Witness Name: Katherine Victoria Burt

Statement No: WITN6392001

Exhibits: WITN6392002 - WITN6392267

INFECTED BLOOD INQUIRY

WITN6392198

1991 — No. 2

The Bulletin

TO PREVENT OR NOT TO PREVENT?

Haemophilia treaters should perhaps look again at treating all people with severe haemophilia with factor VIII or IX prophylactically from an early age, was the message from the British Society of Haematology meeting in Glasgow.

Dr Eric Berntorp, Associate Professor, Department of Coagulation Disorders, Malmo General Hospital in Sweden reported on studies of 60 individuals aged 3-32 years who have received prophylactic factor VIII or IX for 2 to 25 years. The aim of these studies was to stop arthropathy, particularly the progressive destruction of the weight bearing joints such as the elbow or knee.

In those 60 studied there was a dramatic reduction in bleeds (patients with severe haemophilia usually have 30-35 joint bleeds a year without prophylaxis) and subsequent joint damage. Although the studies had no control group "because we find it unethical not to give prophylaxis to boys with severe haemophilia A or B" commented Dr Berntorp, "it is important to give prophylaxis from an early age and to try to prevent factor VIII or IX levels from falling below 1 per cent." He added, "Are we over-treating? The answer is "No". If anything we are still under-treating. The only side-effect of the prophylactic approach is the high cost of treatment!"

Dr Berntorp discussed the fact that it may be possible to increase the efficacy of treatment and reduce cost by implanting a pump which would keep factor levels at around 5 per cent and thereby eliminate the problems of joint damage in severe haemophilia. "However, there are still many technical problems to overcome".

Responding to Dr Berntorp, Dr Geoff Savidge, Director of St Thomas' Hospital Haemophilia Centre reflected on the disparate views of UK treaters. Some considered prophylaxis unethical, non-indicated and not financially viable. Others thought it ethical, indicated and financially feasible.

Professor Arthur Bloom, Director of the Regional Haemophilia Centre in Wales defended prophylaxis. "It is self evident that factor VIII or IX deficiency should be considered in the same light as insulin use in diabetes. The logical and best treatment would be to keep patients in a 'normal' state for as long as we can and on that basis prophylaxis seems to be reasonable." Professor Bloom concluded: "If the material is non-toxic and the economics will bear it, then this is the way haemophilia treatment should progress."

A member of the Society expresses his view on Prophylaxis on page 6.

Report from British Society of Haemotology meeting in Glasgow

CONTENTS

Increased stocks of 8SM from Bio-Products Laboratory

We are happy to report that BPL have increased stocks of 8SM — high purity factor VIII — available. They are described as adequate to meet current demand. Members will recall that we highlighted the advantages of high-purity product in Bulletin No 1 1991.

NOT RELEVANT

HIGH PURITY FACTOR IX REDUCES RISKS

Trials of a new high purity factor IX may eliminate the risks of virus infection and thrombogenic complications in haemophilia B treatment according to Dr Garrett Bergman, Director, Medical and Scientific Affairs at Armour Pharmaceutical Company, speaking at the BSH meeting in Glasgow.

The factor IX under investigation is purified by a monoclonal antibody immunoaffinity column process — the first of its kind. This process eliminates viruses and clotting factors such as II, VII and X which are currently found in PCC (Promthrombin C Complex) the most common treatment for haemophilia B. "In all of the trials, using the high purity factor IX for home therapy or to cover trauma or surgical cover, have we seen any evidence of virus infection or thromboembolic complications" commented Dr Bergman.

The licence for the new high purity factor IX is expected sometime this year.

THE HAEMOPHILIA SOCIETY

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NOT RELEVANT

NOT RELEVANT

YOUR CHILD HAS HAEMOPHILIA

DON'T PANIC

Discovering that your child has haemophilia is a traumatic experience, resulting in a multitude of emotions, some of which may have disappeared, others that will stay with you for a long time. One of these emotions is often fear:- fear of the unknown, if you are unfamiliar with the condition (as in cases where there is no known family history); fear about whether you will cope; fear about your child's safety; fear about recognising bleeds; fear about treatment; and so the list goes on.

A useful strategy for dealing with this fear is to obtain as much information about the condition as possible, but don't attempt to read it all, or absorb it all at once, as it is easy to become "bogged down".

