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DRAFT PAPER TO EXECUTIVE BOARD - CONFIDENTIAL

HEPATITIS C: ISSUES FOR THE NHS

CONTENTS

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HEPATITIS C: ISSUES FOR THE NHS

Executive Summary.

1. This paper draws attention to current issues related to Hepatitis C (HCV) and suggests how they might be handled. Hepatitis C is a blood borne virus which most frequently causes chronic infection and can in some patients result in severe liver damage after a number of years. Whilst the exact prevalence in the UK is unknown, there is sufficient evidence to suggest that a considerable number of people are infected with this virus. There is increasingly a focus on this disease as patients are starting to come forward for treatment. There is lobbying from patient interest groups for hepatitis C to be given a higher profile and for increased resources to be allocated to it centrally.

2. Unlike Hepatitis A and B, there is no vaccine. There are several implications for the NHS, not least in terms of both the specialised manpower needed to treat patients and the cost of drug therapy. These need to be addressed now if the NHS is to be in a position to treat the large numbers of patients who we expect to see coming through with chronic hepatitis C and its sequelae over the next 20 years. Whilst there is a significant programme of activity in hand within the Department to address some of the issues under discussion here, there is a need to co-ordinate this activity and ensure that both the Government and the NHS are in a position to respond effectively. However, it is recognised that this is just one of a number of pressures on the acute sector and that any consideration of the resources required to treat the disease should be seen in that context.

3. **The Board is asked to consider:-**

- whether this should be put to Ministers for consideration of the handling issues raised;

- whether existing HEA and other leaflets should be updated to reflect public health advice on the risks of transmission of hepatitis C through Intra Venous Drug users sharing needles. This presents a dilemma in that a more proactive stance may jeopardise our negotiating position with Treasury if we flag this up as a pressure in PES. However, it would be indefensible to withhold information on the public health aspects of hepatitis C which could help to minimise the risks of transmission simply to strengthen any bid for additional resources for which there is no guarantee of success (paragraph 10 refers);

- whether the long term manpower implications of treating hepatitis C should be assessed with a view to increasing the specialist medical and nursing staff who will be needed as patients who are infected come forward for treatment (paragraph 12);

- our current line when asked how purchasers are to cope with the additional costs of providing drug treatment for patients with hepatitis C is to say that it is for purchasers to determine priorities based on local needs taking account of local priorities and resources. The Board are asked to confirm that this should remain our line in relation to both the costs of the drugs and the other costs associated with treating hepatitis C (even if we raise this as a pressure during the current PES round) (paragraph 17 refers);

- consider whether the work in hand to estimate the impact on resources is sufficient or whether additional work is required to inform discussions with Treasury. The costs identified in this paper comprise manpower, treatment including drugs, testing, counselling and research including sero-prevalence studies. Much will depend on the true prevalence of the disease which is not yet known (see Annex A). It is therefore important that we flag up now the long term resource implications for the NHS;

- how, and whether, we are to ensure that patients are given adequate pre- and post-testing counselling when there may be insufficient resources in place for this. Would purchasing guidance be useful to draw attention to the growing needs of these patients and to highlight the issues to be resolved locally in discussions between purchasers and providers? (paragraph 21 refers);

- whether priority should continue to be given to the voluntary organisations dealing with hepatitis C under Section 64 despite the possibility that the publicity this may attract to funding difficulties for treating hepatitis C may be unfavourable (paragraph 23).

- if we are to raise this as a pressure in this or future Survey discussions, it is essential that we do not say anything to external bodies which indicates that the Department is looking for an exceptional response to the problem by the NHS or considering a policy change. This may conflict with the overriding need to issue clear public health advice both to prevent the further spread of the disease and to encourage people who may have acquired the infection to come forward for testing. The Board is asked for a steer as to how we should best proceed (paragraph 30).

DRAFT PAPER TO EXECUTIVE BOARD - CONFIDENTIAL

HEPATITIS C: ISSUES FOR THE NHS

The Problem.

1. We are aware that there may be large numbers of people in the population infected by HCV many of whom will require assessment by a competent hepatologist and some of whom will need treatment with Alpha Interferon. Depending on the size of this cohort, the resource and cost implications for the NHS in general and the hepatology services in particular could be very significant. Public awareness may be raised in the near future by various initiatives explained in paragraphs 7-9 below.
We need to get a handle on the problem as a matter of urgency.

Treatment.

2. Further details of the natural history of the disease and of the treatment currently available are given in Annex C.

Prevalence.

3. The attached paper at Annex A, prepared by EOR, sets out the best estimates based on the information currently available and gives both the best and the worst cases with confidence intervals. A major problem is the lack of data about the overall numbers involved but something of the order of 100,000-300,000 people could have been infected. The British Liver Trust (BLT) claim that between 0.1 to 1% of the population may be infected but have not substantiated this. (By way of comparison, in the US, there are an estimated 3.5m with chronic hepatitis C[1] which is roughly 1.2%). Details of particular risk groups (patients infected by blood - currently the subject of the "Look back" exercise[2] (see paragraph 6), haemophiliacs, intravenous drug users (IVDUs), health care workers at risk of occupational exposure and patients on renal replacement therapy infected as a result of blood transfusion) are set out in Annex B.

4. Work to establish more precisely the prevalence of HCV is included in the package of research proposals described in paragraph . Revised publicity material to inform patients that specimens will be tested for other infectious diseases including HCV has now been distributed. However, it will be some time before HCV prevalence results are available.

5. EOR's estimates give us some idea as to the approximate prevalence of the disease. This enables us to make some assumptions about the rate at which people might come forward for testing or treatment although it should be borne in mind that the uptake of HIV tests by IVDUs was initially slower than had been anticipated. Those in the known risk groups will be picked up early but ex-IVDUs who are also at risk may be asymptomatic for decades. Assuming that intra-venous drug use was not widespread before the late 1960s, this group may only be starting to develop symptoms now depending on when the virus originated.

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[1] NEJM, June 1 1995, vol. 332 no. 22, page 1509-1511.

[2] This followed a recommendation by the Advisory Committee on the Microbiological Safety of Blood and Tissues for Transplantation in December 1994 that there should be a "Look back" of blood transfusion recipients infected with hepatitis C prior to the introduction of Hepatitis C screening in September 1991.

"Look back" exercise.

6. The "Look back" exercise is well under way; an Interim Report was sent to Ministers in February 1996[3]. This concludes that 1727 donors were positive for hepatitis C who had given blood prior to 1991. 9048 donations have been identified and 2808 recipients have been identified by hospitals of whom 1631 have already died of unrelated causes. The original estimate of approximately 3000 recipients who are alive is thought to be realistic. However, the Look back has taken longer than anticipated due to delays in tracing medical records for recipients identified in the hospital blood banks and due to a shortage of counsellors available to see patients prior to and after testing (see paragraphs 16-18).

Drug misusers.

