liver is such a large organ, tumours can grow quite large before they start causing symptoms and are diagnosed. By then, it is often too late for curative treatment. Second, many traditional cancer treatments are toxic to the normal liver tissue or to other tissues when they are given in doses sufficient to kill the tumour. Doctors have developed some alternative approaches to treating liver cancer that they hope will prolong patient survival.

When a liver tumour is diagnosed, the first treatment considered is complete surgical removal of the tumour. However, only 20% to 30% of tumours are completely resectable. The tumours may be too large to remove or in an awkward location, perhaps surrounding an essential blood vessel. Cirrhosis, too, can make resection impossible. Unfortunately, traditional non-surgical therapy options, such as radiation therapy and chemotherapy, have had disappointing results in liver tumours. Standard radiation treatments are toxic to the liver long before they have an effect on the tumour; there is a high risk of liver failure. Similarly, systemic chemotherapy produces toxic effects in other organs before it affects the tumour. No matter what kinds of drugs are used, the results are pretty dismal, usually 10% or less of the patients respond to systemic chemotherapy. Regional chemotherapy for treating liver metastases from stomach or pancreatic cancers, whole-body treatment is necessary because the cancers often will have metastasised elsewhere. For primary liver tumours, systemic toxicity has limited the tolerable dose of standard chemotherapy drugs to ineffective amounts. Investigators are therefore trying to deliver high-dose chemotherapy directly to the liver.

It has been found that infusing drugs directly into the liver through the hepatic artery would dramatically shrink tumours in a carefully selected subset of patients with advanced hepatocellular cancer. Hepatic arterial infusion of FLAP – a combination of floxuridine (FUDR), leucovorin, doxorubicin (Adriamycin), and cisplatin (Platinol) can decrease tumour size by more than 50%. In several patients, tumours that were originally unresectable became resectable after treatment with FLAP. In modified doses, however, this regimen may prolong life for those who have an adequate amount of healthy liver before treatment.

Another system combines this hepatic arterial infusion technique with hepatic venous isolation and extracorporeal chemofiltration. A chemotherapy drug is infused into the liver through the hepatic artery; the blood coming out of the liver is then captured and filtered to remove the drug. Thus the liver and tumour get a high dose of the drug, but the rest of the body does not. The infusion and the filtering are done through catheters in the neck and groin. Also being studied is the drug-delivery medium called matrix collagen gel. This compound, when mixed with a chemotherapy drug like cisplatin, encapsulates the drug; the drug then does not disperse into other tissues when it is injected into the tumour.

Researchers are also trying other drugs that attack the tumours in different ways. Experimental compounds are being studied, rather than being directly toxic to the hepatocellular cancer cells themselves, may cause the normal liver cells (hepatocytes) to excrete substances that slow or retard the growth of the cancer cells. These compounds have had promising results in trials, producing anticancer responses.

A number of patients with liver tumours – including metastases from colorectal cancers, hepatomas, and sarcomas – have been helped by using cryosurgery. This technique involves inserting into the tumour a thin probe that fills with liquid nitrogen, freezing the surrounding tissue. The freezing destroys the tumour tissue, which is then slowly absorbed by the body over time. The probe insertion and freezing process are monitored precisely by ultrasound.

In the laboratory another technique called bipolar radio frequency ablation (BRFA) is being studied. The opposite of cryosurgery, instead of freezing the tumour, it is heated. Two needles are placed in the liver, one on each side of the tumour, and a radio frequency current is run through the tumour, coagulating it. As for cryosurgery, the dead tumour tissue is slowly absorbed by the body over time. The potential advantage is that the needles used are much smaller than cryosurgery probes and therefore less traumatic to the liver.

The chances for the patient would be better if the tumours were detected earlier, when there are more options for therapy. People appropriate for such screening include those with cirrhosis or chronic Hepatitis B or C infection. Because liver cancer is usually advanced by the time it is diagnosed, any treatments that offer prolonged survival can benefit the patient.

