

aids treatment update

special issue: hepatitis & HIV coinfection

In March of this year, the Department of Health circulated a hepatitis C briefing pack to health professionals in acknowledgment that this viral infection “is emerging as a significant public health problem”. This effort precedes the development of a national strategy on hepatitis C for the UK, where it’s understood that 0.4% of the population are chronically infected with the virus.

A study in the *Archives of Internal Medicine* last year reported that at least 2.7 million Americans are infected, and there are currently eight thousand deaths each years from resultant liver disease. This latter study offered an analysis of costs relating to the US hepatitis C epidemic, finding the bill for medical expenses relating to chronic liver disease and primary liver cancer alone to have been close to one and a half billion dollars in 1997 – about one billion pounds sterling.

Shared transmission routes mean that many people affected by HIV are also affected by viral hepatitis. In the HIV field, the profile of this ‘coinfection’ has increased in recent years. This has had a lot to do with the increased frequency of liver-related illness and medication side-effects. But, as we describe in this month’s issue, interest is also being stimulated by the availability of increasingly effective treatments for both hepatitis C and hepatitis B.

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2 first large study of new hepatitis C treatment in people with both HIV and hep C reports preliminary findings: how will this alter treatment options? by brian west

Hepatitis C (HCV) is a viral infection that is transmitted predominantly through exposure to blood or blood stained body fluids from an infected person. Many people in the UK have acquired it through sharing needles. Some have contracted the virus through contaminated blood products prior to the early 1990's, when screening was introduced. It is also transmitted sexually, although this is not as well documented and may relate to blood exposure during sex. It was first identified in 1989, and is one of a group of different hepatitis viruses which carry an initial after their name to identify them. Like HIV, there are different 'strains' (genotypes) of HCV, and, it is about ten times more infectious than HIV.

In many ways HCV differs from the other hepatitis viruses, and unlike hepatitis B and hepatitis A, there is no vaccine available to protect against infection. Unlike hepatitis B, where most people who are infected eventually produce an effective immune response to the virus and subsequently have resistance to it, only 15-20% manage to eradicate HCV, and it is possible to get re-infected. The majority of those who do not 'clear' HCV show few symptoms in the early years but gradually develop varying degrees of liver damage. This period of 'chronic' hepatitis can lead to scarring of the liver (termed cirrhosis or fibrosis), liver failure, and liver cancer. A group set up to develop HCV strategy for Greater Glasgow Health Board (which reported in November 2000) gave estimates of what this would mean in terms of illness progression. They forecast that 20-30% of people chronically infected would progress to cirrhosis during the first twenty years of infection. Of

those with cirrhosis, about 25% would develop liver failure, with a further 1-2% developing primary liver cancers every year¹. HCV is a major reason for people needing liver transplants in the UK.

Coinfection with HCV and HIV is increasingly recognised as a problem, both in relation to the treatment of either (or both) infections, and because disease may progress more quickly than in people who are monoinfected (infected with one of the two viruses rather than both).

The numbers involved

Estimates of the number of people infected with HCV in the UK range from 0.5-1% of the population, although there are regional differences in the spread of the infection. In Scotland, unlike HIV where most cases of infection (44%) have been in the Lothians, Greater Glasgow has the largest numbers of reported HCV infections (37%)².

Treatment options

Given that HCV is a more recently 'discovered' virus, it is hardly surprising that treatment options lag behind those for HIV. Several other issues have made treatment access more difficult. Firstly, unlike HIV where there have traditionally been protected funds for available therapies, treatment costs relating to HCV have had to be found from within existing budgets. Secondly, most clinical trials for HCV treatments have excluded those with HIV. It has not therefore been clear what benefits and risks these treatments have for people who also have HIV. Thirdly, the genotype of HCV that a person is infected with affects how successful current treatment may be.

There are at least six genotypes of the HCV virus. Genotypes 1, 2 and 3 are most common in Western Europe and the USA. In the UK it is thought that about 66% of people infected have genotype 1, most of the rest being 2 or 3³. Unfortunately, genotype 1 is the least responsive to current therapy.