7. Various pressure groups such as Mainliners and the British Liver Trust are already pressing for increased testing of both current and ex-drug misusers. Current DoH advice published in 1991[4] is that drug misusers should be tested although this seems to have been largely ignored up to now. The Advisory Council on the Misuse of Drugs[5] (ACMD) pressed the Department to issue further advice to drug clinics warning of the dangers of HCV to try to reduce the spread (cf HIV). Colleagues responsible for drug abuse and prevention have agreed that current leaflets (produced by the HEA) should be updated opportunistically to include warnings about other blood borne viruses including HCV and how they can be prevented. The BLT already have a leaflet about hepatitis C and are working on a joint leaflet about the implications for drug misusers with Mainliners. However, the pressure is growing from the ACMD and pressure groups to produce a specific leaflet on HCV which would contain advice on testing and treatment for patients who may already be infected. The BLT are currently working on producing their own leaflet for IVDUs.

8. Whilst we should undoubtedly support publicity on the risks of acquiring HCV which can only help to prevent the disease, such advice would lead to more people being tested and coming forward for treatment with all that would imply for services. There is, however, already anecdotal evidence to back up claims that people coming forward are being denied testing in some areas because of uncertainty as to who should pay for the initial counselling, testing and the subsequent treatment.

9. It is thought that treating patients early has significant advantages in terms of preventing chronic liver failure later on although this has yet to be proven. In addition, the Task Force to review Services for Drug Misusers (set up by Ministers) is likely to recommend that the Department should consider how people who could benefit from treatment for hepatitis B and C could be encouraged to come forward. The Department will be required to respond to this report [DN: needs updating].

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[3] Dr Metters submission to Ms Weatherseed, 5 February 1996.

[4] Drug Misuse and Dependence: Guidelines on Clinical Management, Report of a Medical Working Group.

[5] A statutory committee set up under the Misuse of Drugs Act 1971 with a wide range of professionals and other members which advises the Home Office and Government generally on drug-related issues.

10. **The Board is asked to confirm that initiatives to raise public awareness of hepatitis C should be encouraged and that the NHSE and the NHS generally should take a proactive approach to publicising the dangers of high risk behaviour such as needle-sharing despite the implications for demand for services and the increased pressure that this will place on purchasers.**

Capacity.

11. It would be helpful to have some estimate of the current NHS facilities with the capacity to manage people who test +ve for HCV. Specialist hepatology clinics may be able to cope but it is not clear how many such centres there are in the NHS.
It should be possible to get a rough estimate, if required, informally from professional contacts. It seems unlikely that there will be much unused capacity.

[DN: Dr Doyle's initial enquiries suggest that there are something like 3-5 new HCV cases coming forward each week in every liver unit (he contacted King's, Cambridge, Royal Free and Leeds. This represents something like 20-25% of new referrals. We can update this paragraph following this week's meeting.

Manpower.

12. The main capacity constraint is likely to be manpower. As far as medical manpower is concerned, as well as hepatologists who deal specifically with liver disease, some DGH gastroenterologists also have an interest in hepatology but whether they could give an adequate service needs to be ascertained. Specialist histologists and virologists will also be needed in specialist units treating patients with HCV. Depending on the size of the problem, there may be significant implications for manpower and waiting lists and these need to be assessed. Non-medical manpower is also likely to come under significant pressure, in particular, nursing staff and midwives. If we are to make a PES bid, we need to be able to quantify the training needed to increase medical and non-medical manpower to the level which will be required. The implications for social workers will also need to be assessed.

It may be worth saying something more about current waiting lists/times since we are aware that there are delays in waiting for out-patient referral, (day case) liver biopsy, plus delays in obtaining Alpha IntF where there are funding problems. We may have a clearer idea following the meeting.

13. **The Board is asked whether the long term manpower implications of treating hepatitis C should be assessed with a view to increasing the specialist medical and nursing staff who will be needed as patients who are infected come forward for treatment.**

Drug treatment.

14. Alpha Interferon was licensed for the treatment of Hepatitis C in January 1995 (it had previously been licensed for other conditions, such as Hepatitis B, and is prescribed by GPs for those conditions). It is the only drug so far which has been found to be effective for treating hepatitis C. It is less expensive than Beta Interferon (for treating multiple sclerosis), costing some £2-5K per course of treatment. There is continuing research, some using a combination of interferon and other antiviral agents such as Ribavarin (as yet unlicensed for this purpose), aimed at improving response rates (details of the Health Technology Assessment of this treatment, see Annex D, paragraph 1). Depending on the outcome of this research, it could add to the costs of recommended treatment in the longer term. Annex A includes details of cost-effectiveness and Annex C gives details of the clinical aspects of treatment.

15. Concern has been expressed by some liver physicians about their inability to prescribe this drug from their cash-limited budgets since most purchasers have not contracted specifically for treatment of hepatitis C and hepatologists may be unable to prescribe Alpha Interferon from their cash-limited budgets. These concerns have been echoed by the voluntary sector. Several of the policy and the handling issues raised in relation to the introduction of Beta Interferon for sufferers of multiple sclerosis apply to Alpha Interferon. However, whilst prescribing is unlikely to be initiated in the acute sector which was a major concern in relation to the introduction of Beta Interferon, there is still a same danger of "leakage" to the primary care prescribing budget where consultants request GPs to take over prescribing responsibility as a means of cost-shifting.

16. The issue of handling new drugs and, in particular, the need for clinical guidelines for major new drugs is currently the subject of a submission from CMO to Ministers [DN: data/still in draft form?]. This suggests that there is a need for early warning arrangements for new, potential "blockbuster" drugs. Whilst it is unlikely that Alpha Interferon will be prescribed in such quantities as to place it in the "blockbuster" category, since it is the only treatment available and there are many patients who will wish to try it, it will inevitably add to the existing burdens on the FHS/HCHS budgets. Given its low cost-effectiveness and the high cost of treatment per patient, the arguments about funding and calls for central funding look set to continue. At present, there is undoubtedly geographical variation in the availability of Alpha Interferon which will inevitably lead to some political pressure and pressure on purchasers to allocate additional resources to this area.

17. **Our current line when asked how purchasers are to cope with the additional costs of providing drug treatment for patients with hepatitis C is to say that it is for purchasers to determine priorities based on local needs taking account of local priorities and resources. The Board are asked to confirm that this should be our line both in relation to the costs of the drugs and the other costs associated with treating hepatitis C (see paragraph 25) (even if we are to raise this as a pressure during the current PES round).**

Other strains.

18. A further blood borne virus has been associated with both acute and chronic hepatitis and has been shown can be trasnitted as a result of blood transfusion. It has been designated as hepatitis G. Early work suggests that infection occurs in similar groups to hepatitis C but that the prevalence of hepatitis G appears to be much higher. The clinical significance of HGV infection and of its natural history are unkown and will require further study. This virus may present similar problems to hepatitis C.

Counselling.

19. Another resource question that has to be addressed is the question of who is to counsel patients found to have HCV. Counselling is currently being undertaken by a variety of health care professionals including those counselling specific risk groups such as IVDUs and haemophiliacs. Nursing staff and midwives are already providing counselling in some areas and some are finding it difficult to meet current demand. Guidance issued to the NHS in April 1995 (CMO letter, CMO(95)1) said that patients confirmed to be anti-HCV positive through the Look-back should be counselled on the implications of the test result and referred for a specialist opinion where appropriate.

