Senate Community Affairs Reference Committee

Inquiry on Hepatitis C and the Blood Supply

Submission prepared for Oral Hearings by the Australian Red Cross Blood Service
7th April 2004

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SECTION 1

Introduction

Firstly on behalf of the Australian Red Cross Blood Service ("ARCBS") and the Australian Red Cross Society ("ARC") of which it is a part, I would like to thank the Committee for the opportunity to present to you today.

My name is Dr Brenton Wylie. I am a specialist haematologist and the National Blood Products Manager for the Australian Red Cross Blood Service.

Before I begin, we would like to extend our sympathy to each Australian who has acquired hepatitis C. We particularly extend our sympathy to those who have or will develop symptoms and complications.

We have heard, and hear, the concerns of those who have made submissions to this Inquiry and presented to the Committee. On reading each of the submissions it's impossible not to appreciate the powerful and moving accounts of the challenges faced by individuals, and their bravery. They reflect the experiences that we at ARCBS have had from all of the interactions with patients with hepatitis C over the past years.

We recognise the impact that this disease can have on the person and their family.

We know that the real focus of this Inquiry is on issues such as risks associated with blood transfusion, the difficulties of this chronic illness, discrimination encountered, lack of notification of infection and cost of medical treatment. We will address many of these concerns today, and provide recommendations for the Committee's consideration.

The ARCBS, as part of the Australian Red Cross Society, supports outcomes that will improve the situation of those affected by hepatitis C. In particular, ARCBS wishes to lend its support to a principle of improving the services available for people affected by the hepatitis C virus through the provision of optimal personal, medical and social support.

We also particularly acknowledge the difficult situation faced by patients with haemophilia as described in the submission from the Haemophilia Foundation Australia. Sadly, the high infection rates of people with haemophilia exposed to post transfusion hepatitis C in Australia, as in all other developed countries, is a result of a number of contributing factors and illustrates the risk/benefit dilemma inherent in the use of blood and blood products for treatment purposes.

In my presentation today I will speak to the key issues of the Inquiry including the growth of knowledge about hepatitis C and surrogate testing. I will also explain how the Blood Service operates within the Australian Red Cross Society, the way it is organised and what its services encompass. This will include hearing from a long time donor, a blood recipient, a Sydney haematologist involved in advising on transfusion on a daily basis and an international expert in transfusion medicine.

The Australian Red Cross Society and the Australian Red Cross Blood Service

The Australian Red Cross Society is part of an international movement. The Red Cross (and its equivalent in Muslim countries The Red Crescent) is an international humanitarian non-profit movement active in 181 countries throughout the world. The seven fundamental principles of the movement are:

Humanity, Impartiality, Neutrality, Independence, Voluntary Service, Unity and Universality.

Each National Society is responsible for its own affairs.

More than 80 million units of blood are collected annually worldwide. Over 30% of this blood is collected directly by Red Cross and Red Crescent societies in countries as diverse as the US, Switzerland, Germany, Austria, Finland, Thailand, Japan and Indonesia amongst many others. In addition, another 30% of the blood is collected in countries where Red Cross assists with blood donor recruitment. Overall, almost two thirds of the world's blood supply is supported by Red Cross activities.

The ARC was first established by Royal Charter in 1941. In January 1996, ARC changed its *Charter and Rules* to provide for a national blood service, with a Board of Management and a CEO accountable to the ARC Council for the management of a newly created operating Division of the Society - the Australian Red Cross Blood Service (ARCBS). This new national management structure replaced what was previously eight state/territory based operations.

This change, instigated by ARC itself, resulted in a single national blood service. This has helped ensure uniform policies. Common tests could be introduced universally throughout Australia once approved and with the necessary funding secured.

It is important to note that ARCBS does not work alone in the provision of blood and tissue products to the Australian community. As in the past, we continue to work very closely with State, Territory and Commonwealth health departments and all major decisions about safety and sufficiency are made in consultation with governments.

ARCBS is primarily funded by the Commonwealth, State and Territory governments, with a limited financial contribution provided by ARC. ARC also assists ARCBS through the contribution of volunteers in the recruitment and welfare of donors.