However, unlike HIV where early hopes of viral eradication with HAART have rapidly faded, total clearance of HCV from the human body is known not only to be possible, but is the ultimate aim of treatment. This is measured using an HCV viral load test. To create a standard by which treatments can be compared, a definition of treatment success has been proposed. A 'sustained virologic response' (SVR) is said to have been achieved if there is no detectable HCV viral load six months after a person has completed HCV treatment.

Previous successful trials prompted the UK's National Institute for Clinical Excellence (NICE) to issue guidelines for treatment in HCV mono-infection. One difference between HIV and HCV is that there are no simple blood tests that give guidance on liver disease progression. The main standard used is to study the liver itself (liver histology). The two main elements of this are the degree of fibrosis, and of inflammatory activity.

The two drugs used in combination to treat HCV are interferon and ribavirin. Interferon directly blocks viral entry into cells. Although initially approved as monotherapy, SVR rates indicated that another drug was needed to boost the long-term benefits of the drug. The drug that fits this bill is ribavirin. Ribavirin, a pill taken twice daily, on its own has no effect on HCV viral load, but working with interferon prevents rebound of the virus. The early formulation of interferon required subcutaneous (under the skin) injections to be self-administered three times a week. This has been improved upon by a clever modification called 'pegylation'. Pegylation adds an extra molecule (polyethylene glycol) onto interferon. This slows down the rate that it is absorbed in the body. This has two benefits. Firstly, dosage is reduced to once weekly injections, secondly the 'peaks and troughs' associated with three

times a week dosing are not as marked. This may also help reduce side-effects.

Results published last Autumn in the *Lancet*⁴, showed that this new formulation was superior, especially in people who have HCV genotype 1. In this large study involving 1,530 people solely infected with HCV, two different doses of pegylated interferon were tested in combination with ribavirin. (The amount of interferon used is adjusted according to weight). The marginal differences noted in clearance of the virus in genotypes 2 and 3 were far outweighed by the improvements seen with genotype 1. The SVR in those treated with the higher dose of pegylated interferon increased to 43%, compared to 33% in the group treated with the non-pegylated form. It is suggested that people with HCV mono-infection would be on this regimen for either six or twelve months, depending on genotype and response to therapy. The regimen would involve weekly injections, and twice daily capsules. Major side-effects include flu-like symptoms, and anaemia is not uncommon. Fears for the potential effects of these drugs on the foetus rule out use during pregnancy, and for some time before because the therapy's effects persist for some time after discontinuation. Nevertheless, like HIV therapy, it may seem like the lesser of two evils compared to no treatment at all.

But what do these results mean for people who are coinfected with HIV, and what problems does coinfection bring?

Coinfection problems

At the 9th Annual Retroviruses Conference in Seattle in February, more information accumulated on whether HIV infection encourages progression towards liver disease in people with HCV/HIV coinfection. In a key session, Stuart Ray from the Johns Hopkins University School of Medicine in Baltimore, talked about the poorly understood determinants of disease progression in HCV infection. Having studied some of the usual parameters like ALT, (a liver function test which shows if there are raised levels of alanine aminotransferase; a very common sign in people progressing towards liver problems), genotype, and HCV viral load, he concluded

glossary

- acute** A recently developed condition.
 - antibody** Protein substance produced by the immune system in response to a foreign organism.
 - ALT** Alanine aminotransferase, a liver enzyme. Raised ALT indicates impaired liver function.
 - antigen** Something the immune system can recognise as 'foreign' and attack.
 - antiretroviral A** substance which acts against retroviruses such as HIV.
 - biopsy** A small sample of tissue that can be examined for signs of disease.
 - CD4** A molecule on the surface of some cells onto which HIV can bind. The CD4 cell count roughly reflects the state of the immune system.
 - chronic** A long-term condition.
 - cirrhosis** Scarring of the liver.
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access to pegylated interferon

*Viraferon Peg*TM is the brand name of the version of pegylated interferon which is manufactured by Schering-Plough. *Viraferon Peg*TM is licensed within both the European Union and the USA. *Pegasys*TM is the brand name of the version of pegylated interferon which is manufactured by Roche. It recently received a positive indication regarding its imminent approval in the European Union.



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that none of these were of themselves key markers of disease progression. He did however cite one study⁵, which showed that HIV coinfection accelerated the progression of HCV fibrosis, decreasing the time it takes to move to the highest grade of fibrosis by approximately ten years. Another study linked progression to fibrosis with a CD4 count of less than 400, concluding that HAART should be considered earlier in HCV coinfecting people, before the CD4 count dropped below 400⁶.