20. We are under some pressure to provide additional resources specifically for this. BLT wish either to undertake the work themselves given appropriate funding or to co-ordinate this activity and applied under section 64 for a project grant to take this forward. This was rejected on the grounds that BLT already receive substantial grants from the Department and in any case do not have the infrastructure in place. The Department is supporting an initiative by the Haemophilia Society to undertake a study into the best way to support its members who are infected with the virus, with a S64 grant of over £90,000 in 1995/6 and £117,000 in 1996/7 (in addition to core funding). Transferring responsibility for counselling to the voluntary sector wholesale, however, is not considered a practicable option. Instead, patients should be given adequate information and advice by those assuming responsibility for other aspects of their care.

21. Our response is that this is primarily a purchasing issue since counselling is one important aspect of the whole package of care needed by this patient group and may best be provided by those responsible for the clinical care of the patient. If current facilities for counselling are inadequate, this needs to be addressed by purchasers taking account of local priorities who may need to allocate further resources to this area. It may also be an issue that needs to be addressed in purchasing guidance. **The Board are asked to confirm that this is a reasonable line and to indicate whether guidance on this issue may be helpful.**

Research.

22. In setting up the expert group to manage the "Look back", one of the issues included in the terms of reference was research. Subsequent discussions both within and beyond the "Look back" group have revealed the paucity of knowledge which make it extremely difficult to gauge the impact accurately on the health of the nation in general and on health services. Colleagues within the Department and the NHS, experts on the "Look back" group, the MRC, and the BLT have outlined an initial research agenda which covers the need for research in the following areas:

- pathobiology
- prevalence
- transmission routes
- treatment effectiveness
- natural history of the disease.

Work is planned on all these research priorities and details are set out in Annex D.

Voluntary sector.

23. The role of the voluntary sector has already been touched on. The BLT and the Haemophilia Society are currently being funded under Section 64 to include not only core funding but also projects to enable them to deal with various aspects of hepatitis C specifically (these total £81K for 1996/7). The BLT claim that much of their workload is dealing with hepatitis C. They are working with other voluntary organisation such as Mainliners (who represent IVDUs) to campaign on behalf of patients infected with hepatitis C and to raise the profile of the disease. Regular meetings have taken place between the Trust and the Executive and their role in providing information on hepatitis C is reflected in the priority given through S64. **The Board is asked whether priority should continue to be given to the voluntary organisations dealing with hepatitis C under Section 64 despite the possibility that the publicity this may attract to funding difficulties for treating hepatitis C may be unfavourable.**

24. There has been considerable pressure from some of the voluntary organisations, particularly the Haemophilia Society, calling for compensation for those infected by blood products received as part of NHS treatment. A note about the current position is at Annex E.

Resource implications.

25. The main potential costs to the NHS of handling Hepatitis C have been addressed in this paper and comprise:

- research
- manpower, both medical and non-medical
- linked to the above, the cost of providing counselling
- Alpha Interferon and other drugs including Ribavarin

26. Wessex Institute of Public Health have prepared some expenditure projections for alpha interferon as part of their work on assessing the cost implications of new technology.

Alpha interferon for hepatitis C: Expenditure increases in 1997-98 on 1996-7 to meet incident/prevalent need England NHS 1994-95 prices		
Low estimate	Middle estimate	High estimate
£9m	£30m	£51m

The range reflects uncertain prevalence, take up and duration of therapy. The middle estimate reflects the average of 0.05% and 0.2% prevalence, 50% initial response to therapy and 10% take up. This gives some idea of the costs involved during the first year of the current Survey period and this will be used in discussions with Treasury.

27. Finance colleagues have been kept fully informed and consulted on handling these issues. It is intended that this will be flagged up in this year's Survey discussions depending on the outcome of the work currently in hand.

Conclusion.

28. There is a need to gather further information on the prevalence of Hepatitis C and to initiate action to ensure that there will be sufficient provision to deal with this growing problem. Although the numbers coming through so far may not, so far as we are aware, be very high, they are likely to increase and there are already signs that the liver services are fully stretched and having to devote more and more resources to dealing with chronic hepatitis C and its sequelae.

29. Our current line in response to pressure from groups, such as Mainliners and the British Liver Trust, is that money is not allocated to support specific treatments or for specific segments of the population and that it is for health authorities to assess the health needs of all their local residents and decide which services to purchase and where to place contracts. Hepatitis C is just one of a large number of growing pressures that can be identified on the acute services. This may, however, be a difficult argument to sustain given that there is a growing awareness of the virus and the availability of new drug therapy (stimulated to some extent by the "look back" exercise). In addition, purchasers are unlikely as yet to have identified Hepatitis C as a priority.

30. Hepatitis C is a recently recognised and increasing problem that will inevitably get worse if the numbers we anticipate coming forward for treatment are borne out. **However, if we are to raise this as a pressure in this or future Survey discussions, then it is essential that we do not say anything to external bodies which indicates that the Department is looking for an exceptional response to the problem by the NHS or considering a policy change. This may conflict with the overriding need to issue clear public health advice both to prevent the further spread of the disease and to encourage people who may have acquired the infection to come forward for testing. The Board is asked for a steer as to how we should best proceed.**

ANNEX A

THE PREVALENCE OF HCV AND THE IMPACT ON THE NHS

1. This note sets out an estimate of the prevalence of HCV in the population as a whole. It also considers the evidence on prevalence in certain high risk groups such as ever intravenous drug users (IVDUs) who have ever shared needles, but it does not attempt to build a population estimate by summing estimates for the different risk groups. It goes on to consider the possible demand for services, particularly in the near future, and the cost and cost effectiveness of the leading treatment, alpha interferon.

Prevalence

2. The following data is available on prevalence in different groups:

	Prevalence	Sample
Blood donors[6]	0.05%	800,000
Organ donors 1993[7]	0.24%	838
Organ donors 1994	0.24%	824
Organ recipients 93-94	1.00%	800
Surgical patients	0.00%	267
Dialysis patients	3.58%	1060
Health care workers[8]	0.28%	1053

3. None of these groups is fully representative of the population. Blood donors and health care workers are people of working age. The elderly and middle aged preponderate in surgical patients. Perhaps more importantly, most of the groups have a selection bias against the sub-group most at risk of HCV, ever IVDUs who have ever shared needles. The recommendations addressed to blood and organ donors are likely to have held back donors at high risk of HCV. The group most at risk are unlikely to give blood, donate organs or obtain employment in the NHS. On the other hand, organ recipients are likely to be more at risk of HCV than the general population. Nevertheless these figures do tell us something. The corresponding estimates of national prevalence can be found by grossing up each group's prevalence figure by the total population[9]. These are set out below[10]:

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[6] 1 in 2000 widely quoted.

[7] Data on organ donors comes from UKTSSA (United Kingdom Transplant Support Service Authority).

[8] Zuckerman J, Clewley G, Griffiths P, Cockcroft A. Prevalence of hepatitis C antibodies in clinical health care workers. *Lancet* 1994;**343**:1618-20.