Recently the funding arrangements for the blood system have been changed by Government with the establishment in 2003 of the National Blood Authority, or NBA, which has a national oversight role on behalf of all governments.

Working with donors and clinical partners to provide a service for Australian patients

The mission of the ARCBS is to share life's best gift by the provision of quality blood products, tissues and related services for the benefit of the community. This also encompasses significant programs in the management of organ donation. ARCBS can only achieve its mission through the goodwill and commitment of approximately 500,000 dedicated unpaid donors. Some of these donors have generously donated their blood and provided their time to this activity regularly over their adult lifetime. Whilst a very large proportion of Australians would have given blood at least once in their lifetime, only 3-4% of the adult population are active regular donors. There is a need for donors who are committed to giving blood regularly and over a long period because of the particular demands of a blood service.

The need for blood is constant. Shortages are frequent and can develop rapidly.

Blood must be stored at the correct temperature. It has a short shelf life or use by date. It needs to be collected, processed and distributed on a daily basis. Every day, blood donors are needed (with up to 20,000 donors required weekly). This explains why there are frequent calls for people to donate blood, especially during seasonal trouble spots such as winter time (when people are often ill with colds and flu) and periods of public holidays such as Christmas and indeed Easter which is almost upon us. At these times it is difficult to collect enough blood because of the public holidays. Even something as simple as the weather can affect the blood supply, with wet weather frequently causing fewer collections and thus shortages.

With me today is one of Australia's blood donors, Mr Brian Pepper, whose lifelong effort in donating blood has saved many lives. Brian has been a donor since 1967 and has made over 600 donations.

I invite Brian to share with you his story of becoming and being a regular blood donor.

[Statement by Brian Pepper]

You might ask to whom does the blood go? Firstly, you may not know that from each donation multiple blood components are manufactured greatly increasing the usefulness of a single donation. Red cells, platelets, fresh frozen plasma and cryoprecipitate are the most commonly made so-called "fresh" components. ARCBS records indicate that over 1,000,000 of these components are issued to hospitals each year. The biggest use of red cells is in surgery (37%), followed by cancer patients (16%), patients with gastroenterological problems (16%), burns and trauma patients (9%) and red cell disorders (8%).

Another part of the blood collected, plasma, is immediately separated and the majority of it is forwarded to the Commonwealth appointed fractionator, CSL Bioplasma, which is located in Melbourne, for manufacture into a variety of plasma products. These products are used to treat a range of conditions, including burns and haemophilia. Those products are then returned to ARCBS, which distributes them to hospitals. Again, over 1,000,000 of these products are used every year in Australia.

The supply of blood in Australia does not involve any monetary dealings between ARCBS and CSL. The decision to use CSL to fractionate Australian plasma is made by the Commonwealth government without any input from ARCBS. The Commonwealth pays for the fractionation of the plasma into products, which ARCBS distributes, to treating clinicians and hospitals. The Commonwealth, and now the National Blood Authority, manages its contract with CSL.

There is no requirement for Australian hospitals to maintain a national register of blood component use or to report centrally on usage. An important point is that the ARCBS does not know the identity of patients who are transfused. The privacy of the patient is protected in this way. ARCBS issues the blood component or product to a hospital or doctor and then it becomes their responsibility from that point.

Many patients receive multiple transfusions in one year. Hence, it is not possible to say exactly how many individual patients benefit each year from transfusion. However, we have estimated that approximately 100,000 patients benefit from fresh products (such as red cells and platelets) each year and another 100,000 Australians benefit from plasma products including albumin, intravenous immunoglobulin, special immunoglobulins such as anti-D and

clotting factors. Thus blood collection, component production, testing for blood group and infectious markers and distribution of blood products is an essential part of the healthcare service.

We would like to introduce to you, a recipient of blood, Carole Tozer, to tell her story.