Whilst many studies have agreed that HIV does increase both the likelihood of progression to fibrosis and the speed with which liver problems develop, the second hypothesis, concerning whether HCV worsens HIV prognosis, has been more controversial.

Two key poster presentations in Seattle did however suggest impaired immune recovery in those coinfecting with HCV. The first examined 503 patients who began HAART to ascertain whether CD4 increases were similar between people who were HCV-positive and HCV-negative⁷. The baseline characteristics and type of therapy in both groups were similar, as was the response after twelve months of HAART, (median increase in CD4 was 220 for HCV-negative and 194 for HCV-positive).

However, the differences became more significant after eighteen months, with a median increase of 301 amongst HCV-negative and 233 amongst HCV-positive. This continued to the end of the trial, when at 24 months the figures were 325 and 272 respectively. This study looked at people who had maintained complete HIV viral load suppression. The authors concluded that in people starting HAART, HCV/HIV coinfection was associated with an impaired immune recovery, which became evident after twelve months. A similar study, which looked at both viral load and CD4

count, reached similar conclusions with regard to CD4 count⁸. There was no difference in HIV viral load response.

Several other poster presentations looked at hospitalisation rates. Not surprisingly they had dropped for people who were solely HIV-positive during the HAART era, but had increased for HCV/HIV coinfecting people.

HCV treatment in coinfecting people

This important question has, until now, not been adequately addressed. If we know that coinfection is a problem, that more effective therapies are becoming available, and that both the human and financial costs of HCV will continue to rise, then the efficacy of treatment is paramount. One key presentation at the Seattle conference addressed this issue.

In a large US federal government-sponsored study (ACTG A5071), Chung and colleagues evaluated pegylated interferon and ribavirin (PEG-IFN+RIB), compared to interferon (i.e. non-pegylated) and ribavirin (IFN+RBV); noting that the latter has had low success in coinfecting individuals in the past⁹. Inclusion criteria for HCV included detectable HCV viral load and abnormal liver histology. Inclusion for HIV was either a CD4 count above 100, and a viral load below 10,000, and on stable HAART; or a CD4 count above 300 and not receiving HAART. People were deemed to be HCV virologic responders if their HCV viral load fell below 60. The two groups underwent HCV viral load testing after 24 weeks. Those responding carried on with therapy for a further 24 weeks. Virologic non-responders had a liver biopsy, and only continued treatment if there was a greater than or equal to two point drop in a predefined hepatic activity index.

One hundred and thirty-three people were randomised to one of the two treatment arms.

Using intention to treat analysis (where results from those leaving the trial early are included), the PEG-IFN arm had a significantly higher proportion of viral responders after 24 weeks (44% versus 15%). Histological improvements were noted in those virologic non-responders who underwent liver biopsy at week 24 (26% versus 40% respectively). The PEG-IFN group experienced more grade 4 (severe) side-effects (which is of some concern as pegylation is intended to reduce the frequency of side-effects), but treatment discontinuation was not different between the two groups.

The limitations of these data stem from the fact that the trial is not yet concluded, and so safety issues cannot be fully evaluated. It is worth noting that a third of the people who underwent a liver biopsy at week 24 had a histologic response, implying that there were benefits to be gained even without a full virologic response. This trial also gave us new information on the effect that HCV treatment has on HIV. Total CD4 count fell in both arms, (-111 in PEG-IFN, -77 in IFN), although CD4 percentages stayed the same. HIV viral load detectability did not change.

This is the first trial of this size to show superior results for pegylated interferon and ribavirin in coinfecting people.

And in practice?

So if theory now dictates that HCV treatment may work for people coinfecting, with even genotype 1, should everyone be offered it, would everyone want it, and would it be paid for in the UK through the NHS?

Dr Clifford Leen is a consultant at one of Edinburgh's two HIV treatment centres, the Regional Infectious Diseases Unit (RIDU) of the Western General Hospital. This unit has considerable experience in this field since roughly half of the HIV-positive patients who attend the clinic are coinfecting with HCV. He told *ATU* that he has never had any request to treat a coinfecting person with ribavirin and pegylated interferon turned down. Dr Leen said, "Liver biopsies and the stability of HAART regimens are still key factors in deciding whether to start a patient on treatment,

although obviously with the new information about the success rates in genotype 1, the numbers involved may be greater."

