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The Bulletin

Patron, H.R.H. The Duchess of Kent

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SYNTHETIC FACTOR VIII

The background facts

Many people would have been awakened on Tuesday October 11 to the news that recombinant – synthesised – factor VIII was undergoing clinical trials in the UK. To many this was unexpected and to others it was the fulfilling of an age-old prophecy. Nonetheless, many people were very greatly excited about it and we certainly had a number of phone calls from people who wanted to get on to the material straight away.

One of the problems with such news is that it is easy to give the impression that a clinical trial means that the product is available to everyone. Unfortunately this is not so and the availability is on a strictly limited basis for the one trial which is currently taking place.

However, that does not detract from the importance of this major step forward for people with haemophilia throughout the world. In the longer term it should mean that in this country people will be able to receive prophylactic treatment and in the rest of the world people whose haemophilia has gone untreated may now look forward to the prospect of treatment. It also means that when commercial 'scaling up' has been achieved, a product which is free from all the 'bugs' and infections we currently know about will be available.

Looking further into the future the steps taken so far could lead to the final solution to haemophilia through genetic engineering. That is slightly further off but, again, its value should not be underestimated.

We are proud that this work had some of its origins at the Royal Free Hospital in London. We are equally proud that basic research funding was made available by the Society in the early days of the work that has led to this welcome news.

GRO-A the first recipient in the UK of this product, was reported to have responded excellently to his first treatment which was given on Monday October 3. Over the next six months he – and a few others who will join the trial – will be monitored very closely. GRO-A is attending the Haemophilia Centre daily at first for careful follow-up to study his progress.

The frequency of his visits will gradually lessen, moving towards home treatment, as the safety and efficacy of the new approach is demonstrated. Once this stage is reached, other patients will start to receive similar treatment. The Centre Director, Dr. Peter Kernoff, stresses that caution is vital in view of the innovative nature of the treatment.

CONTENTS

GRO-A

As already mentioned the association between the Royal Free and the recombinant factor VIII dates back some time to work undertaken by Dr. Ted Tuddenham in purifying factor VIII from blood, using new technology and monoclonal antibodies developed by Dr. Alison Goodall. This development led to a joint Anglo-American venture with purified factor VIII and other reagents being supplied by the Royal Free and its UK-backed backer, Speywood Laboratories – to the American biotechnology company – Genentech. Scale-up to the present level of production by Cutter Biological Inc – part of the Bayer Company – presented many problems and took four years to achieve.

Commenting on this brand new treatment, Dr. Peter Kernoff said: "This is a major milestone in a long story involving a huge investment of money and scientific effort. It is encouraging that in this field very basic collaborative research can be translated relatively quickly into a treatment which will benefit patients at a clinical level."

NR

THE HAEMOPHILIA NURSES ASSOCIATION

REACTION SURVEY

THE IDEA

The HNA survey of reactions to blood products was conceived by the Committee in 1983. A number of nurses noted reactions to blood products occurring in their patients, or had had incidents reported to them by patients, parents, spouses, doctors and ward staff. The incidents ranged from the minor to the major, with no common factors, other than that only major reactions appeared to warrant official reporting. Official reporting itself appeared to vary from place to place as did what, in fact was classed as a reaction.

Some papers had been published relating in part to reactions and their causes as in:—

a) **Allain 1980** stating all factor VIII concentrates contain large amounts of non clotting factor related protein, fibrinogen, fibroactin, IgE, IgM, isoglutinins and albumen.
b) **Tilsner and Reuter 1982** stating allergic reactions to factor VIII were largely attributed to IgG and IgM content and that products containing less immunoglobulins were associated with diminished side effects.

However, no comprehensive survey or study had been carried out to cover the areas of concern expressed by the nurses. Areas of concern were:—

- types of reactions
- to what products
- who was reacting
- where and when
- what could be done

The HNA felt that a survey was essential for the following reasons:—

a) To provide evidence that reactions do occur to IV infusions of factor VIII and factor IX concentrate, and to cryoprecipitate.
b) To identify the type of reaction and relate any specific factors which may contribute to the incidence of reactions.
c) To determine if anything could be done to prevent or reduce the incidence of reaction.
d) To instigate programmes of action if areas of deficiency were identified.

The HNA felt it had a membership geographically spaced enough to carry out such a survey, together with the interest and enthusiasm to complete it. With that in mind the haemophilia directors and the Haemophilia Society were approached with the idea. Both parties felt this was a worthwhile project, and Dr Snaipe at Elstree Blood Products agreed to collaborate with the survey as required. Together the three groups formulated and mutually agreed the survey questionnaire. It was also agreed that yearly results and conclusions would be reported to the Haemophilia directors' meeting and the Society.

THE METHOD

At a meeting of the HNA committee on February 29 1984, the survey form, together with a letter of explanation of the format of the survey and its aims and objectives, was agreed. These were circulated to nurses identified by membership of the HNA who were asked to report reactions initially for a six-month period, that was until the end of August 1984. Since then HNA members have been circulated with information annually and some additional information has been requested:—

1. 1985/86 A request that if a nurse had no reactions reported she would forward a nil return.
2. 1986/87 Reactions to DDAVP were included.

The results have been collated annually and presented to the directors' meetings, the Society and the membership of the HNA by means of a newsletter and at general meetings. The results of the 1984/85 survey was presented as in a paper on behalf of the HNA at the World Federation meeting in Milan in 1986.

Certain study limitations were identified:

1. That not all centres would be included in the study as it was appreciated that some centres did not have a nurse with an on-going role.
2. That "total usage" would be of benefit when determining percentage reactions per product, but in asking for that information we could be complicating the survey.

INCIDENCE AND TYPES OF REACTIONS

In comparison with the results of 1984 and 1984/85 study, the number of patients affected by reactions in 1985/86, 1986/87 and 1987/88 has decreased but the number of reaction experiences has increased as noted in the following table:—

Year	Patients Affected	Reactions	Average Reaction per Patien
1985/86	25	51	2.0
1986/87	40	105	2.6
1987/88	25	75	3.0

Reactions such as headache and light headedness associated with speed of infusion were the most common reported reaction up to the end of 1985. These have not been reported since and hopefully with continued good infusion practice and teaching programmes they are reactions of the past.