[9] For example, the prevalence in health care workers is 0.28%. If this rate was typical of the population as a whole, national prevalence would be 0.28% of 50 million (population of England), which is 140,000.

ESTIMATES OF NATIONAL PREVALENCE OF HCV BASED ON DIFFERENT GROUPS	
	Estimate
Blood donors	25,000
Organ donors 93-94	120,000
Organ recipients 93-94	500,000
Surgical patients	-
Health care workers	140,000

These estimates are generally modest. With the omission of the blood donors they collectively point to an estimate of 200,000 with a range of 100,000-300,000, the width of the range reflecting the meagre sample size (3782).

4. An alternative method of arriving at an estimate is by way of an estimate of prevalence in IVDUs noting that this group tends to account for up to a half or more of HCV prevalence in various samples[11]. This method points to a figure towards the higher end of the range 100,000-300,000 or even above it.

5. The prevalence of HCV among drug users who have acquired infection through sharing needles lies in the range 100,000-150,000, to judge from a range of sources using a number of methods. Appendix 1 sets out the detail.

6. It is also possible to make an estimate of prevalence among transfusion recipients. However, in appendix 2 we try to make a direct estimate of the demand for treatment from this group rather than follow an indirect path by way of prevalence.

7. The table below summarises these estimates.

[10] The 95% confidence limits are generally too wide to be worth quoting, except for blood donors: +/-2000 reflecting the large sample.

[11] Neal KR, Jones DA, Killey D, James V. Risk factors for hepatitis C virus infection. A case control study of blood donors in the Trent region (UK). *Epidemiol Infect* 1994;**112**:595-601.

HCV PREVALENCE	
Total	100,000-300,000
High risk groups	
Haemophiliacs	4000
Other blood transfusion[12]	-
Ever needle sharing IVDUs	100,000-150,000
Dialysis patients[13]	-

The Demand for Services

8. Predicting the demand for services over the next few years is unusually difficult. We can make a start by taking stock of the estimates which have been made.

9. It may be as well to set out the sequence of treatments:

Counselling and testing (various stages)
Referral to hepatologist
Liver biopsy
Offer of alpha interferon
Acceptance or decline of treatment

A flow chart[14] is set out below. Appendix 3 catalogues what is known about unit costs.

10. Alpha interferon therapy has been established as effective in removing evidence of HCV in 25% of patients with chronic hepatitis. It also postpones the onset of hepatocellular carcinoma in patients with chronic active hepatitis accompanied by cirrhosis of the liver, with an extra three in ten patients remaining free from this condition after seven years[15].

11. The evidence in the less severe chronic group relates to therapy lasting six months. Questions remain as to whether better results would be achieved with a longer period of treatment or a higher dose or the addition of antivirals or anti-inflammatory agents. But not all the possibilities would increase cost. Most patients destined to respond show signs of doing so within two months and the option arises of discontinuing therapy in non-responders at this point. Moreover, discriminators of

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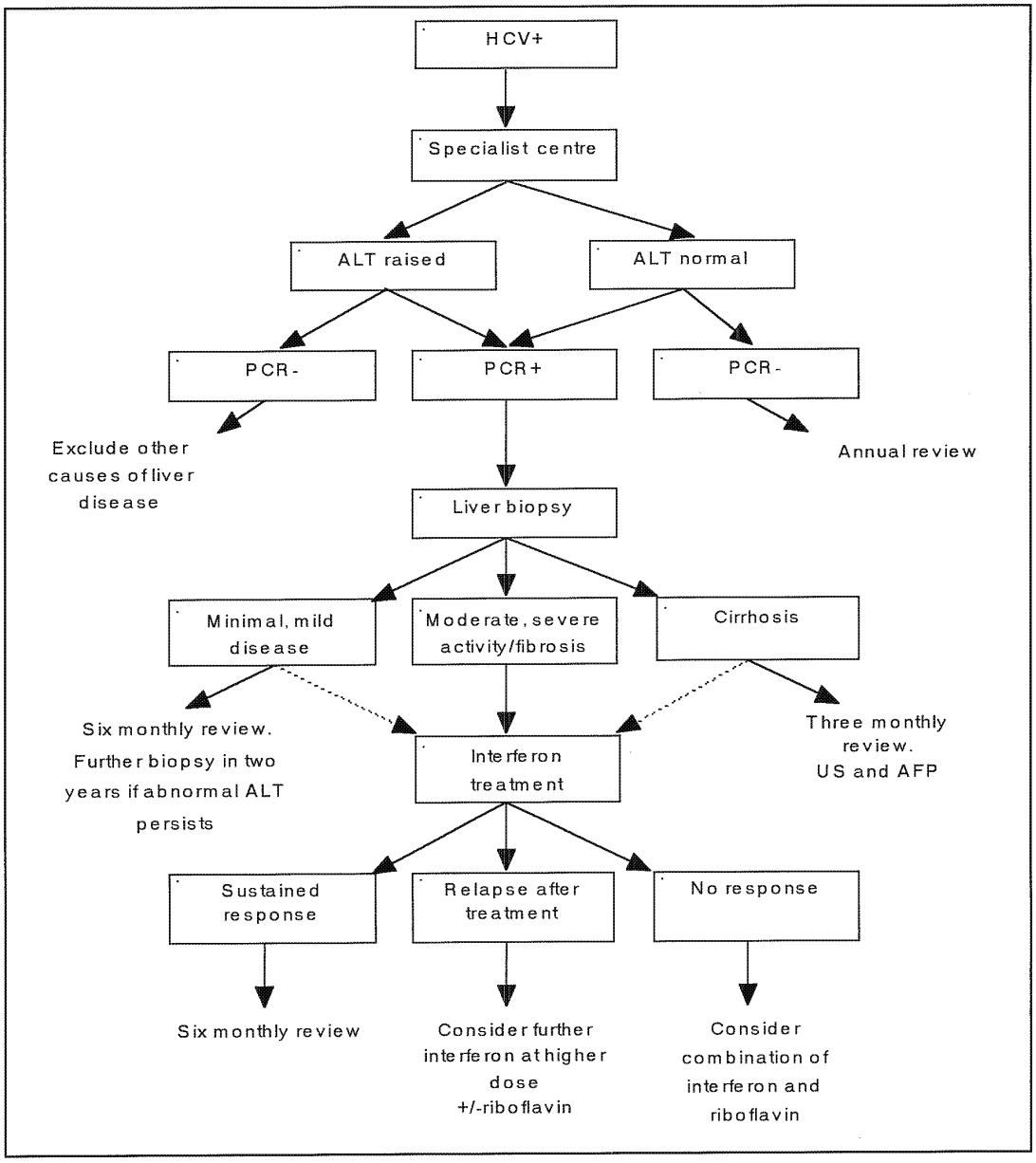
[12] Demand for services calculated directly rather than via prevalence - appendix 2.

[13] The numbers of dialysis patients with HCV is not significant in total population estimates. A prevalence of 3.58% in a stock of 4000 patients points to about 140 cases.

[14] Booth JCL, Brown JL, Thomas HC. The management of chronic hepatitis C virus infection. *Gut* 1995;**37**:449-54.