Dr Leen referred to a time-lag between new treatments becoming available, and people accepting them. He said, "There may be a suspicion of what is, in effect, a difficult regimen, with side-effects. Some patients turned down the first HIV therapies available, and they were probably right!"

However, Dr Leen does see HCV as being a greater problem for many of his coinfecting patients. So, would he encourage greater take-up of HCV treatment? "I'd still rely upon liver biopsies and other key tests. If there was no fibrosis, I would adopt a wait and see approach. If not then it should be considered."

"There may be easier-to-take, oral treatment further down the line. Even if they are five or so years away from being licensed, I would like to ensure that RIDU is in at the trial stages to ensure that my patients have access to them." This is important in a smaller clinic in the northern climes that doesn't have the muscle of some of the larger London centres.

So, treatment of coinfecting people may become more common, and with an aging population the numbers requiring therapy will increase. Hospitalisation costs and liver transplants are not cheap, and coinfection will increase the need for these. Scotland has already had 'disaggregation' of the HIV budget and England and Wales are going down the same path. Where will the money come from for this? Not the HIV budget hopefully, but where else?

key conclusions

- Expect to see pegylated interferon and ribavirin become the standard for treatment for hepatitis C (HCV).
- This is now a viable treatment option, even for people with HCV genotype 1. It may not however suit everyone because of side-effects, and a long period of injections.

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hepatitis B & HIV coinfection

6 several anti-HIV drugs are active against hepatitis B virus too: what issues does this raise for people with both viruses? by megan nicholson

Hepatitis B is a viral infection that can cause serious or even fatal damage to the liver. The word hepatitis means inflammation of the liver. Hepatitis B is caused by the hepatitis B virus, also known as HBV.

HBV is most common in China, Southeast Asia and Sub-Saharan Africa where between 10-20% of the population have been infected. In western Europe and the USA, 0.1-0.2% of the population are infected with HBV.

HBV is usually transmitted through contact with blood, semen, vaginal fluids or saliva of an HBV-infected person. Transmission of HBV from mother to infant accounts for most HBV infections worldwide, though the availability of HBV vaccination has virtually eradicated mother to child transmission of HBV in developed countries. Child to child transmission is another significant vector of HBV globally,

whilst in western Europe, the US and Australia, HBV infection occurs predominantly among gay and bisexual men, people who share drug-injecting equipment, haemophiliacs and health care workers. HBV is many times more infectious than HIV.

Stages of HBV infection

When someone first becomes infected with HBV, they may develop jaundice (yellowing of the eyes and skin), loss of appetite, pain in the abdomen, malaise, nausea, vomiting, muscle and joint aches or fever. The acute illness can be very serious or even fatal. However, most people don't notice any symptoms on infection.

At this point, most people will develop protective immunity to HBV. However, in a significant minority, HBV continues to reproduce in the body long after infection. Some of these individuals may become what

are called 'chronic carriers' of HBV, meaning that they are infectious for life, although they still may not experience any symptoms. About a quarter of chronic HBV carriers eventually develop chronic liver inflammation, which places them at increased risk of liver disease (cirrhosis) and cancer of the liver. HIV-positive people who contract HBV are at higher risk of becoming chronic carriers of HBV, compared to people who are HIV-negative.

Diagnosis and terminology

Blood tests are used to detect the presence of HBV antibodies and antigens, which show whether you have been exposed to, and if so, whether you have cleared the virus. If you have antibodies but no antigen, you have been exposed to HBV but have cleared the virus and so are not infectious to others. If you have been exposed and have not developed antibodies, then fragments of the virus itself, called hepatitis B surface antigen (abbreviated to HBsAg), will persist in your blood for at least six months after exposure to the virus. If your blood test detects HBV surface antigen, this means that you are a chronic carrier. A sub-group of carriers test positive for a specific surface antigen, called the e-antigen. Being e-antigen positive means that your HBV infection is *highly* infectious to others.