However, reactions to products have continued despite purification and better delivery methods. The majority of reactions have occurred during home therapy and have been relatively minor but nevertheless worrying and uncomfortable to those affected. These have included:—

- headache
- after taste
- light headedness
- nausea
- vomiting
- feeling faint
- stomach ache
- flushing

It has to be reiterated that speed of infusion was reported in these cases as being at the recommended rate. Luckily the more severe reactions have occurred in or near to Centres where first-aid has been readily available. These reactions have included:—

- dyspnoea
- rigor
- periorbital oedema
- tachycardia
- bronchospasm
- chest pain

There have been no precipitating factors reported or patients having diagnosed underlying disorders to which the reactions could be attributed.

PRODUCTS USED

Products that have been reacted to over the years of the survey have been unheat treated, heat treated and have become more and more purified. These are listed as follows:—

1. NHS Factors VIII and IX
2. Cutter products
3. Alpha products
4. Armour products
5. Cryoprecipitate
6. DDVAP
7. FFP
8. Porcine

Reactions to cryoprecipitate and FFP have been well documented in the past but averaged out in the HNA survey at 5.8% of the total reactions from 1984 to date. It is felt that this is perhaps not a true reflection of reaction, the reason being that there could be more acceptance of reactions in view of previous reporting and the use of preventative measures.

Many difficult products were assessed and reactions varied considerably. However without every reaction being recorded

(Continued on next page)

LETTERS TO THE EDITOR

The Editor is always delighted to receive letters for publication or with ideas for future articles.

Writers' names and addresses must be supplied, but if so requested, will not be published.

Jury Service

Sir,

I refer to the last Bulletin's article on Haemophilia and Jury Service. I thought the Society together with the leading directors of Centres, encouraged haemophiliacs to lead active normal lives. In the last paragraph we seem to be encouraging people to get out of their duties.

Yours etc.

B

Sir,

We are all aware that there are families whose lives are restricted because of haemophilia. They require and deserve all the support the Society can give. I would not presume to comment on any individual circumstances but I would question the wisdom of the Society encouraging people to use haemophilia as an excuse to opt out of the sort of duties anyone in this country might be asked to perform.

We are constantly at pains to emphasise to schools, employers and the general public that haemophilia (and HIV and AIDS) is not to be feared, nor does it prevent people from leading a normal life and making a contribution to society.

If a person with haemophilia needs help he should go to his Centre or the Society to get it. But, we all know that there are a few people with haemophilia who are happy to use it as a good excuse to avoid the responsibilities of normal life – they also need help, but not of the type suggested in this article.

Yours etc.

C

Information required for TV film

I am preparing a 30 minute documentary film for BBC-2 about harassment and discrimination suffered by people with AIDS, and those who are HIV antibody positive.

If any of the readers of The Bulletin has experienced problems at work or with housing or insurance, schools or the social services – whether through actually having the HIV virus, or through fear that they MIGHT have it – I would very much like to talk to you.

I should make it very clear that at this early stage of the research, our conversation would be entirely OFF THE RECORD and any information would be treated in the strictest confidence. If, at a later date, you agreed to allow me to use some of the information, there are many ways of keeping your identity secret – perhaps by allowing an actor to use your words.

You can contact me on my direct line at work GRO-C (There is an answerphone after 6 pm). If you prefer, you could write to me at GRO-C GRO-C London GRO-C

Thank you.

Deborah Perkin
Producer,
BBC Documentary Features

REACTION SURVEY

(Continued from previous page)

and knowledge of total usage, no one product can be implicated. All products had attributed to them, flushing, headache, after taste feeling shivery and feeling cold. Nausea occurred in all products except DDVAP, FFP and Porcine. Periorbital oedema occurred in FFP, Alpha, Cutter and NHS products. Rigor occurred in Armour, NHS and Alpha products. The combination of reactions appeared to be endless, we found no one reaction specific to any one product.

OTHER FACTORS

From data collected the most commonly affected age group is between twenty and thirty years. The person giving the infusion was found to be most frequently the patient or a relative, followed by a nurse. Doctors appear to be only giving a small number of infusions. All reports from 1985 have recorded that recommended diluent volume and recommended infusion rates were correct. Increase in usage of antihistamines and steroids has continued.

CONCLUSIONS AS THEY RELATE TO THE ORIGINAL AIMS

a) Evidence has been found that reactions do occur to IV infusions of factor VIII/IX concentrates, cryoprecipitate and DDVAP.

b) Identification of types of reactions have been noted. The relation to specific factors has been found especially in the area of speed of infusion.

c) Training programmes in home therapy for staff and patients have been suggested as a means of helping to prevent or reduce the incidence of reactions to the use of existing material such as the Centre directors' handbook is recommended. Examination of methods of first-aid in the event of reaction merits study.

d) Programmes of action in areas of deficiency were identified, are suggested as follows:—
   - Drawing up treatment administration guide lines to a required minimum standard which would form the basis of ongoing training programmes.
   - Provision of updated home therapy programmes at regular intervals.
   - Continued surveillance of reactions to blood products, perhaps with a wider remit. The reference Centre directors of the United Kingdom are setting up a working party to look at blood products in general. This will include reactions and maybe the outcome will be a co-operative study.

The committee of the HNA would like to thank all the nurses who have participated in the study over the years. Thanks also to Susan Battersby and Eileen Barraclough (secretaries at Bradford Royal Infirmary) for their patience and support in typing various manuscripts.

DISCRIMINATION

Discrimination surrounding HIV infection has become a major concern for many people with haemophilia.

The Society would like to compile a collection of experiences from people with haemophilia who have been discriminated against, however slightly, on account of HIV/AIDS. With this information we will therefore be able to work on various projects to attempt to reduce such prejudice.

If you or your family have been discriminated against please write to GRO-D explaining what happened.

There is no need for you to put your name on the correspondence and all information will be treated confidentially.

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DARE TO SURVIVE – DOES THE CHALLENGE EXIST?

A recent front page article in The Bulletin, 'Haemophilia and AIDS: A personal view', captured many peoples' imagination. It talked positively about living with HIV infection and pointed out that a diagnosis of AIDS is not necessarily the automatic death sentence that it is perceived to be.

The author, a man with haemophilia and AIDS, also pointed out that Centre staff and people with haemophilia can collude together in not diagnosing HIV related symptoms, "neither party wanting to hear the bad news".