Over a period of time through contact with your Centre, your own reading and meeting other families or using the Haemophilia Society literature, your knowledge will grow and your confidence will also increase.

Whilst gathering information it is a good idea to find out certain information from your Centre that will enable you to use your Centre and its staff to your best advantage. Table 1 contains the information you need to find out about your Centre.

When visiting your Centre, don't be afraid to ask questions, no matter how trivial they may seem. The staff will be only too happy to answer your queries, if they can! If you think of questions when you are at home jot them down on a piece of paper and take them with you next time you visit the Centre. This will help you to remember what you wanted to ask, as often in the flurry, activity and anxiety that surrounds treatment the questions are forgotten until you reach home again!!

Many parents worry in the early days about how to recognise a bleed — try not to! Most bleeding episodes are undramatic and become obvious whilst observing your child in his normal activity. He may seem reluctant to use one particular limb whilst playing, or cry or complain of pain when you touch a part of his body in washing or dressing.

Until your child becomes mobile, it is likely that he will have few problems. As he becomes more active he may experience more bleeds. Table II provides a quick guide to bleeds. The main thing to remember is that if you are worried or in doubt either phone or attend your Centre.

Another common cause of concern for parents is that every little fall or knock will result in a major bleed. Obviously this anxiety often makes parents want to wrap their child up in cotton wool, but it is important to remember that children need to learn about their own space and how to move around in a world full of obstacles without hurting themselves. If a child is not allowed to move around freely like other children he will not learn that the world has corners!

All children need supervision, in order to protect them from danger, but try not to restrict your child any more than you would a child who does not have haemophilia. As your child grows your Centre may advise you to discourage certain sporting activities, but normal safety precautions are sufficient for the pre-school child.

If you have no transport and need to go to the Centre, because you think your child has a bleed, you are entitled to use the 999 ambulance service. Show the ambulance person your child's green medical card (this should be supplied by your Centre) and make sure that they take you to your Haemophilia Centre and not a local hospital even if the local hospital is nearer.

It is a good idea for your child to wear an SOS talisman or bracelet, containing information about his haemophilia, in case he is taken to hospital in an emergency, when you are not with him.

Remember, you are not alone. Although the staff at your Centre cannot know exactly how you feel, they can help you in lots of ways so don't be afraid to ask. Table III shows some of the ways that your Centre may be able to help you. Unfortunately not all Centres have the same resources but the Haemophilia Society, especially if there is a local group can provide you with many support services. Although living with haemophilia often seems difficult, remember that your son has a condition that can be managed effectively and he can expect to have a happy, healthy future.

Sister Angela Westoby, Birmingham Children's Hospital

TABLE I

What to find out about your Centre
— Who's who?
When your child has a bleed:-
— Where should you go?
— Is it the same place day/night/weekends?
— Who should you contact? doctor/nurse?
— How is this done at your particular hospital?
— Is it possible to phone for advice?
— What is the phone number?
— Who should you ask to speak to?

TABLE II

Quick Guide To Bleeds

1. **Superficial bruises** — these do not necessarily need treatment but large hard bruises, especially on the bottom, should be seen at your Centre.
2. **Knocks to the head** — Your child should always be seen at the Centre following hard knocks to the head.
3. **Mouth/tongue bleeding** — Attend the Centre.
4. **Prolonged/severe nose bleeding** — Pinch the nose firmly for five minutes, holding head forward. If bleeding has not stopped or restarts, attend the Centre.
5. **Blood in urine or stools** — Attend the Centre.
6. **Swelling or pain anywhere** — Attend the Centre.

TABLE III

What Your Centre Can Do To Help

1. Source of information about:-
haemophilia
treatment
benefits
local contacts
other Centres (for holidays etc)
2. Provide teaching for home therapy
3. Provide a listening/support/advice service
4. Assist in negotiations re childcare/nurseries/schools
5. Provide support for specific difficulties (eg social worker/psychologist)
6. Assist in organisation of support groups/activities
7. Home visiting

NOT RELEVANT

GRO-D *is definitely in favour*

My Key To A Normal Life Style

There is, understandably, much despondency amongst people with haemophilia and their families today. I refer, of course, to the scourge of AIDS which has become such a dominant influence in the lives of so many and changed them so much.