HIV and HBV coinfection

Several studies of HBV infection in gay men, injecting drug users and people with haemophilia have shown that the infection does not hasten HIV disease progression or severity. However, new information presented at the Seattle Retroviruses conference in February suggested that HBV/HIV coinfection significantly increases the risk of death in people with HIV. A study of participants in the Multicenter AIDS Cohort (MACS, a large cohort of American gay men), found that men who were HBV surface antigen positive (chronic carriers) were eight times more likely to die of liver-related causes when compared to men with HIV who did not have HBV¹.

The MACS investigators prospectively followed a cohort of 5,293 gay men between January 1984 and March 2000, testing them every six months for HIV and HBV infection. Three

hundred and twenty-six (6%) were HBV surface antigen positive, of whom 213 (65%) were also HIV-positive. In comparison, 47% of the 4,967 HBV surface antigen negative men were HIV-positive. Liver-related deaths were thirteen times more common among surface antigen positive men than surface antigen negative. Among those men who were chronic carriers of HBV, only one HIV-negative individual died of liver-related causes, compared with 61 liver-related deaths amongst coinfecting men.

Licensed treatments for HBV

The aim of treatment for HBV is to reduce liver inflammation, lower levels of HBV viral load and, ideally, to eradicate HBV antigens and produce antibodies. There are currently two licensed treatments for chronic HBV infection, and these are effective in about one third of recipients: alpha interferon and lamivudine. Alpha interferon is also used to treat hepatitis C virus, as described in the accompanying article. Lamivudine is more commonly known to many people with HIV as 3TC, and that's how we refer to it in this article.

Alpha interferon is usually given for four months as an injection of five million units daily, or ten million units three times per week. It generally leads to viral clearance in 20-40% of recipients. Key side-effects associated with alpha interferon include flu-like symptoms, aches and pains, depression, bone marrow suppression, and auto-immune responses.

3TC inhibits both HIV and HBV and is a licensed treatment for both infections. The dosage of 3TC used for the treatment of HBV infection is 100mg taken orally once daily (while as an HIV treatment, the drug is taken at a higher dose of 150mg twice daily). As a treatment for HBV, 3TC results in viral clearance in about 20-30% of people after one year of treatment. The optimal duration of 3TC treatment for HBV has not been established. Studies have generally treated people for one or two years, but longer therapy may be required.

As in the case of anti-HIV therapy, combining drugs to treat HBV is generally regarded as more effective than the use of a single drug.

glossary

continued from page 3
clinical trial A research study with people, usually to find out how well a new drug or treatment works and how safe it is.

enzyme A protein which speeds up a chemical reaction.

fibrosis Scarring of the liver.

genotype The genetic make-up of an organism.

HAART Highly Active Antiretroviral Therapy, term used to describe anti-HIV combination therapy with three or more drugs.

hepatic Pertaining to the liver.

placebo A pill which looks and tastes exactly like a real drug, but contains no active substance.

randomisation The process of selecting by chance the treatment that a clinical trial participant will receive.

regimen A drug or treatment combination and the way it is taken.

resistance A drug-resistant HIV strain is one which is less susceptible to the effects of one or more anti-HIV drugs because of its genotype.

viral load Measurement of the amount of virus in a sample. HIV viral load indicates the extent to which HIV is reproducing in the body.

hepatitis B & HIV coinfection continued

However, two studies of the combination of alpha interferon with 3TC failed to show the benefit of combination over single drug therapy. Combination therapy studies are currently ongoing with the two approved treatments and a wide range of experimental agents.

As with HIV, HBV can become resistant to 3TC, so there is a need for new HBV therapies which are effective not only in their own right, but as treatments for people whose HBV is 3TC resistant. Prolonged use of 3TC (as an HBV therapy) leads to HBV resistance in about one third of individuals.

Emerging HBV therapies: adefovir

Adefovir is a drug which has anti-HIV activity, but its development was stopped because it was only weakly potent against HIV, and caused a high level of kidney side-effects. However, 10mg adefovir daily is well-tolerated and effective against HBV. Importantly, it is active against HBV which is resistant to 3TC. According to new information presented at the Seattle conference, adefovir reduced HBV viral load by over four log in HIV coinfecting people.