The article closed by discussing the availability of effective treatment in managing HIV problems. More importantly, however, it touched on the need for the individual to come to terms with his diagnosis and take an active role in living with and controlling AIDS. As was emphasized, *Dare to survive".*

As a result of the article there has been a steady stream of enquiries concerning any new treatment for HIV infections. There has also been an increase in requests for information on the general principles of *"Wellness"* or holistic medicine.

HOLISTIC MEDICINE

The idea of the latter is that it works alongside established medicine. However whilst that treatment is concentrating only on one specific symptom, "Wellness" approaches the body as a whole and follows the belief that positive health can only be achieved by using the mind, body and spirit. The theory behind Wellness is that there are no simple solutions to our state of health but if we do combine the control of our whole body with established medicine we can improve our general state of being.

Holistic health is not an easy process. It demands an active commitment on the part of the individual to draw on his or her own healing powers. This can be done through various means but often involves using techniques such as visualisation, imagery, meditation and positive affirmations. The object is to develop a strong, positive, mental self-image, but individuals are free to take what fits them and discard what they do not feel comfortable with.

Holistic health and Wellness programmes can by no means cure HIV although some people have claimed startling results. However, the principle of holistic health is that it offers a general improvement in the quality of life, thus by implication a reduction in stress. Clearly such a situation can have positive affects for people with haemophilia and HIV, even to the extent that one man with the virus, who swears by positive living and holistic health, bounced in to the Society recently and announced that he had been informed by his Centre director that his T4 Cell count ratio was *higher* than normal!!

The challenge to *"dare to survive"* can be taken up. Control of mind, body and spirit can be restored. At the same time a general increase in awareness and a hightened sense of being can arise. If people with haemophilia, their partners, families and friends are interested in finding out more about Wellness, please contact Jonathan Cooper at the Society. He has established links with recognized authorities in this area and will therefore be able to advise you on this subject.

GRO-D

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W.F.H. – 25th ANNIVERSARY

The World Federation of Hemophilia celebrated its 25th year with the publication of a special issue of its journal. The following article was written for the publication by Dr. Tony Britten. Dr. Britten, GRO-C *works with the League of Red Cross and Red Crescent in Geneva.*

The 25th Anniversary of the World Federation of Hemophilia, provides an opportunity for reflection. Frank Schnabel's genius has given us a remarkable organization, a unique international collaboration of patients and professionals. That Frank will not be with us in person on this occasion is Marthe's tragedy and our loss too, but his spirit is irrepressible and lives on among us.

Frank's creation has generated much action, excitement and change for the better, but also tragic disappointment. I shall not attempt a full historical review, but shall refer to highlights as I remember them.

I first met Frank in 1964, in Amsterdam, at the second meeting of his small international team. These were the days of excited optimism; treatment with plasma products was becoming accepted. There was a new freedom, and it was Frank's dream that it could reach haemophiliacs everywhere.

The 1968 W.F.H. Congress in Montreal was an important milestone. It was the first major scientific event in the series. Cryoprecipitate was clearly a reality. Lyophilized concentrates were increasingly available. Surgery was becoming safe for most haemophiliacs. Carol Kasper reported outpatient dental extractions. This was a time when there seemed to be no limits. The following year, in Moscow, I proposed a toast "to the time when normal people wish that they had haemophilia!" The International Haemophilia Training Centres were born.

DECADE OF CONCENTRATES

The 1970's was the decade of concentrates, of growing industrialization. The profiferation of products provided a new opportunity – home treatment – the freedom for a haemophilic family to give infusions without direct supervision. The resulting independence made travel safe and simple. It made daily life possible without the inevitable interruptions for medical treatment.

The 1970's also brought widespread use of prophylaxis, a more controversial development. It was now possible by regular infusions to prevent bleeding. For those who could afford it, and tolerate the burdensome routine, prophylaxis brought a new level of certainty to life. Severely affected haemophilic boys were beginning to compete in contact sports. Nothing was impossible, it seemed.

Prophylaxis also rewarded the industry. Profits were soaring, especially in the Federal Republic of Germany where liberal national insurance laws provided incentives to increase doses and elevate prices. Spectacular successes were reported using massive doses to treat inhibitors. In some cases the annual cost ran into millions of dollars. Where would it all end?

This industrial affluence created a new problem. Directors of treatment centres could influence these profits through changing prescription patterns. It became essential for manufacturers to court these powerful decision-makers; free travel and research grants came to be expected. This method of securing the industrial oligarchy has become entrenched in the haemophilia care community.

Stormclouds began together in the '70's. Reports of liver damage and, occasionally, death from liver disease provoked urgent research. We thought testing for hepatitis B would be the answer, but then we learned about non-A non-B. Treatment with concentrates was evidently not free of danger.

The conspicuous failure of modern therapy to reach the poorer nations was another troublesome problem. Could this be lack of knowledge? . . . or money? Actually it was due to lack of organized blood transfusion services.

SUCCESSES AND FAILURES

These successes and failures were inter-related and, in their relationship, accounted for the only important lapse of judgement of the leadership of W.F.H. The great faith in industry and its products and the lack of interest in basic blood transfusion (cryoprecipitate and plasma) had the effect of restricting treatment to the wealthy. Production in the hands of only a few companies, dominated by the United States, led to worldwide dissemination of those chronic viral infections transmitted by factor VIII concentrates.

The 1980 Bonn Conference, the start of the decade of the '80's was a splendid affair, launching a new initiative to improve the availability of plasma products, comprehensive care and haemophilia organizations. It was my privilege to play a small part in the first of these, working with a task force including Fereydoun Ala, Charles Carman, Franz Etzel and Cees Smit Sibinga. Quickly it became clear that there were grave difficulties in many developing countries.

Lack of money blocked importation of concentrates. Lack of organization blocked domestic production of cryoprecipitate and plasma. Haemophilic patients were dying untreated. Our final report to the 1984 Rio de Janeiro Congress was depressing, but it led to the formation of W.F.H.'s Blood Resources Committee, chaired by Cees Smit Sibinga.