BIRCHGROVE IS A FORUM FOR:

- The treatments of haemophilia and HIV
- Taking best care of ourselves, through informed debate
- Staying healthy with both haemophilia and HIV/AIDS
- Ways in which HIV affects love and sexuality
- The social and psychological aspects of haemophilia and HIV

PEOPLE WITH HAEMOPHILIA AND HIV

- Can be empowered and enabled to deal with HIV/AIDS through relevant information and mutual support
- Can improve their health and extend their lives by expressing feelings and confronting the issues directly
- Have needs that are best understood by drawing on the experiences of those in the same situation
- Should be heard and have their needs recognised and not suffer in fear and isolation
- Have a role in the work of the HIV/AIDS community to inform and challenge the ignorance that exists about HIV

Individual leaflets are free of charge to those directly affected by Haemophilia and HIV. For non-members, we ask a contribution of 50p per leaflet/newsletter to cover the cost of postage.

Newsletter Back Issues

- ☐ *Issue 3 – General Issue*
- ☐ *Issue 4 – General Issue*
- ☐ *Issue 5 – General Issue*
- ☐ *Issue 6 – The AIDS Hypothesis...*
- ☐ *Issue 7 – The Sex Issue...*
- ☐ *Issue 8 – The Drugs Issue...*
- ☐ *Issue 9 – Death and Dying...*

Information Leaflets

- ☐ HIV and Itchy skin
- ☐ An ABC of Hepatitis
- ☐ Liver Disease and HIV
- ☐ HIV and Vitamins & Minerals

FOR FURTHER INFORMATION:

The Haemophilia Society,
123 Westminster Bridge Road,
London SE1 7HR
Telephone: 0171 928 2020

The Birchgrove Group (HIV)
P.O. Box 9, Abertillery, NP3 1YD
Telephone: (Lo-call) 0345 697231

The Manor House Group, (HCV)
P.O. Box 128, Nantwich,
Cheshire, CW5 8PQ

National Hepatitis C Support Group,
Mainliners, 205 Stockwell Road,
London, SW9
Telephone: 0171 738 4656

The British Liver Trust,
Central House, Central Avenue,
Ransomes Europark, Ipswich IP3 9QG
Telephone: 01473 276326

FIVE QUESTIONS TO ASK YOUR CENTRE DIRECTOR

- For how many years have I had Hepatitis C?
- How many times have I been re-infected with Hepatitis C?
- Can Hepatitis C make my bleeding worse?
- Was I infected with different Hepatitis C genotypes?
- Does my clotting factor make my liver work harder?

FIVE QUESTIONS TO ASK YOUR INTERFERON SALESMAN

- Can Interferon-α damage my immune system?
- If my liver is so bad, how can Interferon-α do any good?
- Can my liver get worse, when I stop taking Interferon-α?
- Can my hair fall out with Interferon-α?
- Why do less than 4% of haemophiliacs get any permanent improvement?

FIVE QUESTIONS TO ASK YOUR LIVER

- Fancy a good drinking binge?
- Why are you worse in the winter?
- Why can't I eat late at night?
- Are you sure you wouldn't like a hot curry or a good fryup?
- Red palms, hardened tendons, swollen glands, itchy skin, mood changes, irritability, depression, muscle pains, skin eruptions, liver cancer, abdominal pains, jaundice, fluid retention, enlarged and bleeding veins, brain damage, you are joking aren't you?

FIVE POSITIVE STEPS TO ASSIST YOUR HEALTH

- Rest when you feel unwell
- Learn some stress management/relaxation techniques, seek counselling if you have ongoing problems.
- Maintain a nutritious diet which is well balanced and low in fat. Avoid alcohol or drink only small amounts of it.
- Anti-oxidant vitamins and some herbs may have a beneficial effect if used sensibly.
- Talk to other people who are Hepatitis C positive.

The Birchgrove Group, P.O. Box 9, Abertillery, NP3 1YD. Telephone: (Lo-call) 0345 697231.
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