However, in my own life a change has also taken place over the past five years, but a more positive one. I have severe haemophilia with a factor IX deficiency. As I am aged over 40, I lived through that post-war era of the fifties and early sixties when, effectively, there was no treatment available for the likes of me. Others have written in *The Bulletin* recently of this period, characterised by long spells in hospital, plasma drips, intense pain and permanent joint damage.

It is not my intention here to dwell on the past but to look to the future and to explain how my own lifestyle has improved. Yes, I am fortunate in being HIV negative, but in the early '80s the toll of 30 years + of joint haemorrhages was really beginning to tell. The situation was further exacerbated by my wife's developing multiple sclerosis, with a gradual loss of mobility and balance characterised by that condition.

Where is all this preamble leading you may ask? Well, my joints were deteriorating, my wife's health worsening (she had to give up her job altogether) and my own periods of absence from work were becoming more frequent. Although surgery on my right knee in 1981 was a great help, if I was laid up by a joint bleed my wife and I were effectively isolated, being unable to drive, go shopping etc.

It was at this stage that the Director of my Haemophilia Centre made the decision that I should try a course of prophylaxis. So I commenced injecting 2000 units of factor IX twice a week. That was in May 1985 and I have not stopped since, apart from one brief spell in hospital, following an accident, where I was treated for injuries in the normal "on demand" way.

REMARKABLE

The past five years have been remarkable. The number of spontaneous and traumatic bleeds during that time can be counted on the fingers of one hand. If it wasn't for my legacy of 30 years untreated joint bleeds I would certainly be able to lead a totally normal life. As it is I cope with looking after my wheelchair-bound wife, maintain a full time job and do most of the shopping and housework.

Although our local Social Services have been marvellous, I would not be able to manage if I were still subject to that uncertainty that many of us know so well — the sudden, painful, crippling joint bleed that leaves you helpless so quickly. So, prophylaxis equals no bleeds, which equals being able to live at home and care for a disabled wife, which equals no spells in hospital, which equals being able to earn a salary, maintain myself, my home and my wife — which equals being normal!

Much could be said about the cost of maintaining a single patient on 4,000 units a week for five years. Not much is said about the alternative in my own case. This could be the cost to the Department of Social Security of fully maintaining two people, probably not in their home, but in state or local authority accommodation, plus frequent hospitalisation for myself. I consider that the NHS has got itself an economic deal with myself on prophylaxis!

So there we are, every Monday and Thursday evening, rain or shine, Christmas Day or whatever, in goes those precious 2,000 units. Mind you, it requires an organised lifestyle to ensure there are always enough units, syringes, etc, available and the 100 mile round trip once a month to collect them does become a bit of a chore!

But I wouldn't have life any other way now. I've done it for five years and will continue indefinitely to stop prophylactic injections now would, I am sure, bring my life down around me in ruins.

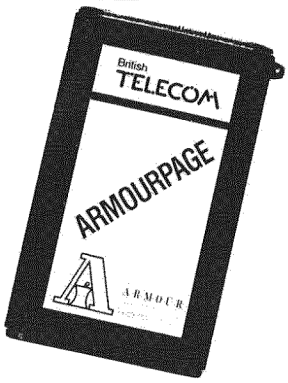
"Cheap imported products"

DO NOT BE ALARMED AT MEDIA STATEMENTS

Some of our readers may have been alarmed by statements in the media on Friday 26 April regarding the potential of a threat to the safety of their blood products.
We would like to immediately reassure you that, to the very best of our knowledge, there is no known problem associated with any blood products currently in use in the UK for the treatment of haemophilia.
In recent months we have welcomed the introduction of new methods of production and purification of factor VIII concentrates and know of no reason for you to feel threatened in the manner suggested by the media. The argument which is being conducted in the medical press relates to changes in the structure of the NHS and the decision to allow 'market forces' to determine the levels of, for instance, the new BPL product 8SM manufactured which we highlighted in our last edition.
In the short-term there is absolutely no cause for concern: whatever product you are currently receiving is safe. The Society prefers patients to be treated with monoclonal or solvent detergent products above all others and regard that level of safety as more significant than the 'paid' and 'unpaid' donor arguments which held more validity in the past than they do now.