While all this was going on, other events were overtaking us. In 1982 we learned of AIDS. Its appearance in haemophiliacs suggested a new infection but there were many bewildering features. Some of us, myself included, were slow to realise the gravity of what was happening. Now tens of thousands are infected and several hundreds of cases of AIDS have been reported in haemophiliacs. Many of us have lost friends from this disastrous illness. One must face the additional fear of spread to wives and loved ones.

More cheering has been news of improved products for treatment. Factor VIII can be prepared almost pure from monoclonal antibody columns. Promising methods are available for viral inactivation.

Still more exciting is the progress made towards commercialization of human factor VIII produced in cultures of non-human cell strains.

RECOMBITANT FACTOR VIII

Even recombinant factor VIII, when perfected, will not be a cure. But new genetic engineering technologies offer promise. The future is much brighter than it was for those who grew up when the only effective therapy was family love.

In ending this piece I must refer to one other aspect of haemophilia. As infusion therapy became routinely available I saw many families become obsessed. A haemorrhage became evidence of failure. Parents would infuse their sons at the slightest sign of bleeding. The resulting anxiety became a way of life for these young men. Life became the full-time task of dealing with haemophilia. Treatment Centres asserted a dominant influence in the lives of these families, a medical tyranny from which escape became increasingly difficult. The battle against haemophilia became a battle for independence from the doctors.

Haemophilia must not become life's central focus. It is a challenge to be conquered so that one can get on with more important business. It should be ignored again. One is not a haemophliac struggling to avoid disaster. One is a normal citizen, with a personal problem. Conquering this problem brings strength of its own. The essence is independence.

I think that Frank would have endorsed this principle. He led an extraordinarily full life and, through his inspiration and leadership, enriched life for the rest of us. It was a privilege to have known him. He has made it easier for the next generation of haemophiliacs to take their future into their own hands.

(Acknowledgements to the World Federation of Hemophilia)

NR

THE ROYAL FREE HOSPITAL HAEMOPHILIA CENTRE

Christine A. Lee. MA MRCP MRCPath

The Katharine Dormandy Haemophilia Centre at the Royal Free Hospital, Hampstead, opened ten years ago. This was made possible by a generous financial contribution from Mr GRO-D In one way, it was a sad occasion because the director, Katharine Dormandy, who had the inspiration, for the new centre died shortly after it opened. However, she did see in 'concrete' terms the culmination of many years' work and the beginning of a new era in haemophilia care.

THE BEGINNINGS

The Royal Free Haemophilia Centre started in 1964 with five patients and the specific objective of providing a good treatment service for haemophiliacs living locally. The space for the developing centre was very cramped. Outpatients were given infusions at the end of one of the wards of Lawn Road Hospital, an old fever hospital, which occupied part of the site of the modern Royal Free Hospital.

There was a small amount of laboratory space for coagulation work and office space for the consultant and research assistant was the partitioned end of a staff coffee room. A significant land-mark was the donation of a large caravan by the Haemophilia Society in 1965. This provided accommodation for the two research assistants who were studying the medical and schooling problems of young haemophiliacs in South East England. This caravan was to remain a prominent land-mark at Lawn Road until demolition in 1973.

THE WFH

As a consequence of patients who were registered at the Centre seeking advice about treatment facilities when travelling abroad, together with reciprocal requests from patients living abroad, the Centre became an agency to whom patients and staff telephoned or wrote from all over the world. In 1968 the World Federation of Hemophilia brought about a scheme for correlating such information and Dr. Dormandy's research assistant, Mrs Peggy Britten, became a regional secretary for the WFH.

Doctors, technicians and medical students were soon regular visitors to the caravan-office to discuss the haemophilia problems in their home-towns and to see the Royal Free Haemophilia Centre.

GROWTH OF THE CENTRE

By 1970, the Centre had 180 patients. With this fast growth an out-patient treatment unit became a necessity and this time the Haemophilia Society provided for a pre-fabricated extension on the verandah of ward 7 at Lawn Road. At that time treatment was predominantly on an out-patient basis with infusions of fresh frozen plasma.

CRYOPRECIPITATE AND HOME TREATMENT

It was in 1970 that the Centre took part in the trial production and clinical evaluation of cryoprecipitate. The production of cryoprecipitate was soon taken over by the North London Blood Transfusion Centre. In 1971 the first patients were begun on home treatment with cryoprecipitate. This was soon to become a routine in the Centre and later was commenced in other parts of the country. It, of course, provided a great freedom for patients who no longer needed to attend the Centre each time they had a bleed.

By 1972 there were 220 patients with inherited bleeding disorders registered at the Centre. These included 132 with Haemophilia A (factor-VIII deficiency), 28 with Haemophilia B (factor-IX deficiency), 52 with von Willebrand's disease, 1 with factor-VII deficiency and 7 with factor-XI deficiency.

THE NEW KATHARINE DORMANDY HAEMOPHILIA CENTRE

The present director, Dr. P. B. A. Kernoff together with Dr. E. G. D. Tuddenham, who has now left the Royal Free, joined the centre in 1978.

At that time treatment with freeze-dried clotting factor concentrate was gradually replacing treatment with cryoprecipitate and most severely affected haemophiliacs were becoming established on home treatment.

During the past ten years there has been an enormous expansion of the Centre which is reflected in the number of patients registered (all patient data is entered on to the Centre's Computer when he or she is first registered.): 981 for the period 1987-88 : 424 with haemophilia A, 95 with haemophilia B, 204 with von Willebrand's disease, 68 with factor-XI deficiency and 142 with congenital platelet disorders. These patients attend from a wide variety of areas : 39% from the North West Thames region ; 30% from the North East Thames region ; 21% from other National Health Service regions and 7% from abroad.

Patients of all ages are registered with the centre and almost one hundred are less than ten years old. We are also a haemos-

The present Haemophilia Centre.

THE ROYAL FREE HOSPITAL

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tasis unit and of 550 new patients seen in 1987, about half had problems of clotting.

This increase in patient numbers has required more staff. The staff of the Centre now includes the medical director, Dr. P. B. A. Kernoff, a consultant haematologist, myself, an associate specialist, Dr. Eleanor Goldman, the staff for the routine laboratory and a small genetics laboratory, a senior Scientist, Dr. Ron Hutton, a research development scientist, a research team, three nursing sisters including the Clinical Nurse Manager, Patricia Lilley, a data processing officer, an office manager, secretaries and reception co-ordinator.