[15] Sánchez-Tapias JM, Rodés J. Interferon in chronic hepatitis C. *Lancet* 1995;**346**(suppl):11.



poor response have emerged - genotype 1b, a high level of viraemia among others - raising the possibility of a selective policy.

12. Interferon may well not give a good cost effectiveness performance in some kinds of patients and if resources are constrained it may be necessary to set priorities.

13. An estimate of the demand for services in France, where the population prevalence lies rather above estimates for this country, suggests that the stock of patients suitable for interferon now is about 3500 to 5000 - with an annual incidence of about 600[16]. The cost to prescribing budgets of clearing a backlog of 3500-5000 cases is then about £9m-£13m[17]. However, the annual incidence of 600 would impose fairly modest annual expenditure below £1½m.

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[16] HCV prevalence in France is half a million. *Br Med J* 1995;**311**:1187-8.

[17] using the quoted price of £2600 for a course of treatment lasting a year: drug cost only.

14. Rather similar estimates are found on this side of the Channel. The estimate that 10% of current injecting drug users screening positive will require immediate treatment with interferon[18] corresponds to 5000 cases[19] and an expenditure of about £6m[20]. This estimate assumes an average six months of treatment to take account of early termination of treatment in non-responders. It is difficult to translate these figures into a pattern of need over the next few years. Clearly, the backlog will take some time to work off while subsequent recruits to needle sharing IV drug use keep coming forward. There may occur a troublesome bulge in demand. Once the backlog has been worked off, the upper limit of annual numbers among drug users should be equal to new notifications. However, these numbers are rising. For what it is worth, new notifications of injecting drug users in 1993 were about 5000 of whom about 2500 will have shared needles. These figures correspond to an annual interferon caseload of 2500 at an annual expenditure of about £3m[21].

15. Figures for the whole population can be found by applying the proportion of HCV positives accounted for by drug users. Using a figure of about 50%, the cost of meeting the immediate need for interferon treatment will be about £12m, with the annual steady state caseload costing at most £6m.

16. Current information does not suffice to extend these estimates to the demand for tests for HCV antibody (though it seems probable that most drug users in contact with services will already have had a test), referral to hepatologist, liver biopsy to test for hepatitis. However, some evidence may suggest that fears of services becoming snowed under with demand may be overdone. There appears to be some unwillingness among those testing positive for antibody to undergo further investigation. Moreover, the majority of HCV positives do not currently belong to any risk group, are unlikely to come forward for testing and in the absence of a campaign to test everyone will not come to light whilst asymptomatic.

17. Forecasting the demand for services in the longer term is even more difficult, and has not been attempted in this note. It seems quite possible that many of those infected but who have no other health deficits may prove more resistant to progression of the disease.

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[18] Hepatitis C and intravenous drug misusers. DH/AMCD Meeting June 1995. Para 17.

[19] 0.2% of the population are injecting drug users according to *Sexual Attitudes and Lifestyles* - 100,000; about half share needles - 50,000. Number of cases requiring interferon = 50,000(needle sharing current IVDUs all assumed HCV positive) x 0.1(10% immediate need) = 5000.

[20] on this source's assumption of a six month course of interferon therapy costing £1300.

[21] 2500x£1300

Cost Effectiveness of Interferon Therapy

18. The effectiveness of interferon alpha is different at different stages of the disease and this pattern may have consequences for setting priorities and for the timing of treatment. For example, it would save a great deal of money if it were to prove cost effective to defer treatment until the onset of cirrhosis because only a minority of patients with chronic active hepatitis develop cirrhosis. Happily, an Australian paper on cost effectiveness sheds some light on these important questions[22]. However, the cost effectiveness ratings apply to the assumptions the authors have made about a range of factors and do not always extrapolate readily to other situations.

19. Interferon is much less effective in clearing HCV in patients with cirrhosis than in those still at the stage of chronic active hepatitis. But the cost effectiveness is not much less because only one in five chronic active hepatitis patients will go on to cirrhosis so that at least four fifths of the therapy falls on stony ground. Those with cirrhosis have a four in ten chance of dying from HCV disease, half from liver failure and half from hepatocellular carcinoma. Those with chronic active hepatitis have an 8% chance of dying from HCV disease. Interferon clears virus in 4% of those with cirrhosis and 26% of those without cirrhosis. The table explains and summarises these figures:

EFFECTIVENESS OF INTERFERON IN TWO GROUPS OF PATIENTS		
	Chronic active hepatitis	Cirrhosis
Without interferon		
Proportion going on to cirrhosis	20%	100%[a]
Death rate from HCV disease	8%[b]	40%
With interferon		
Proportion cleared of HCV	26%	4%
Average number of lives saved per person treated	0.021[c]	0.016[d]

[a] by definition
[b] 20% go on to cirrhosis and suffer the 40% death rate
[c] 26% clearance rate applied to the 8% death rate
[d] 4% clearance rate, 40% death rate

20. On these figures interferon is not very effective. In patients without cirrhosis it saves life in 2.1% of those treated; in those with cirrhosis the rate is a little lower at 1.6%. The much lower clearance rate in cirrhosis is offset by the proportion chronic active hepatitis patients in whom the disease does not progress.

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[22] Shiell A, Briggs A, Farrell GC. The cost effectiveness of alpha interferon in the treatment of chronic active hepatitis C. *Med J Aust* 1994;**160**:268-72.

21. Interferon therapy does not appear to yield significant savings in the cost of a lifetime treatment career. The unit costs and cost effectiveness ratings are as follows:

COST EFFECTIVENESS OF INTERFERON IN TWO GROUPS OF PATIENTS		
	Chronic active hepatitis	Cirrhosis
Net cost of therapy per person treated	£3200	£2500
Rate of lives saved per person treated	0.021	0.016
Life expectancy gain per life saved	6	16
Cost per life saved	£150,000	£156,000
Cost per life year saved	£25,000	£10,000

22. These cost per life year figures are high. They are much higher in those without cirrhosis because terminal HCV disease develops much later and the gain in life expectancy is correspondingly less. There are many better uses of health care resources, but on the other hand the NHS carries out treatments such as renal dialysis whose cost effectiveness is comparable to treating the non-cirrhosis patients.

23. The study is perhaps a little pessimistic on some issues. For example, terminal HCV disease reduces quality of life. Preventing it therefore yields quality of life gains to add to the gains in life expectancy. In other words the cost per quality adjusted life year (QALY) would be lower. Secondly, the cost of therapy makes no allowance for discontinuing therapy at 12 weeks in those showing no response. An allowance for this would reduce the net cost to £1600 for cirrhosis patients[23], £2825 for those without cirrhosis[24]. On these figures the cost per life year saved would be £6250 for cirrhosis patients, £22,400 for those without cirrhosis. The further analysis below assumes discontinuation in non-responders.

[23] 60% do not respond. A year's therapy costs £3000. A year's therapy for 40% and six months for 60% costs on average £2100: 0.4x3000 + 0.6x1500.

[24] 25% do not respond. A year's therapy for 75% and six months for 25% costs on average £2625: 0.75x3000 + 0.25x1500.