Benhamou and colleagues treated 35 HIV/ HBV coinfecting people with 10mg adefovir daily². All were taking 3TC as part of a HAART regimen and in all cases, their HBV was resistant to 3TC. After a median time on adefovir of 72 weeks, the average decrease in HBV viral load was -4.77 log. Four of 33 people became HBV surface antigen negative during treatment, and three developed HBV antibodies. Liver function tests also improved, and 17% achieved normal ALTs, a measure of liver function. In fourteen people who underwent liver biopsy on entering the study, and again at week 52, median liver inflammatory scores (a measure of liver disease) decreased. Four people stopped their treatment, including two who stopped because of side-effects (diabetes and insomnia).

Gilead Sciences has applied for marketing approval for adefovir (as an HBV treatment) in the European Union and the USA, and is offering an expanded access programme that will make the drug available before marketing approval is granted. People with 3TC-resistant hepatitis B will qualify for this programme in the USA, European Union and Australia, but the start date for the programme will depend on the speed at which it is approved by local licensing authorities.

Emerging HBV therapies: tenofovir

Tenofovir, like adefovir, is produced by Gilead. Having been recently licensed for treatment of HIV, tenofovir is now under investigation as a treatment for HBV. Two small studies of tenofovir in coinfecting people found substantial reductions in HBV viral load of between 3.4 and 4.6 log, according to reports in Seattle.

Cooper analysed a subgroup of fourteen HIV/ HBV coinfecting men from Gilead's Study 907 (a randomised, double-blinded study of 300mg tenofovir daily in 550 HIV-positive adults)³. Twelve of the subgroup received tenofovir and the remaining two were randomised to placebo. HBV viral load levels fell by an average of -4.63 log compared to an average increase of 1.23 log amongst those on placebo. Response was not affected by the presence of HBV resistance mutations, which were present in seven individuals. Two tenofovir recipients achieved normal liver function tests and one man became surface antigen negative. Study 907 has already reported its main findings, regarding the effect of tenofovir on HIV infection. In this HBV substudy, HIV viral load declined by -0.75 log in the tenofovir group, compared to no change in the placebo group.

In a separate study, Bochet followed ten HBV/ HIV coinfecting people with 3TC-resistant HBV⁴. All were treated with 300mg tenofovir daily, in addition to ongoing antiretroviral

therapy for their HIV infection. Median HBV viral load fell by -3.34 log after twelve weeks of tenofovir, suggesting the drug is active against 3TC-resistant HBV.

Issues in treating HBV/HIV coinfection

Regardless of its cause, hepatitis or other forms of liver disease can have a significant impact on treatment options and strategy in people with HIV.

Firstly, a number of anti-HIV drugs may cause increases in liver enzymes, which may already be raised in people with viral hepatitis. In particular, ritonavir is associated with hepatic (liver) side-effects. However, other drugs can also trigger liver toxicity, including indinavir, nevirapine, AZT, ddI, sulphur-based antibiotics, ketoconazole, and pentamidine.

A recent analysis of the development of liver toxicity in people starting HAART found that HBV infection itself, alongside other viral forms of hepatitis, is an important risk factor⁵. Reisler retrospectively analysed 1,841 people who were followed for a 36 month period from September 1999 to August 2001. Five point seven per cent were chronic carriers of HBV, 17.4% had hepatitis C (HCV) antibodies, and 1% were HBV/HCV/HIV coinfecting. After 30 months, 21% of all patients had experienced a grade IV (serious) adverse event; 4.8% a liver-related grade IV event; and 6.4% had died. Comparing those with and without viral hepatitis, 25% versus 20% had any grade IV event; 8% versus 4% had a liver-related grade IV event; and 8% versus 6% died. People with HBV, and/or HCV, faced a five times greater risk of grade IV liver-related events than those who were HIV infected only.

The damage to liver cells which occurs as a result of HBV infection is not caused by HBV itself, but by the body's own immune response to the infection. This means that acute episodes

of HBV, known as "hepatitis flares" can occur as a consequence of immune recovery. For people who are HBV/HIV coinfecting, the rebuilding of the immune system (which is associated with taking effective HIV treatment) can provoke hepatitis. This is one reason why some experts believe that people with HBV infection who commence HAART should begin treatment for HBV infection at the same time, in order to reduce the risk that HAART will lead to HBV-related liver damage.