Professor Roger Hardisty, who recently retired from Great Ormond Street Hospital, has joined us as Emeritus Professor. Three members of our current staff, Mr David Bone, Senior Chief MLSO, Mrs Riva Miller, the medical social worker, and Mrs Peggy Britten, our volunteer data processor, worked at the haemophilia centre at Lawn Road hospital.

THE REVIEW SYSTEM

All patients are regularly reviewed. Those with severe haemophilia are seen every six months and those with mild haemophilia and other inherited disorders of coagulation are seen annually. The reviews provide an opportunity for regular assessment of the haemophilia, general medical health, dental care, the need for hepatitis B vaccination and social aspects of care.

All patients complete home treatment forms and information from these is entered on to the computer. This enables a printout of annual or six-monthly treatment usage to be provided at each review. It also provides precise information about the number of bleeds into each joint and hence target joints.

A monthly Orthopaedic Clinic is held jointly with the consultant orthopaedic surgeon, Mr J. C. A. Madgwick. These clinics are also attended by the physiotherapist, medical social worker, regional liaison sister and a sister and doctor from within the Haemophilia Centre. Patients can self-refer to these clinics, but more commonly problems are found at the regular review, necessitating referral to other departments.

ORTHOPAEDIC SURGERY

Patients admitted for orthopaedic procedures are admitted to an orthopaedic ward.

There is close co-operation between the orthopaedic team and the haemophilia centre. All factor concentrates are administered by the sisters from the haemophilia centre and there is careful monitoring of the levels by the routine laboratory. The surgeon will not operate unless the pre-operative factor level is known. The orthopaedic nursing is carried out by the ward nurses and there is close liaison with the laboratory when nursing procedures or physiotherapy are required.

GENETIC COUNSELLING

This has always been an integral part of the clinical work, but more recently with the advent of genetic probes, enabling DNA analysis, this work has expanded and there is now a small genetic laboratory devoted entirely to it. Although this is primarily an NHS service, the Haemophilia Society provides substantial financial support.

Chorionic villus sampling is performed at the Royal Free Hospital to ascertain whether a foetus has haemophilia.

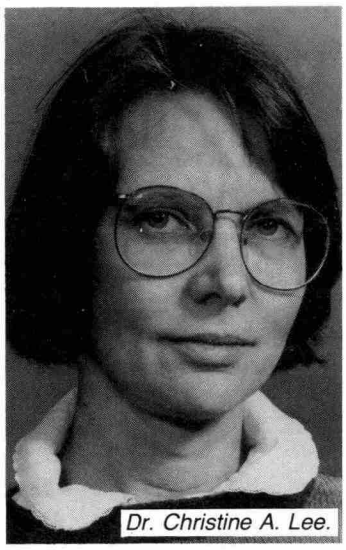
However, foetal blood sampling for factor VIII or IX levels in the foetus is performed at King's College Hospital. An unusual aspect of this work is the genetic counselling for families with factor- XI deficiency.

The Royal Free Hospital is situated in Hampstead District, which has a large Jewish population, and thus a relatively high number of patients with factor-XI deficiency are registered at our centre. There is the additional problem of the advisability of home circumcision in such patients.

THE IMPACT OF HIV

The comprehensive care which our centre gives has provided a natural framework to help cope with the devastating problem of HIV infection. All patients who are HIV positive are seen for at least six-monthly review : 90% of these patients have severe haemophilia. These reviews provide an opportunity not only for a full medical assessment, but to address HIV-related issues and to ensure that patients have full information about their situation.

Now, with the advent of specific anti-viral therapy, particularly AZT, patients are seen more frequently, on a two-weekly basis, to monitor blood counts. A number of patients are receiving nebulised pentamidine as a prophylaxis against pneumocystis pneumonia. This is administered



Dr. Christine A. Lee.

by one of the sisters to outpatients in the haemophilia centre, and we hope to move to home therapy.

Patients who are ill with HIV infection and need in-patient care are admitted to one of our beds on a general medical ward. This ward also has beds for patients with chest disease and there may be in-patients with AIDS due to other risk factors. The staff of this ward are thus developing increasing expertise in the care of AIDS. There is always close liaison with the staff of the haemophilia centre.

COUNSELLING

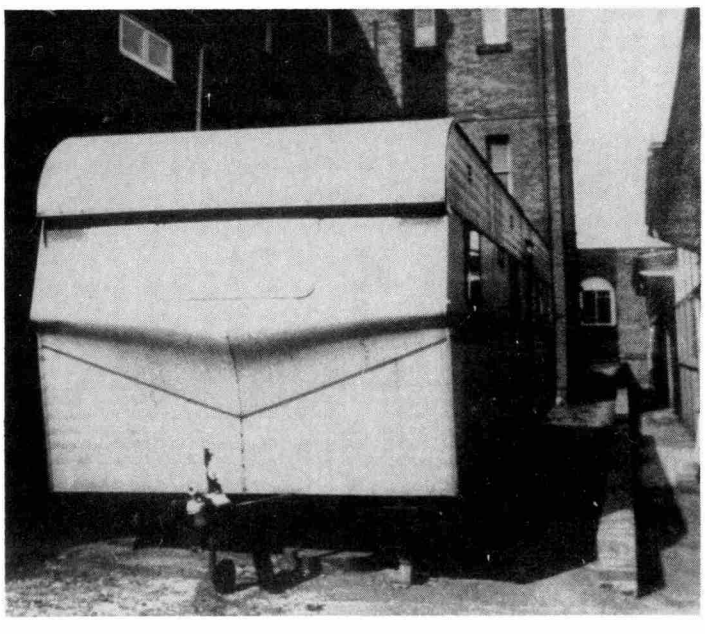
Our medical social worker, Mrs Riva Miller, has always applied the techniques of family therapy and is one of two trained family therapists (the other being Dr. Eleanor Goldman) within the Haemophilia Centre. Patients are seen by her at the time of reviews and are encouraged to bring relatives and/or close friends to such interviews. Sometimes, if there is a specific problem, a family interview will be especially set-up. This way of working has naturally extended to HIV-related problems and it has been used to help address dreaded issues.