[Statement by Carole Tozer]

As there is no database of blood recipients in Australia it is difficult to extract a clear picture of blood recipients. However, we know from comparative studies in other developed countries that the average age of blood recipients is aged 60-65. The majority are seriously ill, including cancer patients and trauma victims. Sadly, because these people are so sick, survival of blood recipients is quite poor, in that around 50% of blood recipients die from their underlying disease or condition within 12 months of any given transfusion. Nevertheless, many recipients do recover and go on to lead healthy lives. Others face a lifetime of dependence on blood products because of their particular disease.

Important partners in the provision of this service are the doctors, scientists and nurses in the healthcare system. Although the bulk of transfusions occur in the large tertiary hospitals in the capital cities, over 300 hospitals around Australia transfuse blood, many of them located in regional areas. Both private and public hospitals use blood services. Thus, it is a very complex system involving hospitals run by 6 states and 2 territories and both public and private facilities.

It is important to note that blood and blood products in Australia are provided to both the private and public hospital system totally free of charge to patients. The involvement of Australian Red Cross in the provision of blood services is based on the support of voluntary non-remunerated donors and the free provision of blood and blood products.

Advances in medical practice frequently depend on support through blood transfusion. Examples over the past thirty years include complex open-heart surgery, liver transplants, bone marrow transplants, new treatments for cancer including more powerful chemotherapy and new burns treatments. The specialist area of medicine, which has the expertise in managing blood transfusion and maintenance of normal blood function including clotting factors, is known as haematology. Haematologists also look after patients with blood disorders and clotting disorders such as haemophilia. We have invited here today an experienced Australian haematologist, Dr David Rosenfeld, Head of Haematology for the South West Sydney Area Health Services, one of the largest and busiest services in Sydney.

[Statement from Dr Rosenfeld– See Appendix One]

So this is very much background to the issues we know are of interest to this Inquiry.

However, what we are here today to discuss is the important question of how to manage the safety of the blood supply and minimise risk of harm to the patient. Nothing in life is 100% safe. Blood transfusion is in many cases a life-giving procedure, however as with any medical procedure; there are some risks associated with its use for the individual patient. How can we reconcile the risk for an individual patient with the overall benefit? The Blood Service does all it can to minimise risk in the product itself but there are risks beyond the Blood Service's control, for example what happens in the hospital, how the transfusion itself is given and how the patient is managed.

These days, statistically there is a greater risk of an error in getting the correct unit of blood to the patient than there is of viral transmission through a transfusion.

Infectious risks in the last 25 years have primarily been Human Immunodeficiency Virus (HIV) and hepatitis. HIV became a problem in the eighties. The introduction of stricter criteria for selection of donors, eliminating those donors with risk factors, and the introduction of specific testing for HIV in 1985 largely solved the problem of transmission of HIV through blood transfusion. The current risk of transfusion acquired HIV has been modelled at 1 in 4.8 million units transfused.

Hepatitis was known to be a risk since World War II. Identification of hepatitis B and finding a test for this helped to reduce post transfusion hepatitis in the early seventies. Hepatitis not attributable to hepatitis A or B soon became known as non-A, non-B hepatitis. In 1989 it was shown that most non-A, non-B hepatitis was due to a new virus, hepatitis C.

In a review of the introduction of specific hepatitis C screening in developed countries, Australia was the second country in the world (after Japan) to introduce this testing in 1990. A table detailing these dates is included in our written submission (page 30).

Table 1: Screening of blood donations for antibody to hepatitis C virus

Date	Country
Dec 1989	Japan
Feb 1990	Australia
Mar 1990	France (1 March): Luxembourg (new donors only, 1 March)
Apr 1990	Finland (1 April) - all donations: partially started 1 February
May 1990	USA (2 May): Austria: Amsterdam (other Netherlands centres later)
June 1990	Canada: Germany (by 1 July)
July 1990	Belgium (1 July)
Aug 1990	Switzerland (1 August)
Sept 1990	Luxembourg (all donors)
Oct 1990	Spain (all by 12 October, some started earlier)
1990 / 1991	Norway
Jan 1991	Sweden (legal requirement published 24 January to start as soon as possible)
Mar 1991	Portugal (mandatory, some earlier): Cyprus: Greece: Hungary: Iceland: Malta
June 1991	Netherlands
June 1991	Denmark
Aug 1991	Italy
Sept 1991	UK (1 September)
Sept/Oct 1991	Ireland
Aug 1992	New Zealand

The risk of transfusion-acquired hepatitis due to non-A, non-B hepatitis (now known as hepatitis C) in Australia and the US is also shown in a table provided in our written submission (page 27).