NOT RELEVANT

Armourpage Voted An Overwhelming Success



NOT RELEVANT

Armourpage is a British Telecom tone pager which operates in selected regions around the homes of parents/guardians of children with haemophilia. The parents/guardians are given a simple British Telecom Tone Pager; and the school a 10-digit telephone number. In the case of an emergency, the school simply dials the number which makes the pager "bleep" within minutes, alerting the parent, who knows to contact the school immediately.

The happy family, complete with Armourpager.

In April 1990 the Haemophilia Society was pleased to be able to offer on behalf of Armour Pharmaceutical Company Ltd and British Telecom, a free paging service "Armourpage" for all parents/guardians of children with haemophilia (under the age of 16). 463 families took up the offer, the majority of whom had not previously used such a service.

With this in mind the Haemophilia Society has just run a survey amongst Armourpage users to see just how useful the service has been and check up on any problems.

The results were both staggering and extremely encouraging. Over half those approached responded within just two weeks and everyone replying said they would recommend other parents

INCREASED FREEDOM

in their position to apply for an Armourpage. No-one had any problems that couldn't be resolved by a quick battery change or a chat with a Telecom engineer.

Many families felt that having had an Armourpage "life would be impossible without one" regardless of whether they had received a call on the service. The

"We are free to go anywhere with peace of mind. Simple as it may seem to most, it means a lot to us."

Armourpage offered them increased freedom and peace of mind and enabled them to lead a "normal" life again, knowing that they were constantly contactable.

In some cases reluctant schools had been more willing to enrol the child and to allow them to go on school trips and join after-school clubs, knowing that if anything happened the parents would be a simple call away. The children also benefited from not having "mum being dragged along" on school trips — embarrassing even for the shyest of children!

Children gained in confidence and mums and dads resurrected their social life. As one parent explained that before Armourpage "on many occasions my pleasure was lost and therefore the outing a fruitless exercise". Often the outing was a

"The greatest thing since sliced bread."

simple one that many people take for granted. "Little things like going out to do some gardening, having a cup of coffee with a neighbour, going out for a meal with my husband and not having to ring home every half hour to see if. . . has a bleed," explained another.

At a more practical level the use of an Armourpage also reduces the time lag before treatment. This helps ease the pain/discomfort much more quickly and the child can be back on his feet within an hour, whereas in the past it could have taken longer than that just to contact the parent.

"The Armourpage has unlocked the door to freedom from haemophilia."

"It's like a new lease of life for me and my family."

Overall the comments about the scheme varied only in the language used spanning from "the best thing since sliced bread" to "It is a Godsend". As one parent put it "It is the most wonderful thing I possess" — which says it all.

Hot Foot

The majority of parents received calls while shopping. One parent's lighthearted account of receiving a call on their Armourpage:
"The very first time I was out buying some boots. The pager went off, everybody looked at me, and I was convinced the boots I had on my feet were alarmed. The boots might not have been but I was! Without the pager I would not have gone shopping. The shop let me use their phone and I hot footed it!"

"I am now a human being. I don't have an umbilical cord attached to the phone!"

NOT RELEVANT

NOT RELEVANT

Scotland Launches Its New FVIII Product For The 1990's

Dr R.J. Perry, Director of SNBTS Protein Fractionation Centre

Excellent Prospects For Safe Treatment

For those involved in the manufacture of blood products recent years have been dominated by the search for technologies and manufacturing methods to enable patients with haemophilia to be treated with products which are effective and free from the risk of virus disease transmission.

It is gratifying that this search within the UK has proved successful and both the SNBTS and BPL currently manufacture and supply coagulation factor products which enjoy a safety record second to none.

The technology developed and used by both manufacturers in the UK employs the use of severe heat treatment of the product in the final container and provides a high degree of safety which is internationally recognised.

The prospects for the safe treatment of people with haemophilia have never been better. The stringent safety and quality standards for both factory VIII and factor IX concentrates manufactured within the UK and abroad have never been higher.

In additional to these significant technical achievements other advances have been made in the field of coagulation factor concentrate manufacture and processes now exist which can isolate factor VIII from plasma to a level of purity and at a yield which hitherto has not been possible. These techniques have been pioneered by commercial and not-for-profit organisations alike and the new generations of coagulation factor products are becoming increasingly available from a range of manufacturers. Each manufacturer has selected its preferred combination of manufacturing technologies and will doubtless seek to convince both the scientific community and consumers that their product is the one of choice for doctors, patients and health authorities alike, for that is the nature of the consumer market place.