An integral part of the counselling is the organisation of groups. These meet on an average 6-12 monthly basis. We have groups for parents of children, adolescents, wives, adults and more recently HIV positive patients. Such groups are carefully structured and last about 1½ – 2 hours on a weekday evening. They are certainly not a forum for gossip, but provoke hard and sometimes painful discussion. We also have a staff support group which is held monthly, mainly for 'hands-on' carers, particularly the nursing sisters who are very heavily involved in all aspects of patient care.

THE ROUTINE LABORATORY

The routine laboratory provides the essential facility for the diagnosis of new patients and the monitoring of registered patients

The caravan at Lawn Road hospital.



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THE ROYAL FREE HOSPITAL

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who are receiving treatment. There is also an active development team for the introduction of new laboratory tests. The NEQAS headquarters has been recently situated within the haemophilia centre and this provides for a national quality control of laboratory tests.

RESEARCH

The Haemophilia Centre has always been closely involved in the development of safe blood products. Treatment of patients with inhibitors using porcine factor-VIII was pioneered at the Royal Free Centre. The purification of factor VIII by Dr. Tuddenham and his co-workers led the way to the production of genetically engineered factor VIII and this will start to be evaluated in patients in our centre within a few weeks.

The incidence, prevention and therapy of hepatitis associated with blood product therapy is part of the research programme. The immunological response to blood product therapy and the way in which this is affected by HIV and hepatitis infection is also being studied. There is a team of scientists working on platelets, particularly the platelet membrane and this will help in the treatment of patients who have congenital platelet disorders.

EDUCATION

In 1974 the centre was designated as an International Haemophilia Training Centre to which staff from centres worldwide could be sent on training fellowships. In addition we are frequently visited informally by staff from other centres and this is reflected in entries to our visitors' book 1987-8 with entries from India, China, New Zealand, Poland, Egypt, USA, Australia and Ireland.

As part of a medical school we regularly teach medical students about all aspects of haemophilia care. Every six months there is a two-week course for doctors who are near the end of training as haematologists and who will soon become consultants. This has a particular emphasis on the laboratory aspects of haemophilia care.

THE FUTURE

Our aims for the future are in the improvement of patient care – particularly in the evaluation of safe blood products; in the provision of efficient and accurate genetic counselling; in the development and utilisation of effective laboratory tests; and in research and the continuing build-up of education.

This article has been written by a young man with haemophilia who is a PH.D working in the field of AIDS. He is HIV positive.

TRIALS OF AZT
TO ENROL . . . OR NOT TO ENROL

Very soon some people with haemophilia who are HIV positive but show no signs of disease (i.e. asymptomatic) will be given the chance to enrol in trials of AZT; if you are one of those people, should you or should you not take up the offer? This drug, also known as Retrovir and Zidovudine, is the only drug to have any proven beneficial effect in HIV disease (ARC and AIDS); it decreases the incidence of infections and illness, and sometimes also increases the numbers of while blood cells that became depleted during the disease (T4 cells), although not restoring the immune system to its former glory.

In spite of its efficacy, there is evidence that for at least some AIDS patients the benefits of AZT are temporary, so it in no way should be seen as a cure for AIDS. AZT also has side effects in about half of AIDS patients taking the drug, causing anaemia.

Given this background, what then are the possible advantages of going on an AZT trial if there is nothing wrong with you? What are the potential disadvantages? I have briefly summarised below my own thoughts on this matter in the hope that they may be of some benefit to others who have this awkward issue to face.

POTENTIAL ADVANTAGES

1. AZT is perhaps of limited use in AIDS because the immune system has already become damaged by the virus. AZT works by slowing the rate of reproduction of the virus, but it does not directly boost the immune system. On the other hand, if it is introduced before the virus gets a grip, it may stop the virus causing any damage and halt progression to ARC/AIDS.

2. Toxic affects of AZT are worse in AIDS patients than in ARC patients; limited evidence suggests that toxicity will be slight in asymptomatics; a recently published trial (Lancet, February 1988) showed little sign of drug-related problems in 18 asymptomatics.

3. Over an eight-to-ten year period post-infection it seems likely that about half of HIV positive people will become diseased, many with AIDS. If you are unlucky enough to be one of those people you are, from the above arguments, probably better off trying AZT now.

POTENTIAL DISADVANTAGES

1. Even if half of us do get ill, then by the same argument half of us will not and there remains a reasonable chance that an asymptomatic will remain stable for several years and perhaps for much longer. By then the situation regarding AZT will be clearer and other treatments may become available. In such a case the patient on trial may have been unnecessarily exposed to AZT.

2. Although the short-term toxic affects of AZT seem unlikely to be serious in asymptomatics, long-term toxicity is a possibility as with any new drug. AZT has not been tested long enough to know if there will be new problems after years of exposure to it.

3. Going on a trial entails the inconvenience of regular visits to hospital and lots of tests.

4. Half the people entering the trial in the hope of getting AZT will not get it, but will be put on a dummy drug (placebo); this is so that there is a randomly selected group of untreated patients to compare with the treated group in as strict a fashion as possible. Not even the doctors knows if the patient is taking AZT or placebo. In essence, half the people on the trial will be given AZT and thus will benefit from its good effects but may suffer any side-effects; the other half will be spared any side-effects but will receive no positive benefit from going on the trial. The authorities have insisted on setting up the trials this way, which is over-fussy of them, but they are like that sometimes.

The choice of whether to give yourself an even chance of taking AZT is a very hard one. All that can be done is to consider the issues, weigh up the odds, and gamble one way or the other. There is no way of predicting the outcome. The choice is a personal, instinctive one, but it is to be urged that every healthy seropositive person thinks things over and makes a decision, one way or the other. Good luck!

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EVALUATION REPORT ON THE LIVERPOOL SEMINAR, 1988

This article is a shortened version of the full evaluation report prepared by GRO-D copies of which can be obtained from Head Office.

THE SEMINAR

Since its inception the seminar has been one of the highlights of the Society year. It has proved as popular with the membership as with the professionals.

But it was realised in the planning stage that the 1988 seminar was going to be different.

In the first place it was recognised that the theme of living with haemophilia and HIV positive would prove highly emotive and sensitive and would be likely to attract a large number of people who have been identified as HIV positivity. It was felt that success would hinge on proposed group work as many issues could not adequately be dealt with in lectures.

It was accepted at an early stage that analysis of data collected at the seminar would be very important for the planning of future seminars.