Table 2: Declining risk of post-transfusion hepatitis C in Australia between 1979 – 2002 compared to the US

Year test introduced in Australia	Risk of transfusion NANBH/ Hepatitis C transmission in Australia as % units[1] transfused	Risk of transfusion NANBH/ Hepatitis C transmission in US as % units transfused
1979 – 1980 Unscreened (for hepatitis C antibody)	1:333	1:100
1990 Hep C 1st gen test	1:3435	1:3,333
1994 – 1995 Hep C 2nd gen	1:234,000	1:103,000
1997 Hep C 3rd gen	1:311,956	1:120,000
2000 – 2002 Hep C 3rd gen + NAT	1:3,112,000	1:2 million

This table tells us several things:

1) The blood supply has generally carried a higher risk of hepatitis infection in the US than it has in Australia.
2) The risk of acquiring hepatitis in Australia fell from approximately 1 in 300 per bag of blood transfused to approximately 1 in 300,000 by the mid 1990's and to less than 1 in 3 million today. A table detailing this has also been provided in our written submission.
3) The blood supply today is now extremely safe in respect of hepatitis C.

It should be noted that while the introduction of first generation hepatitis C antibody testing was a major advance, it did not detect all donors who were infectious. Although first generation testing was not perfect, it was the best available. Some true hepatitis C positive donors were not detected by the first generation test. The second generation test introduced in 1991 was an improvement and third generation tests were even more sensitive. Thus a number of patients in the 1990's acquired hepatitis C through transfusion because some infectious donors were not detected by the first tests available. We are aware of 13 known cases between 1995 and the introduction of NAT testing in 2000. NAT testing is very sensitive because it directly detects genetic material of viruses such as HIV and hepatitis C

It should also be noted that a very small risk of post-transfusion hepatitis remains even today. Why is this so? Even with the best testing available today it is not possible to completely eliminate the window period. What this means is that there is a period of time that a newly infected donor will be infectious and yet their hepatitis C virus infection will not be detected by *any* test, even the very good ones now available. (The window period now for hepatitis C is around 7 days). We can never say that the blood supply is 100% safe as blood is a biological product and there is always a small degree of risk.

[1] Please note that the data is expressed as % UNITS transfused, a different figure from % PATIENTS transfused. A unit corresponds to a bag of blood obtained from a single donor. For the 1979 – 1980 and 1987 - 1990 periods the figures for % patients transfused in Australia were 1.7% and 1% respectively.

It is important that today's patients are aware of the context of risk of acquiring an infectious disease if they have a blood transfusion.

As you can see there is a very small risk that this could occur – for hepatitis C in the range of 1 in 3 million for each unit transfused.

We have described the current risk of transfusion acquired Hepatitis C as being a very small risk. How does it compare with other risks that Australian patients face?

- The risk of death definitely attributable to an anaesthetic is in 1 in 150,000 procedures
- The risks of hospital acquired infection from clean surgery is currently 1 in 100
- The risk of an adverse event occurring to a patient admitted to an Australian hospital was been estimated recently as 1 in 10

These risks are from The Australian Council for Safety and Quality in Healthcare "Safety in Numbers Report" 2001.

We provide these risks to convey an understanding that all medical and hospital procedures do carry an element of risk, and to put into context transfusion associated risks, which are currently low by comparison.

We urge the Committee in its recommendations and public statements to be aware of the real danger of alarming today's patients unnecessarily.

It is the mission of the Blood Service to "Share life's best gift by the provision of quality blood products, tissues and related services for the benefit of the community." Minimisation of risk is the key task here.

The ARCBS, like all in the health care system, strives to reduce risks wherever possible. However, all medical procedures involve risk and there have been, and continues to be risk in blood therapy. Blood is a biological material and it is never possible to say that there are no associated risks; accordingly there is inherently a balance of risks and benefits involved in its use.