Against this background and the launch of BPL's new product for the 1990's the Haemophilia Society has kindly invited the Scottish Transfusion Service to outline its plans for the coming decade and indicate what products will be available from the SNBTS to treat patients in Scotland and Northern Ireland. This is a welcome opportunity to communicate with our ultimate customers and the invitation is warmly received.

WE ARE DOING A GREAT DEAL

So, what is the SNBTS doing in response to all these world wide developments in haemophilia care?

A great deal is the short answer — involving major building programmes to increase manufacturing capacity, improved stock and distribution management, increased plasma collection programmes to produce the essential raw material to assure short, medium and long term availability of product supplies and, last but not least, a major product development programme to ensure that our customers receive the best possible materials for treatment in terms of product quality, safety, continuity of supply, and value for money.

In January of this year the SNBTS announced its factor VIII Development programme for the future following a 12-month period in which all possible options for a new product were examined. Consultation with Haemophilia Centre Directors has been an important part of this process and the final decision effectively represents a joint decision of the SNBTS and Haemophilia Directors in Scotland and Northern Ireland and has been given formal approval by the Management Executive of the NHS in Scotland.

These decisions were clearly not taken in haste! The final outcome is that the SNBTS is now committed to a programme for the manufacture and

Report from SNBTS

supply of a high potency factor VIII product which will be manufactured using a combination of existing Scottish technology and state-of-the-art purification methods developed by our colleagues in the French Transfusion Service (Centre Regional De Transfusion Sanguine) at Lille.

The product itself will possess all the features of a first class modern high purity factor VIII concentrate, involving very high purity, low dose volume and rapid solubility and will meet the foremost requirement of virus safety through treatment with the well established solvent/ detergent method. Moreover this technology has been selected by the SNBTS to ensure that:

- Patients in Scotland and Northern Ireland will continue to receive the best possible products for treatment derived from the safest source of plasma —the non-remunerated voluntary donor.
- The SNBTS will be able to maintain continuity of supply of NHS product to all patients in Scotland and Northern Ireland for whom the product is suitable —the vast majority.
- Additional manufacturing costs are kept to a minimum so that it will not be necessary to restrict supplies in order to contain Health Service expenditure; nor will this development divert resources from other areas of the NHS in Scotland or Northern Ireland.

MORE THAN ONE ROUTE TO EXCELLENCE

But why not the monoclonal antibody technology I hear you all ask? The simple answer is that the SNBTS has conducted an extensive evaluation of the technical options available — including the detailed assessment of both monoclonal and non-monoclonal technologies offered to the SNBTS for potential use under licence. We have come to the firm conclusion that it would be neither necessary nor cost effective for us to incorporate such technology in our development programme.

Alternative purification processes have been made available to the SNBTS which will deliver a product which in all respects will meet the requirements of prescribing clinicians and the aspirations of patients with haemophilia. These processes will ensure that the wider goals of the SNBTS in respect of self sufficiency and continuity of supply will be achieved and maintained whilst at the same time ensuring that patients receive safe, effective and convenient products. Monoclonal antibody technology is not the exclusive route to these goals nor should we conclude that products derived from alternative technology are somehow inferior. They are not. There is more than one route to excellence!

There is a danger that if policies are defined in restrictive terms consumer choice will be restricted rather than widened. Monoclonal antibody products have set a standard in terms of product purity but it would be wrong to conclude that this is the only way of achieving this particular quality objective, nor would such a conclusion be in the best interest of patient, prescriber nor in the long term of the manufacturer.

But enough of all this — suffice to say that the SNBTS product will possess all the best features of monoclonal antibody produced materials — but without the monoclonal antibody. There is a body of opinion that would regard this as an added quality advantage. This type of product has been routinely manufactured by our French colleagues and used to treat patients in France for over two years. This provides the SNBTS with the unique opportunity of drawing upon their substantial existing manufacturing and clinical experience of the techniques involved prior to launching our own Scottish product.

As with all major product developments this new SNBTS product will not be available immediately or initially in quantities to treat all patients.

The SNBTS development programme launched in January of this year is, however, very much a fast track affair designed bring the product into use at the earliest opportunity.