EVALUATING THE SUCCESS OF THE SEMINAR

Such an evaluation posed potential pitfalls and constraints which might affect the objectivity aimed for. As evaluator I was unable physically to observe everything, therefore I employed different methods:

(i) my own personal observations,
(ii) questionnaires,
(iii) interviews,
(iv) diary entries.

It soon became apparent that these techniques were adequate but not totally appropriate.

Firstly, given the highly sensitive and personal nature of living with HIV positivity, it was inappropriate for me to observe the centrally important group work. My intermittent presence in different groups would have had a disruptive influence on the group dynamics and would have seriously prevented group members confidentially building support and trust for each other.

Secondly, I abandoned the use of interviews as soon as I became aware, after beginning to process the questionnaire that my proposed one or two interviews would have presented a distorted, positive or negative view of the seminar.

Ultimately, I relied upon questionnaires and diaries from both participants and professionals to satisfy the following objectives:

(i) to be aware of their reasons for attending the seminar,
(ii) to ascertain their expectations for, and reactions to the seminar,
(iii) to discover if their expectations were met or surpassed,
(iv) to provide information for future planning.

PROGRAMME

The Seminar programme was designed to meet the following objectives: To promote a positive image of living with haemophilia and HIV positivity,

(i) by providing the opportunity for participants to discuss supportively in groups, problems related to living with haemophilia and HIV positivity
(ii) by providing information about living with haemophilia and HIV positivity through lectures and discussion groups.

QUESTIONNAIRE RESULTS

Pre-Seminar Questionnaire
Professionals and Participants.

Of 130 people who attended, their reasons for being there included personal interest, representing a local group and professional interest. By attending they hoped to gain knowledge and understanding; to meet, support each other and share experiences freely.

Post-Seminar Questionnaire
Professionals and participants.

The questionnaire revealed the following information: Professionals and participants were in general agreement as to the positive value of the seminar, although there were some minor disagreements. This was to be expected because of the different roles for each group.

Participants: The following aspects of the seminar were very useful, financial assistance, orthopaedics, fears/anxieties, inter-personal relationships and self-esteem. The following aspects were less useful, diet, money and benefits/allowances.

Professionals: The following aspects had the greatest relevance for participants, fears/anxieties and psychological state. The following aspects were poorly received by participants, healthy living, diet. Again, this represents a general degree of agreement between the two groups.

Participants: Aspects not included were as follows: lack of time, employment, compensation, more depth, dental care, stress-management, wives and mothers.

Professionals: Aspects not included were as follows: stress-management, prejudice and the Macfarlane Trust.

Participants: Would have liked more time to explore: stress, HIV+ groups, personal relationships, wives groups, adolescence, working in other groups, diet, healthy living, support, Macfarlane Trust.

Professionals would have liked more time to explore: support groups in local groups, smaller, more homogeneous groups, HIV+ groups, haemophilia separate from HIV +, diet, healthy living, wives, stress and interpersonal relationships.

Participants felt that the following aspects made for a successful Seminar: meeting and talking with others with similar problems, expressing fears/anxieties, helping with HIV+ problems, bringing people together and being informed.

Professionals felt that the following aspects made for a successful Seminar: letting people vent their feelings, group work, meeting others in similar situations, sharing and supporting, communicating between mothers and haemophiliacs, being in a supportive and caring atmosphere – part of a big family.

Participants gave the following ideas for improving future seminars: more flexible groups, homogeneous groups, smaller groups, more time, more group work.

Professionals gave the following ideas for improving future seminars: regional seminars to reach more people, homogeneous groups, better defined agenda, less egotistic and patronising lectures and similar future themes.

Participants A large majority stated a preference for more group work and fewer lectures.

Professionals A small majority preferred less group work and fewer lectures.

CONCLUSION

I have represented only the main results in this abridged version of the seminar evaluation report and I have also omitted results from personal diaries. However, it is clear that generally speaking the Liverpool seminar was found to be very successful and relevant to both professionals and participants who attended.

(Continued on next page)

GROUP SEMINARS COULD BECOME IMPORTANT

Identifying the issues

Many local groups have always responded to their members' needs by organising social activities that often include elements of fundraising. It is obvious that their popularity should ensure their continuing success.

It is noticeable however, that some groups are beginning to extend their repertoires by introducing a wider range of activities and meetings for their members. One trend that I think is particularly important, because it represents a change of perception, is in the area of group development. Two major contributory factors I feel have generated this situation. Firstly, recent Society seminars I have attended have been successful in raising members' and groups' awareness of issues and problems and to some extent in pointing towards a methodology or ways of examining these issues and problems. Secondly, groups are becoming more aware of an obligation to identify and respond to members' needs and this has resulted in a greater sensitivity by them in addressing local issues. The consequence of these two factors alone, means that groups are becoming more confident about organising their own seminars in the knowledge that they are satisfying members' needs.

With the exception of Northern Group who held one about six years ago, more recent initiatives by North West, Birmingham and North East Groups in organising their own local seminars point to an exciting development, nationally and show how some groups are able to adapt to changing circumstances.

I recently attended the North East Group's seminar in Leeds and was encouraged by their success in staging such an event. The seminar was a result of them asking their members to identify the issues to be dealt with and I am sure this was largely responsible for such a good attendance and positive response.

If groups would like to examine and discuss the possibilities of organising their own seminars, the Group Liaison Working Party of the Executive Committee would welcome enquiries. This is a challenging time for the Society. We have seen many changes and developments in recent years and I am sure there are more to come. We need to look continually at ways of responding to those changes as they occur and the development of groups is centrally important to that process.

GRO-D

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SEMINAR EVALUATION

(Continued from previous page)

As previously suspected, it's success greatly depended upon the quality of the group work provided and whilst it was not possible to observe group work, many participants valued the opportunity to deal with the sensitive issues in this way.

Members of the Executive Committee will look more closely at the results to assess the extent of the seminar's success and will especially take on board the responses when planning future seminars.

Already, planning has begun on organising a regional seminar in the south west of England in response to a need for regional seminars mentioned at the most recent national seminars.

Finally, as evaluator, I would like to record my thanks and appreciation to all those people who contributed to the results of this report and also to Diane Daniel, who chaired the Seminar Working Party, and to David Watters and his staff who made the Seminar possible.