Conversely, the other reason for treating both HBV and HIV simultaneously is that treating HBV alone, using standard HBV therapy, may induce HIV drug resistance. This could occur if your HBV regimen includes treatments which are active against HIV but are not part of a regimen which itself is sufficiently potent against HIV to shut down HIV replication.

key conclusions

- New research suggests that hepatitis B (HBV) infection hastens disease progression in people who have HIV.
- Two experimental treatments for HBV appear effective against HBV which is resistant to licensed HBV treatments.
- 3TC and tenofovir are licensed to treat HIV, but may also be used to treat HBV. This allows the option of treating both viruses at the same time, but whether this is the best strategy is unclear.
- People with HIV and viral hepatitis experience more liver problems when taking HAART than people with HIV infection alone.

hepatitis B vaccine

There is an effective vaccine against HBV which is recommended for people at high risk of exposure, including gay men, injecting drug users, health care workers and the partners of people infected with HBV. The vaccine is perfectly safe for people with HIV to take, although compared with uninfected people, a higher proportion of HIV-positive people may not develop protective immunity against HBV following vaccination, and those who are successfully immunised may be more likely to lose their immunity over time.

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Safety of protease inhibitors in HCV / HIV coinfecting people

People coinfecting with HIV and hepatitis C (HCV) taking dual-protease inhibitor (PI) containing regimens are just as likely to have to stop therapy because of treatment-related liver toxicity as people taking a single PI regimen, according to Canadian doctors.

Researchers at the University of Ottawa Hospital's HIV clinic reviewed the medical records of 66 patients coinfecting with HIV and HCV who started antiretroviral treatment including either one or two PIs between 1994 and 2001. The researchers also looked at whether a person was taking a treatment regimen containing ritonavir, which has been particularly associated with liver toxicity, in either a single or dual-PI regimen.

A review of the medical records of all the patients indicated that after a year of treatment, dual-PI therapy was not associated with greater liver toxicity and discontinuation of treatment than single-PI therapy with nearly 50% of both groups stopping their initial therapy within twelve months. Of these, 9% had stopped therapy because of liver toxicity and a further 15% because of gastrointestinal problems. Rates of discontinuation for liver toxicity were similar between those receiving a single-PI and those on a double-PI.

Nor was discontinuation of treatment any more common in those taking ritonavir compared to people taking another PI. This was the case when ritonavir was given as either the single-PI or as part of a dual-PI regimen.

Rates of liver toxicity associated with different nucleoside analogues were also analysed. The Ottawa team were particularly keen to see if suggestions that d4T (stavudine) was associated with liver toxicity in HIV/HCV coinfecting individuals were demonstrated. d4T-containing regimens were found to be no more liver toxic than regimens containing other nucleoside analogues.

The Ottawa researchers conclude that the high rate of discontinuation of treatment within a year demonstrates the difficulty people coinfecting with HIV and HCV experience in maintaining antiretroviral therapy, and suggest that the sustainability of NNRTI-based regimens should be explored for this group as an alternative.

Source: L Curtis. CID 2002;34, 1259-1263.

Hepatitis G: an emerging infection

A US study has found that people seeking treatment for a sexually transmitted disease (STD) are more likely to be infected with hepatitis G and other hepatitis infections than people who have not had an STD.

Discovered in the early 1990's, research so far suggests that hepatitis G does not cause liver disease or worsen disease caused by other hepatitis viruses. Some evidence also suggests that people coinfecting with both HIV and hepatitis G may experience a slower rate of HIV disease progression.

These data add to the evidence that hepatitis G is sexually transmittable as well as being spread by contact with infected blood via blood products or shared injecting equipment.

Between December 1995 and February 1998, researchers at the University of St Louis compared rates of hepatitis G between a group of 453 people seeking treatment for an STD and 491 people who had never had an STD. Using both assays to test for the presence of hepatitis G, and antibody tests, they found that those who were seeking treatment for an STD were substantially more likely to have been infected with hepatitis G and other hepatitis viruses. When the results of both tests were combined 36.6% of the STD group were found to have hepatitis G against 8.8% of those who had never had an STD.