24. In view of the deadweight expenditure associated with therapy in those who do not have cirrhosis, it may be worth questioning the value of the poorly targeted policy of starting treatment before patients develop cirrhosis. The improvement in life saved is 0.018 per person[25]. The number of life years saved per life saved is the same - six. The chief difference in cost lies in giving interferon therapy to five people instead of one, an extra £11,300 per person[26]. There would also be additional costs due to time discounting since treatment would be many years earlier, but this has been neglected here. The cost per life year is then over £100,000, an expensive method of buying life years.

25. There is therefore a case for confining interferon therapy to those in whom cirrhosis has developed. This analysis relates to a cohort at average age of 42 at the start of treatment. For patients ten years younger, the corresponding cost per life year would be £42,000 from treating now rather than waiting for cirrhosis to develop and the argument in favour of deferral still has some force.
26. It should be possible to pinpoint the best age to begin treatment on given criteria, but such fine tuning is not attempted here.

27. The estimates set out above rely on information which remains uncertain and possibly contentious. A later study of interferon therapy reaches lower estimates of cost per life year saved[27,28]. It focuses on patients without cirrhosis and puts the cost per life year at £2000 to £9000 depending on the rate of progression to cirrhosis and the subsequent death rate.

28. The report of the later study is unclear on certain points, ruling out full reconciliation with the Australian paper. The age of the group studied, the lives saved per person treated and the life years saved per life saved all differ from the Australian paper but not by enough to account for more than a small proportion of the discrepancy. The key difference appears to be the duration and cost of therapy needed to achieve a 25% virus clearance rate, the later study assuming six months and the earlier study a year. Differences in the costs of lifetime treatment careers also play some part.

29. Noting that interferon should improve the quality of life as well as increasing life expectancy, the later paper also presents ratings in terms of cost per QALY. Cost per QALY at £1500 to £2000 compares favourably with other uses of health care resources.

30. An editorial in the same journal criticises this study as overoptimistic[29]. It quotes the response rate as 5%-20% rather than 25%. However, this criticism also applies to the Australian paper.

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[25] Starting with a cohort of 1000 without cirrhosis, interferon therapy saves 21 lives. In the absence of treatment 200 go on to cirrhosis where therapy saves 0.016 lives per person treated, or 3.2 lives. Net saving from early treatment is 17.8, a rate of 0.0178 per person.

[26] £2825x4

[27] Dusheiko G, Roberts J. Cost effectiveness of alpha interferon treatment of chronic hepatitis C. Unpublished speaking notes and slides.

[28] Dusheiko GM, Roberts JA. Treatment of chronic type B and C hepatitis with interferon alpha: an economic appraisal. *Hepatology* 1995;**22**:1863-73.

[29] Koff RS, Seeff LB. Economic modelling of treatment in chronic hepatitis B and chronic hepatitis C: promises and limitations. *Hepatology* 1995;**22**:1880-2.

31. The discrepancies between the two papers suggest that a reliable cost effectiveness rating requires firmer information as to the effectiveness of different durations of therapy.

32. A French study of this very factor suggests increasing returns to higher durations of therapy instead of the more usual diminishing returns[30]. This result implies that if any duration passes muster the longest should be selected. The implications for expenditure are considerable.

33. The three and a half year French study investigated three different interferon regimens. Various measures of response were used. The regimens are as follows:

Interferon Regimens	
1	18 months @ 9m units a week
2	6 months @ 9m units a week; then 12 months @ 3 units a week
3	6 months @ 9m units per week; repeat once if serum ALT still raised.

It is possible to compare the regimens in terms of cost per response (judging by a normal serum ALT after three and a half years). The cost and cost per response are as follows:

COST EFFECTIVENESS OF INTERFERON				
Regimen	Response rate %[31]	Cost of regimen £	Cost per response £	Incremental cost per response £
1	22	4212	19,145	15,600
2	10	2340	23,400	22,932
3	8	1881	23,517	23,517
D&R	25	837	3,348	-
Shiell et al	26	3170	12,192	

[30] Poynard T, Bedossa P, Chevallier M, et al and the multicenter study group. A comparison of three interferon alfa-2b regimens for the long-term treatment of non-A, non-B hepatitis. *N Engl J Med* 1995;**332**:1457-62.

[31] percentage with normal serum ALT after three and a half years; D&R: after six months [DN check]

The French study implies much higher cost per response than Dusheiko and Roberts (D&R) and higher than the Australian paper. The declining incremental cost per response with the longer durations indicates increasing returns. It is not possible to be precise about the corresponding cost per QALY but it would also fall with duration. However, the incremental cost per response even for the longest duration is higher than the cost per response which corresponds to a very high cost per life year in the Australian paper. As a result it may be that none of these regimens gives good value for money.

34. A tentative round up of the results on cost effectiveness emerging from these studies is as follows:

    a. Cost effectiveness depends on a factor which is not yet certain: the effectiveness of different durations of therapy.

    b. Analysis of cost effectiveness performance suggests that patients with cirrhosis should have priority over those at an earlier stage in the natural history of the disease. There may be better uses for health service resources than treating HCV patients who do not have cirrhosis.

35. The implications for expenditure highlighted by the cost effectiveness analysis are as follows:

    a. The level of expenditure depends heavily on the duration of treatment and decisions about the stage of disease at which treatment is offered;

    b. Given the increasing returns in the duration range studied and the high cost per response at any duration, there remains a danger of spending a great deal of money which only just satisfies vfm criteria.

Appendix 1

THE PREVALENCE OF HCV AMONG IVDUs

1. The Addicts Index provides a base on which to make an estimate of prevalence of ever drug addicts in the population, ie the prevalence implied by this year's incidence - "new notifications". There are two methods.

Prevalence estimate based on 1993 new notifications

2. The first method projects annual incidence. Annual incidence 10,124. The average age of a new notification is twenty five - proportion of population of 830,600 twenty five year olds: 1.2%. Since new notifications always remain one time drug addicts, prevalence in the population 25 and over is 1.2% if drug addicts have average life expectancy, but their life expectancy may be lower.

3. The proportion in the whole population needs to take account of population under 25 not affected. This leaves only 34m population so whole population prevalence is 34/51 of 1.2%: 0.8%. The proportion of drug addicts currently injecting is 56%. This proportion may understate the proportion ever injecting since some of those not currently injecting may have done so in the past or may do so in the future. But using the current rate of 56% ever injecting drug users prevalence is 0.45%. And about half of these will not have shared needles[32] and so will not be at risk of HCV. Numbers of notified drug addicts at risk from HCV: 0.23% of population: 115,000.

4. This estimate counts only serious addicts, though this is also the group exposed longest. Moreover, since annual incidence has been rising using current incidence as a guide to prevalence is a source of overestimation.