SECTION 2

What is hepatitis C and why is it associated with Blood Transfusion?

History of post-transfusion hepatitis

The occurrence of hepatitis following blood transfusion has been recognised both in Australia and internationally since the Second World War. As described in our written submission a significant advance was the discovery of hepatitis B and the subsequent development of a hepatitis B screening test for donors in 1970.

After that it emerged that not all post-transfusion hepatitis had disappeared and the concept of "non-A, non-B non- hepatitis" was established around the mid-seventies. What was not established was whether it was one virus or several viruses. In fact through the decade and a half from the mid-seventies to the end of the eighties there were dozens of reports from scientists in different parts of the world claiming to have discovered a new hepatitis virus, most of which were quickly discredited.

In Australia there was concern amongst the blood services about non-A, non-B hepatitis although very few cases were reported to the Blood Services throughout the 80s - something of the order of dozens of cases through the whole decade of the 80s across all states and territories. Because of this, it was not seen as being a common problem and it was seen as a disease, which often had no symptoms and was very hard to diagnose.

However, it *was* taken seriously. Sufficiently seriously that the Red Cross commissioned a study in 1979 to carefully study a group of 842 multiply transfused patients undergoing heart surgery in Sydney. The patients were followed for 24 weeks after their operation to look for signs of illness and monitor them with the crude blood tests available at that time and the donors of all blood products these patients received were also tested carefully. They received an average of 5.7 blood transfusions each. This revealed a rate of 2.0% per patient – less than one fifth of the rate found in similarly constructed studies in the US and Canada at the time. The patients did not seem to have a major problem as they were mostly without symptoms and did not appear to be seriously ill. Their donors were all well. So non-A, non-B hepatitis was hard to diagnose with certainty and generally the patients had no symptoms that could be readily attributable to a hepatitis virus.

Surrogate testing

The fact of the matter was that until 1990 there was no specific test for non-A, non-B hepatitis, later known as hepatitis C. However, during the mid eighties there was much debate in the literature about whether any good might be achieved by testing donors with surrogate tests and this proved controversial.

Two such surrogate tests were proposed. They were not direct tests specific for non-A non-B hepatitis but were indirect tests used for other purposes –

- the ALT test one of various tests that monitor liver function and
- the anti-core test is a marker of past infection with hepatitis B.

The National Institutes of Health Hospitals in Bethesda, Maryland, USA adopted ALT screening in 1981 and in the first 3 years found no decrease whatsoever in the risk of non-A, non-B hepatitis after transfusions.

The decision was taken in Australia through the National Blood Transfusion Committee not to recommend the introduction of surrogate tests, following an evaluation of the scientific evidence for surrogate testing because the evidence that it would be effective was not convincing. This was the case except in one state, Queensland, which took a contrary view to the rest of Australia and elected to introduce the ALT test only.

The US Blood Banks adopted these surrogate tests at various time intervals up to mid 1987. The FDA, which is the regulatory agency in the US and the equivalent of the Therapeutic Goods Administration in Australia, met to consider these tests three times and never decided to recommend the tests should be done. However, the American Association of Blood Banks, an industry association, in 1986 recommended to its members their introduction and this happened in 1986-87.

The debate then continued through the rest of the world as to whether there was any value in the tests being adopted elsewhere. The countries which introduced surrogate testing in the mid 80s were the minority. Most countries did not introduce them. No European country was performing anti-core testing and only parts of Germany and Italy were doing ALT testing. Germany had ALT in place since the 70s but still had a very high reported rate of post-transfusion hepatitis of 17% which suggested that ALT was not an effective test in their population.