Other factors associated with an increased likelihood of having hepatitis G were injecting drug use, a history of exchanging sex for drugs or money, and the receipt of blood products. Rates of infection with hepatitis B and C were also substantially higher in the STD group. The researchers conclude that infection with another STD may facilitate infection with hepatitis G.

Source: SE Frey. CID 2002:34, 1033-37.

Abacavir licensed in UK for use in children

The nucleoside analogue abacavir (*Ziagen*TM) has been approved for paediatric use as part of HAART in the UK.

In July 1999, abacavir was licensed across the European Union for use by HIV-positive adults, and the drug will now be available for the

treatment of children aged 3 months to 18 years of age.

The 6 April 2002 edition of the medical journal, the *Lancet*, includes an article on the PENTA 5 clinical trial which demonstrated that abacavir was generally well-tolerated in paediatric use, and that the incidence of the potentially life-threatening side-effect, the abacavir hypersensitivity reaction, was similar in children to that seen in adults, at approximately 4%.

As with the adult dose, abacavir is licensed to be taken twice daily by children in combination with other HIV antiretroviral drugs. A strawberry-banana flavoured paediatric solution of abacavir will be available for children as will the existing tablet formulations.

May NAM forum on coinfection with HIV and viral hepatitis

Continuing the theme in this issue of *ATU*, this month's NAM Information Forum is on hepatitis and HIV coinfection, and takes place at the University of London Union, Malet Street, London WC1 on May 27th, 7-9pm. A guest speaker will discuss recent developments in the treatment and care of hepatitis viruses, and take questions from the audience.

Entrance to NAM forums is free and all are welcome. Refreshments, and a sign language interpreter are provided.

more HIV & AIDS news at [aidsmap.com](http://www.aidsmap.com)

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credits

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AIDS Treatment Update
founded by Peter Scott

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design
Alexander Boxill

printing
Cambrian Printers

ISSN
0969-4706

charity number
1011220

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NAM's treatments information for people living with HIV is provided free thanks to the generosity of:

Department of Health, London HIV Commissioners Consortium, International HIV/AIDS Alliance, Crusaïd, British HIV Association, Elton John AIDS Foundation, GlaxoSmithKline, Bristol-Myers Squibb, Roche Products, Bristol-Myers Squibb Pharma, Abbott Laboratories, Positive Action, Boehringer Ingelheim, Merck Sharp & Dohme, Gilead, Roche Products Hep C Division, Roche Molecular Systems, Serono, Visible Genetics, Virco, and these health authorities: Barking & Havering, Birmingham, East Surrey, East Sussex, Brighton & Hove, Manchester, Newcastle and North Tyneside, Norfolk, North Nottinghamshire, Salford & Trafford, Stockport, West Pennines, West Surrey, West Sussex, Wigan and Bolton, and Manchester City Council



any questions

For an introduction to HIV treatment issues

The booklets in NAM's Information Series for Positive People are free to people with HIV. This easy-to-read series includes: Anti-HIV Drugs, Clinical Trials, Glossary, Lipodystrophy, Nutrition, Resistance, and Viral Load & CD4.

The HIV & AIDS Treatments Directory

This 600 page book, published twice a year, is a comprehensive guide to the medical aspects of HIV. Available at only £12.95 to people with HIV, £64.95 to professionals.

<http://www.aidsmap.com>

NAM's resources are also available online at [aidsmap.com](http://www.aidsmap.com). These include our extensive and searchable treatments database, the latest news on treatment developments, our online directory of AIDS service organisations, hundreds of links to recommended HIV-related sites, and free downloadable resources.

Monthly NAM information forums in London

Each month an expert speaker discusses a treatment-related topic. Entry is free. Future forums are advertised inside this newsletter.

THT Living Well Phonenumber 0845 9470047 Mon-Thu 6-9pm

i-Base Treatment Phonenumber 0808 8006013 Mon-Wed 12-4pm

NAM recommends that you discuss all your treatment decisions with your doctor.



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AIDS Treatment Update is available free to individuals in the UK affected by HIV or AIDS.

Professional/organisational rate: £75/year.

Voluntary organisation rate: £55/year.

Overseas rate: within EU add £10/year; outside EU add £15/year.

AIDS Treatment Update is available on audio tape, and can be emailed to you as a pdf file for viewing with Acrobat Reader. Telephone NAM on 020 7627 3200 for details.

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