Estimate based on cumulative incidence

5. Injecting drug abuse dates from the late 1960s. Cumulative incidence since about 1970 therefore gives an estimate of current prevalence, after adjustment for survival. The Home Office Statistical Bulletin gives data for new notifications back to 1983. Rates between 1970 and 1983 can be estimated by linear interpolation. The same source gives data on death rates by number from first to the seventh year following notification. Death rates for earlier years can be found by extrapolation. This method gives the number of drug addicts surviving as 112,000 for UK. Using the estimate of 56% injecting and half of those sharing needles, the estimate of notified drug addicts at risk is about 30,000. It would be reasonable to expect all of this group to be HCV positive.

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[32] Johnson AM, Wadsworth J, Wellings K, Field J. *Sexual attitudes and lifestyles*. Blackwell Scientific Publications. Oxford. 1994.

Estimate based on surveys

6. The *Survey of sexual attitudes and lifestyles* included injecting drug abuse and the proportion ever sharing needles. It found no respondents over 44. The number of those ever sharing needles is 60,000 (cf the number of ever injecting drug abusers: 120,000[33]).

7. A Home Office survey[34] found that less than half of one per cent of the population aged 16-59 had ever injected drugs, ie less than 150,000, a figure broadly consistent with the estimate in the previous para and implying a similar estimate of those ever sharing needles.

Estimate based on methods used in the AIDS projections

8. In 1988 the Department of Health AIDS working group made an estimate of needle sharing injecting drug users based on 1987 notifications[35]. Replicating the calculation using the latest data gives the following result. Notifications in 1993 were running at a rate of 24,000. This is believed to represent one tenth of the total, giving about a quarter of a million current addicts of notifiable drugs. The AIDS estimate doubled this figure to take account of non-notifiable drugs: half a million. Applying the latest data on the proportion injecting takes the figure to 280,000. A third of this group share needles: giving 90,000 current drug users at risk of HCV. And an allowance for those who have stopped taking drugs would have to be added in.

Discussion

9. The main drawback of the estimate based on the AIDs projections is that it depends too much on the tenfold uplift to take account of underreporting. Moreover, since the estimate aspires to cover only current IVDUs, and we need ever IVDUs it leaves us rather up in the air.

10. The method based on inferring prevalence from current incidence only works in steady state. Since incidence has in fact been rising quickly, it is too simple.

11. The cumulative method based on notifications and the Sexual Attitudes figures at least deliver estimates of the stock of needle sharing ever IVDUs. Both carry the drawback of incomplete coverage. However, their gaps may be to some extent complementary. The fear is that the Sexual Attitudes survey misses the more serious cases, while if anything the notifications are likely to be the more serious cases. Adding the estimates from the two sources runs the risk of overlaps and gaps covered by neither. The estimate so based is about 90,000.

Conclusion

12. Despite all the uncertainties, the evidence points to a prevalence of about 100,000 ever IVDUs who have shared needles and who are therefore likely to be HCV positive. However, prevalence up to half as much again 150,000 remains a possibility.

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[33] at least judging by the combination of the age specific proportions quoted in table 9.4 and the population in the relevant age groups - the text itself quotes 175,000.

[34] Mott J, Mirrlees-Black C. *Self reported drug misuse in England and Wales: findings from the 1992 British Crime Survey*. Research and Planning Unit paper 89. London: Home Office. 1995

[35] Hillier H. Estimation of HIV prevalence in England and Wales - the direct approach in *Short term prediction of HIV infection and AIDS in England and Wales*. Department of Health 1988.

Appendix 2

THE PREVALENCE OF HCV AMONG TRANSFUSION RECIPIENTS

1. A figure of 40,000 for HCV prevalence among recipients of blood transfusions has gained some currency, in line with a "crude actuarial model" developed by Dr Renton.

2. However, HCV prevalence is only a stepping stone on the way to an estimate of the likely demand for services. In the group infected through transfusion there may be a more direct method. (There are reliable figures for haemophiliacs who are not considered further here.)

3. The direct approach is based on the age distribution of transfusion recipients. We begin by taking stock of the distribution of deaths by cause by age in those known to have HCV antibody. This data shows that few who have acquired HCV over the age of fifty or so would be likely to experience HCV related morbidity, because they would die of other causes first. Moreover, the age specific death rates of these patients are likely to be raised by the condition they were being transfused for.

4. Apart from the elderly[36], the main group receiving blood transfusions is children under five. We can therefore usefully approach the likely need for services by estimating the numbers in this age group who have received contaminated blood.

5. Data for Edinburgh hospitals shows that in 1992 about 400 children under five received blood, two and a half units each on average. The corresponding rate for the population of England is 27,000[37].

6. Calculating the current prevalence of HCV in this group requires two further pieces of information: the period during which HCV contaminated blood donations; and the proportion of HCV positive donors. The risk of HCV contaminating blood probably lasted for 21 years, from 1970 to 1991. The number of children under five transfused over this period is therefore about 560,000. Information on the prevalence of HCV among blood donors is more difficult to estimate, though it is possible to say something definite about the trend. Prevalence is likely to have built up progressively from 1970 onwards with a fall in 1983 when IVDUs were asked to exclude themselves and again in 1985 following the introduction of HIV testing, until screening virtually removed the risk in 1991. The current prevalence rate of 1 in 2000 in new donors will serve as a working figure for the whole period.

7. On these figures the demand for services from the group infected by blood transfusions is unlikely to be on a major scale. The chance of contamination is only about 0.125%[38]. With 560,000 people exposed to a risk of 0.125%, 700 are likely to have acquired infection. With allowance for other groups, it appears that the demand for services may be in the region of 1500, provided that treatment is not offered to those unlikely to survive long enough to develop cirrhosis.

8. The hepatitis C lookback exercise will provide further information on numbers and their breakdown.

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[36] Some young adults receive transfusions, mainly during surgical procedures, with road traffic accidents (RTAs) the most likely reason. But only a small minority of RTA cases receive blood transfusion and many of these die of their original injury.

[37] Edinburgh hospitals serve a population of about three quarters of a million.

[38] 0.05% (HCV prevalence in donated blood) x 2.5 (average number of transfusion episodes per patient under five transfused).

Appendix 3

Unit Costs

HCV: Unit Costs of Procedures	
Test for HCV[39]	
ELISA	£2.50
RIBA	£25
PCR	£100
Referral to hepatologist	
Liver biopsy[40]	
Day case	£360
In patient case	£1270
Course of interferon	£2000-£5000

[39] 1990 prices.

[40] OPCS code J13 - diagnostic percutaneous operations on the liver

ANNEX B

Patients at high risk of infection.

Patients infected by blood.

1. The "Look back exercise" aims to identify people infected with HCV as a result of receiving contaminated blood. It is estimated that this will detect about 3,000 patients who have been infected and are still alive.

Haemophiliacs.

2. All haemophiliacs who were treated with Factor VIII concentrate prior to 1985 may have been infected. Since 1985, heat treatment and other measures will have destroyed HCV in Factor VIII. Thus something in the order of 3,500-4,000 haemophiliacs have been infected. Among this group are the 1200 who were also infected with HIV, half of whom have now died of AIDS. Approximately 50 haemophiliacs have died of liver disease (presumably mainly HCV) in the period 1988-1994. Most haemophiliacs at risk will already have been tested and many of them, where it is felt appropriate, will already have commenced or indeed finished a course of interferon. Colleagues in CA-OPU have investigated claims about the lack of availability of interferon treatment for haemophiliacs on financial grounds; in the main they appear to be unsubstantiated.