At its meeting in May 1987 the Council of Europe's Committee of Experts on Blood Transfusion and Immunohaematology concluded that:

> *"Arguments against the introduction of surrogate testing include the variability of data from one country to another, the non-specific nature of the tests proposed, loss of apparently healthy donors, difficulty in follow up of the donors and the continuation of transfusion-transmitted NANBH in spite of the tests."*

After studying the situation the Council of Europe's Working Group on surrogate tests reported in November 1987:

> *"The introduction of non-specific tests could lead in some countries to a severe depletion of blood donors which could compromise the blood supply and this is a factor which must be taken into account."*

In May 1988 it was announced that a new virus had been discovered (later called HCV, or hepatitis C), and that a test would soon be made available. Research tests arrived in Australia in August 1989 and were immediately applied to the post-transfusion hepatitis study. The Australian Red Cross moved with all haste to introduce the specific test, which was universally in place by February 1990.

The NTBC, which included representation from all Australian Blood Services and the Commonwealth government and Commonwealth Serum Laboratories (strictly speaking part of the Commonwealth in those days), closely monitored all the available scientific evidence both locally and internationally. It made the decision not to recommend the introduction either of the surrogate tests because they were considered to be blunt and inaccurate tools with the potential to create blood shortages without any demonstrated benefit to public safety. The surrogate tests had not been proven to be effective in reducing post-transfusion hepatitis. Several studies in European countries such as England and France showed no benefit.

As already stated, in the USA one hospital at National Institutes of Health did introduce ALT and after three years when they reviewed their results the rate of post-transfusion hepatitis in transfusion patients had not fallen at all.

A major concern was that it was estimated that at least 5% of voluntary blood donations would be rejected although they were mostly expected not to be infectious. This was because the ALT test might give a positive result if the donor was overweight or had had a heavy night drinking before donating or was taking certain medicines. In a time of great concern about the adequacy of the blood supply (following the advent of AIDS there was a well documented fall in blood collections in the mid eighties) the Red Cross was very concerned about serious blood shortages occurring if they threw away at least 5% of their blood. Added to this - what were the Blood Banks to tell these donors? Should they be referred to liver clinics for investigations and biopsies when in all probability they did not have infectious hepatitis? Was it right and fair to worry people unnecessarily when there was very little evidence that these people were ill?

The introduction of surrogate testing would have meant referring many thousands of donors for investigation and possibly even a liver biopsy, a procedure with risks of its own, even though the great majority of donors would be healthy.

Such a move might also have been counterproductive, due to the fact that to replace the lost donors there would need to be a consequent increase in new donors, which also brings an increase in risk. New donors were known from experience with HIV and hepatitis B to have much higher rates of infectious disease markers than repeat donors were.

Commercial considerations played no part in the decision making. It is important to note that cost was not a consideration and has never been claimed to be an issue in the decision making on this surrogate testing in Australia. Red Cross funding at that time was not reliant on the volume of collections therefore any fall in collections did not affect funding. However as the blood supply is traditionally very finely balanced, a fall in collections caused by having to reject blood from donors with high ALT levels would have caused real and immediate problems in supply.

Was it the right decision for the NBTC in conjunction with the health authorities to make? We believe it was and still remains so. Surrogate testing meant that a lot of good blood was discarded for no good reason and the tests were very poor at actually detecting infectious donors. Anti-core antibody testing (a test for hepatitis B virus) was shown not to be effective in several countries (France and the Netherlands) for reducing post-transfusion hepatitis and retrospectively it was shown in the post-transfusion study in Australia not to have been of any benefit at all. See also the written submissions from Professor McCaughan and from the Australian Hepatitis Group for more detailed arguments about the inadequacies of surrogate testing.

It was not possible during the eighties to measure how effective the surrogate test was, but in 1990 a proper test for hepatitis C became available. Then, retrospectively it was shown using the new test in the US that 91% of US donors with an elevated ALT were hepatitis C antibody negative. **That is, 91% of the rejected blood was perfectly OK**. Not only that, but the surrogate test **missed** around 80% of the real positives (ALT normal but hepatitis C antibody positive). The AABB in the nineties admitted that it was impossible to say in retrospect whether the surrogate tests had been of any value in the US.

Essentially surrogate testing was casting a very wide net in which you may have caught just a few of the infectious donors but also a lot of good safe donors got caught up as well. You might say you were "throwing out the baby as well as the bath water".