GRO-D

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LEGAL ACTION OVER HEPATITIS

This brief and anonymous case history is provided by a solicitor who represents the interests of a lady who is a carrier of haemophilia A and who was given factor VIII *for the first time* in 1983 and at a time when the use of concentrates in such cases was contra-indicated because of the risk of hepatitis. **You should note that it was crucial to the outcome of legal action that the lady had not previously received concentrates and that there was good reason for not using them at the time they were used.**

GRO-A who was born in 1931 was diagnosed in 1978 as being a carrier of haemophilia A with a basal factor VIII level of about 20%.

In 1983 her dentist advised her that she needed to have teeth extracted and in view of her haemophilia background referred her to the local general hospital for them to carry out the removal of the teeth.

At the hospital GRO-A was given an injection of factor VIII concentrate so as to prevent excessive bleeding from the tooth extraction.

Unfortunately the hospital failed to heed the clear warnings as to the administration of factor VIII to GRO-A who had not previously received blood product. Tragically GRO-A developed non-A non-B hepatitis from the injection of factor VIII. She subsequently sought the advice of solicitors.

Proceedings were started against the particular health authority and an application was made for summary judgement under Order 14 of the rules of the Supreme Court. However, immediately prior to the Court hearing, solicitors and counsel on behalf of the particular health authority and on behalf of the Medical Defence Union, who were acting on behalf of the doctor who administered the factor VIII injection, admitted liability and judgement was accordingly entered against the health authority.

A small interim payment of damages was paid to GRO-A However, it is proving very difficult for GRO-A and her medical advisers to get any firm idea of her future health prospects because of the lack of knowledge of this particular strain of hepatitis.

GRO-A's solicitors are attempting to compile a profile of her health prospects so that an application can be made for damages to be assessed by the Court if negotiations with solicitors on behalf of the Medical Defence Union fail. This profile is proving to be difficult to build up because of lack of general knowledge.

The National Directorate of the National Blood Transfusion Service

In October 1987 the N.H.S. Management Consultancy Service presented to Ministers their report on the organisation of the N.B.T.S. The report confirmed that the Regional Transfusion Centres (R.T.C.s), through their regionally managed services, were able to ensure that sufficient blood and blood products were available to satisfy clinical demands in regional hospitals but in the vast majority of instances there were underlying problems.

The absence of reliable management information made comparisons of effectivness and performance between R.T.C.s difficult to make; there was difficulty in the London regions in satisfying demands and a lack of co-ordination of the supraregional activities of R.T.C.s and between R.T.C.s and the Central Blood Laboratories Authority. The latter aspect is currently of considerable importance as the new Blood Products Laboratory increases production of fractionated products in an attempt to provide national self-sufficiency.

Following consideration of this report by the N.H.S. Management Board, Mrs. Edwina Currie announced in the House of Commons on Thursday July 28th 1988 that new management arrangements were needed for the supraregional and national dimension of the N.B.T.S. Operational responsibility at the national level for the N.B.T.S. will be exercised on behalf of the Health Ministers of England and Wales by the N.H.S. Management Board and undertaken by Mr. Graham Hart, its Director of Operations.

Day to day national strategy will be delegated to Dr. Harold Gunson, the new National Director of the N.B.T.S. and a small supporting staff. Regional Transfusion Centres will continue to be managed by their Directors for the Regional Health Authorities.

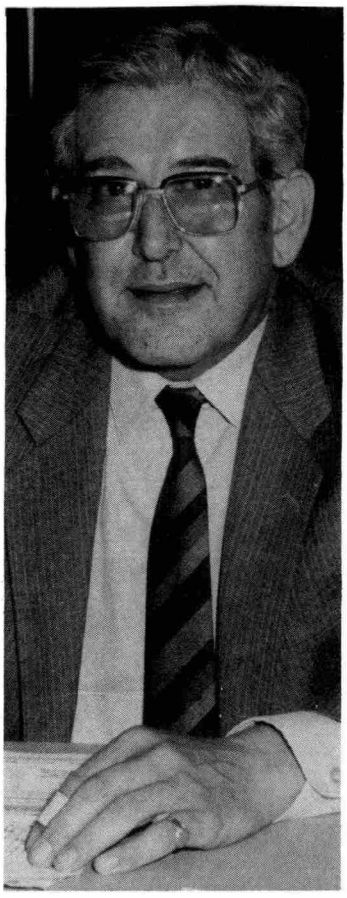
Dr. Gunson, who will head the National Directorate, entered the N.B.T.S. in 1959, following a five year period spent in Canada working in Pathology with a special interest in blood transfusion. After an appointment as Senior Medical Officer at the Manchester Regional Blood Transfusion Centre in 1964 he established and became Consultant-in-Charge of the Transfusion Centre in Lancaster.

Between 1975 and 1980 he held the appointment of Director of the Oxford Regional Transfusion Centre before returning to Manchester as Director of the North Western Regional Transfusion Service.

Since 1981 he has been the Consultant Adviser in Blood Transfusion to the Chief Medical Officer of the D.H.S.S. Dr. Gunson is also President of the British Blood Transfusion Society and President-elect of the International Society of Blood Transfusion.

Dr. Gunson took up his appointment as National Director on October 1st 1988. His prime objectives are to co-ordinate the activities of the R.T.C.s and the C.B.L.A., to implement a cost-effective strategy for ensuring an adequate supply of blood throughout England and Wales and plasma to the Blood Products Laboratory and promote the efficiency of the N.B.T.S.

The National Directorate will operate from the Headquarters of the North Western Regional Health Authority in Manchester.



Dr. H. H. Gunson, D.Sc., MD., F.R.C.P., F.R.C. Path.

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HEPATITIS B VACCINE

Enquiries arriving at the office suggest that there is some confusion about hepatitis B vaccine. The very first point to make is that **if you are concerned about the vaccine 'talk to your Centre Director'.**

In very general terms the system for vaccination should work like this:—

Everyone who is likely to be treated with, or come into contact with blood products, should be tested for hep. B antibody. If no antibody is present, that person is eligible for vaccination. **This extends to staff in Centres, patients themselves and their immediate family members.** The vaccination process consists of three injections over a six-month period and on the whole they produce a good antibody response which lasts up to five years.

It should be stressed that the vaccination is safe and is now available in synthetically produced materials.

EDITOR: Andy Cowe

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