Intravenous Drug Users.

3. The most frequent mode of transmission of HCV in the UK is believed to be through the sharing of blood contaminated needles and injecting equipment by intravenous drug misusers. Transmission may have occurred in people who only injected for a short period and perhaps many years ago. Available evidence would suggest that 50-80% of users currently in touch with services will have been infected depending upon where they live (even higher rates are claimed in parts of Scotland).

Patients on Renal Replacement Therapy.

4. Some patients on Renal Replacement Therapy may also be infected with HCV, most likely as a result of previous blood transfusion but there are also concerns about transmission within renal dialysis units. The Public Health Laboratory Service have been commissioned to draft up-to-date guidance to prevent the spread of blood borne viruses, including Hepatitis C, in renal units and it is hoped that this work will be completed by the Summer in 1996.

Health care workers.

5. [DN: Consider adding paragraph here although occupational risk appears to be low.]

ANNEX C

Natural history of hepatitis C and treatment with Alpha Interferon.

1. Following infection with hepatitis C the natural history varies widely. Some patients may recover spontaneously and completely. However it is currently thought that the virus may persist in perhaps 80% of those who have been infected with HCV. Many of these will go on to get varying degrees of liver damage often without symptoms but some will develop the more severe chronic active hepatitis. 20% of infected patients are likely to develop cirrhosis, sometimes only after 20-30 years. A much smaller number may then go on to develop hepatocellular carcinoma (primary liver cancer). End stage liver disease resulting from infection with hepatitis C now accounts for a significant proportion of liver transplants carried out in the UK.

2. Current advice is that those found to have been infected should be referred to a specialist with an interest in the condition for further assessment. This will include sophisticated tests to detect the continued presence of the virus (PCR) and in most cases a liver biopsy. Patients considered to be at risk of progressive liver disease may be offered treatment with Alpha Interferon. The recent granting of a product licence for the use of Interferon in cases of chronic hepatitis C and the testing and referral of patients recommended by the 'Look back' exercise, are likely to raise expectations in other groups who may have acquired hepatitis C.

Alpha Interferon.

3. In general, Alpha Interferon has been used in patients with HCV who have chronic active hepatitis in an attempt to prevent progressive liver disease, though overall the results are somewhat disappointing. 50% of patients show an initial favourable response to treatment (this response usually occurring within 12 weeks of starting therapy). However relapse rates are high with approximately 50% of those responding relapsing within the first year of stopping treatment. Thus only 20-25% of patients with HCV have a sustained response to Alpha Interferon. Interferon treatment is recommended for between 6-18 months, and may cost in the region of £2-5K per patient. Costs could be reduced by terminating treatment after three months in the 50% in whom there was no response, but that begs the question of what should be done for such patients. Studies are currently underway using a combination of Interferon and Ribavarin; if beneficial this could increase the costs further but may be more clinically effective.

4. There are no clear guidelines for the use of Interferon. It is recommended for all patients with moderate or severe inflammatory activity in the liver but at present not for patients with minimal or mild hepatitis on liver biopsy. Such patients are kept under observation with repeated liver biopsy every 2-3 years. Further research may point to the benefits of earlier treatment and there may be increased pressure from patients for this. Thus it is difficult to say what proportion of patients may be offered treatment at the time they present. We are aware this can range from estimates of 10% to 50% in different clinics, but there is no indication they are seeing either the same sort of patients or using the same criteria to determine who to treat.

5. Some experts have suggested that Interferon should not be offered to patients with a history of depressive illness (as these symptoms can become exaggerated and patients feel suicidal) or to patients where there is evidence of ongoing alcohol or intravenous drug abuse. This is related to the difficulties which people with unstable lifestyles face in complying with a rigid and prolonged course of treatment (non-compliance and missing doses is liable to result in the patient not responding) and also because of continuing risks of re-infection with HCV. Interferon depresses the bone marrow, so regular monitoring of blood counts is required. However, any proposal to limit treatment in this way

or to discriminate between patients on the grounds of how they contracted the disease would not be acceptable here although it is open to individual clinicians to decide that a patient who is a current IVDU may not benefit from treatment.

ANNEX D

Research initiatives.

1. The MRC and the NHS are taking forward research on the basic science and treatment effectiveness issues. Effectiveness of treatment is a key area for research; evaluation of the use of Interferon in the treatment of hepatitis C was identified as a top priority for the NHS by the Standing Group on Health Technology in November 1995. The Standing Group recommended a multi-centre controlled trial to assess the effectiveness and cost-effectiveness of Interferon in the early treatment of the hepatitis C virus. The use of Interferon in the prevention of relapse-recurrence was also recommended as an area for assessment.

2. The MRC is currently considering a proposal on hepatitis C which may address these questions. The proposal goes to the MRC's Board in June. The MRC and NHS HTA programme are working together to ensure that a high quality trial is taken forward without delay in this area. This work will complement ongoing R&D, such as the development of other antiviral agents through the pharmaceutical industries.

3. In addition, funding of £1m has been identified by the Department for research. Advertisements calling for research proposals will appear on 20 April. Research will be in:

- *prevalence:*

  see main paper and Annex A;

- *transmission routes:*

  this research will help predict the spread of the condition and increase our knowledge about groups at potential risk;

- *natural history of the disease:*

  research on the natural history of the disease will help inform and advise those at risk and establish the pattern of demand on the NHS. It is, for example, unclear what proportion of those who are HCV positive will progress to liver disease and how quickly.

4. Additional work will involve compiling and maintaining an archive of patients of known date of infection. This will draw on those involved in the "Look back" exercise and those who have been infected via other transmission routes.

ANNEX E

COMPENSATION

1. The main pressure for compensation has come from the Haemophilia Society with significant political support (200+ MPs have signed an EDM calling for compensation and the subject is regularly debated in the house). The principle claim is on behalf of haemophiliacs who were infected with HCV through the use of blood products prior to 1985 (when measures were introduced to destroy viruses in Factor VIII products). Best estimates suggest that some there are around 3,000, who are not already covered by the HIV compensation scheme, are involved. The Society is also seeking extra compensation for the latter group bringing the total nearer to 4,000. Additionally, if compensation were conceded, it would also be very difficult to exclude those infected through blood transfusion. The Lookback exercise is expected to identify some 3,000 such cases but it is likely that the true number is very much higher.

2. Ministers have held the line that the Government is opposed to any form of no-fault compensation but in recent times the Society have been encouraged by what they see as a softening of Ministers' position. Confidentially, Ministers have been considering the possibility of limiting compensation to those most severely affected by HCV infection (eg using cirrhosis as a marker). Official advice has been that (a) objective clinical markers are not easily identifiable or workable and (b) a scheme that was reasonably "cheap" would be unlikely to satisfy the compensation lobby. Estimates based on the Haemophilia Society's own expectation put the cost at over £300m over the next ten years. This takes no account of the administration costs nor the likely knock-on effect in terms of potential claims in respect of other iatrogenic disorders.

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