Thus far the programme is on schedule. The necessary building modifications at the Protein Fractionation Centre have been completed and the first trial production batches are in preparation. When they are complete the SNBTS will be scaling-up and increasing its production output — targeting December 1992 as the date by which the entire needs of patients in Scotland and Northern Ireland will be met by the new high purity product. In the meantime clinical requirements will be met by continued supplies of z8 to supplement the small but growing supply of the new factor VIII.

We look forward to and expect a successful outcome to this major development programme.

Finally and perhaps most importantly we would wish to take this opportunity of thanking our French colleagues at CRTS (Lille) whose support and co-operation has played and will continue to play a key role in supporting our drive always to serve the best interests of patients now and onwards into the 1990s.

NOT RELEVANT

HAEMOPHILIA AND LIVER DISEASE

By Dr C.R.M. Hay, Director, Mersey Region Haemophilia Centre,

INTRODUCTION

Post-transfusion jaundice, caused by hepatitis viruses, became a problem as soon as blood transfusion became relatively commonplace during the second world war. Blood products were also found to cause jaundice when many thousands of GIs were infected with what became known as serum hepatitis from an infected batch of yellow fever vaccine in 1941 / 2. Twenty five years were to pass, however, before the causative agent could be identified as the hepatitis B virus and reliable tests for the virus were not widely available until the nineteen-seventies. Most of these episodes of hepatitis were mild, and although some deaths occurred, almost all patients appeared to make a complete recovery.

Until the end of the nineteen-sixties haemophilic patients appeared largely untouched by this side-effect of replacement therapy, partly because very little treatment was given by present day standards, and partly because the only available treatment came from single blood donations (eg plasma or cryoprecipitate).

Haemophilic patients were thus exposed to blood from very few donors. Isolated episodes of hepatitis B following treatment with cryoprecipitate or plasma were reported in 1969/70 but at this time only 11 per cent of haemophilic patients had biochemical evidence of chronic liver disease.

All this was to change following the introduction of factor VIII concentrate in the mid nineteen-seventies. 77 per cent of haemophilic patients were found to have biochemical evidence of chronic hepatitis by 1978.

Although thought to be caused by transfusion transmitted viruses, it was not immediately clear which virus was responsible for this liver disease. Although a high proportion of these patients had antibodies to the hepatitis B virus suggesting that they had been exposed to hepatitis B, few had a history of jaundice or had the chronic hepatitis B carrier state which is associated with chronic liver disease. It was argued that since haemophilic liver disease was not caused by hepatitis A (infectious hepatitis, not transmitted by transfusion) and not usually caused by hepatitis B that it should be attributed to the newly described non-A, non-B hepatitis (NANB).

ACUTE NON A, NON B HEPATITIS

Although the clinical concept of NANB was first described in 1974 the main causative agent, the hepatitis C, virus was not discovered until 1989. Infection in the general population is probably by contaminated food. Sexual transmission is unusual, and infected patients seldom infect members of their family. The infection seldom makes the patient jaundiced or sick and so most patients are unaware that they have contracted the infection unless blood samples are taken at frequent intervals to look for raised liver enzyme levels.

Despite this, and even if they make a complete recovery, infected patients frequently remain carriers of the hepatitis C virus for life and blood from such individuals will transmit the disease. Since almost 1 per cent of blood donors are carriers of this virus, and since factor VIII and IX concentrate are made on an industrial scale from plasma pools containing thousands of donations, it naturally follows that all factor VIII concentrate not subjected to a special viral inactivation step will be contaminated with hepatitis C.

With hindsight, it is not surprising that a study in 1983 found that all haemophilic patients developed NANB hepatitis after their first injection of factor VIII concentrate, and that there was no difference between American and UK brands in this respect.

HAEMOPHILIC LIVER DISEASE

Although we now know that, in the days before heat-treatment, all haemophilic patients treated with concentrate contracted NANB hepatitis, most did not become ill, and were unaware that they has been infected. Chronic hepatitis, as shown by abnormal liver function tests, developed in 70-80 per cent of individuals but these patients were also usually very well.

Early liver biopsy studies tended to confirm the general impression that haemophilic liver disease was a benign condition causing the patient no problems, and which should not give cause for concern. It was not until the mid eighties, well into the HIV era, that further liver biopsy studies whilst confirming some of the earlier findings showed that serious liver disease did occur in a significant minority of patients.

These studies showed that at least three quarters of haemophilic patients had very mild inflamation of the liver unlikely to progress or to cause problems. About 25 per cent of patients were found to have more severe inflamation of the liver. Although this improved in some patients it progressed in others resulting in cirrhosis of the liver in 15 per cent of patients, usually after many years.

Although probably more benign than some other forms of cirrhosis, cirrhosis following hepatitis C does carry a significant mortality.

PREVENTION

Increasing awareness of transfusion hepatitis during the nineteen-seventies led to the universal adoption of hepatitis B testing of all blood donations, and the closure of American skid-row blood banks. This greatly reduced the frequency of hepatitis B after transfusion, but had little impact on the prevalence of tranfusion hepatitis as a whole since it was usually caused by non A, non B hepatitis, The hepatitis C test is only now becoming widely available after the discovery of the virus in 1989, and all blood donations will be tested for this virus within the next few months.

All tests for antibodies to viruses suffer a common limitation called the "window period". This is the period during which an infected individual may be infected with a virus before the tests for the virus or

HAEMOPHILIA AND LIVER DISEASE

antibody to it become positive. For hepatitis B and C and HIV the window period lasts about three months. If an individual donates blood during this period the infection may be transmitted by that blood or blood even though the tests are negative.

For this reason testing of blood donations can very greatly reduce the transmission of blood-borne viruses but can never eliminate it entirely. This has long been recognised by the plasma fractionators who have been searching for an effective way to render factor VIII concentrate virologically safe since the early eighties.

Early attempts to heat-treat factor VIII concentrate to render it virologically safe were ineffective. Factor VIII was denatured and the end product would not dissolve. Factor VIII of greater purity than had previously been available had to be produced before the problem of loss of solubility following heat treatment could be overcome and before the factor VIII concentrate could be heated sufficiently to kill the viruses.

Indeed, although heat treated concentrates were widely adopted as safe from HIV in 1985, some batches of the concentrates available at this time still transmitted hepatitis B and C since these viruses were very much less sensitive to heat treatment than HIV.

Pasteurisation destroyed viruses effectly but also denatured 50 per cent of the factor VIII. A clinical trial of such a product began in Germany as early as 1981 but continued throughout the eighties and was published only in 1989. Supplies of this product became available much too late to have an impact on the HIV epidemic, are still in limited supply, and have only been licensed for use in this country for about 18 months. Pasteurisation and solvent/detergent treatment of concentrate has now largely replaced dry heating, and all concentrates currently licensed can be regarded as completely safe from hepatitis and HIV

TREATMENT

transmission. Haemophilic patients newly treated in the last three or four years no longer suffer this complication.

Although patients recently treated with concentrate will not become infected with hepatitis, most older patients with severe haemophilia will have been infected with hepatitis C at sometime in the past. Most of these patients will not require treatment, having only very mild liver disease, but a minority with more severe liver disease are at risk from clinical complications of liver disease, and in these patients some form of treatment would be desirable. The only form of treatment currently undergoing trial for such patients is alpha-interferon. This is given by self-administered subcutaneous injection three times a week, and in the doses effective in hepatitis C, has few side-effects.

Early results are extremely encouraging, but this form of treatment may have to be given for a year or more, or possibly intermittently over a period of years, to control the liver disease. The length of time for which interferon should be given, and the patients to whom it should be offered remain to be determined by clinical trial but at present this form of treatment would appear to offer the best option for patients with severe haemophilic disease. One disadvantage of such an approach is that the severity of liver disease can often only be reliably determined by liver biopsy.

CONCLUSION

For newly diagnosed haemophilic patients, haemophilic liver disease is of historical interest only since current licensed concentrates are virologically safe. For older patients, it is usually not an active concern since most will have recovered or will have mild liver disease. A minority of patients are at risk from more serious problems and may require treatment with alph-interferon however, even though the role of such treatment is still under investigation. Certainly, it is one of the functions of every haemophilia centre to monitor all patients for evidence of chronic liver disease and the clinical problems that can result from this.

NOT RELEVANT

NOT RELEVANT

ARMOUR
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We extend our grateful thanks to the Armour Pharmaceutical Company Limited who have kindly donated a sum to the Society to pay for the publication of The Bulletin throughout 1991.

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