I would now like to introduce Dr Paul Holland, Medical Director and CEO of BloodSource in Sacramento, USA, and international expert on transfusion medicine, to provide an international perspective on the debate surrounding efficacy of surrogate testing. We have invited Dr Holland to appear before the committee at our expense because we think he is uniquely placed to provide an expert opinion.

[Paul Holland's statement - See Appendix Two]

How much blood did surrogate testing needlessly waste?

We can estimate this from figures in Queensland, which alone amongst the States introduced a surrogate test (one only, the ALT test) in July 1987. Over four thousand four hundred donations were estimated to have been discarded by Queensland over the 3-year period that ALT testing took place before hepatitis C testing was commenced. This did create problems for Queensland because they suddenly increased the number of new donors to make up for the shortfall they had. New donor rates rapidly increased in Queensland in the period 1987-1990 and exceeded the new donor rate per thousand population in the other Australian states by a factor of about 30% during 1987-1990. New donors are known not to be as safe as regular repeat donors and hence this introduced a counter effect potentially increasing other infectious risks in the blood supply. Moreover, the volume of plasma forwarded by Queensland for fractionation into plasma products fell in 1987-1988 by 9% - the only time there was a fall in a 6 year period of otherwise growing volumes, which would have negatively affected the volume of plasma products available for patients in that state.

Moreover, retrospectively it was clear that 92% of the blood Queensland rejected was in fact good blood.

How many hepatitis C positive donations were missed in Queensland over the same period? The Queensland figures suggest that at least 75% of the infectious donors were not detected by the ALT tests so it is not surprising that there were still many hepatitis transmissions in Queensland during this period.

In summary, surrogate testing as a means of maximising patient safety was very seriously considered by Australian blood services and health authorities. However, the evidence was not there to support its introduction across Australia.

What else was done?

So the question might be asked what did the Australian Blood Services do about the threat of hepatitis? In fact there were a number of things that were done. Firstly the Red Cross consistently warned doctors and hospitals throughout the seventies and eighties that in spite of hepatitis B tests there was still a risk of transmitting hepatitis through transfusion. In its publications including a film and a booklet both entitled "Blood Components and their uses", the Circular of Information which was issued with blood products, information sheets issued to resident medical officers, "Notes for Nurses", a "Guide to Blood Transfusion" and "Blood and its products – A practical guide to handling and usage" there were sections explaining what non-A non-B hepatitis was and the risks of transmission. Letters and reports describing the viral risk were transmitted to blood user groups. Non-A non-B was a regular topic of discussion and concern at Australian scientific meetings of the time.

Secondly experts and advisors from US and Europe advised Australia in the mid eighties to conduct our own study to determine how great the problem was in Australia and what impact the introduction of the tests would have in the Australian population because American and European studies showed variations in different populations. The Red Cross endorsed such a study and over 1200 patients were enrolled in the study from 1987 in Sydney and Perth and followed for 52 weeks. When the results were analysed in 1989 it was found that the rate of post-transfusion NANBH in patients who had had multiple transfusions had fallen considerably from 1.7% in 1979-1980 to 1.1% in 1987-1989. There were 8 cases of post-transfusion hepatitis recorded and seven of these were shown to be due to hepatitis C. In all over 3,400 units of blood had been given to 736 patients. Not one unit of anti-core positive blood was actually infectious for hepatitis C. Of 126 units of blood transfused which had raised ALT levels only 4 units were actually anti-HCV positive (3%). Also overall ALT testing failed to detect 22 out of 26 hepatitis C positives. The results of that study have been published in the Medical Journal of Australia in July 1995 and thus were made fully available for scrutiny and discussion as detailed in our written submission.

During the eighties there were a number of other initiatives introduced by Red Cross to make the blood supply safer, including the development of the first Australian Donor Guidelines. Important measures were the introduction of donor interviews, stricter donor questioning and a declaration form and these measures undoubtedly contributed to improving the safety of the blood supply. When the rate of post-transfusion hepatitis was compared in the early eighties and the late 80s the rate was seen to have fallen in many countries that never introduced surrogate testing. This included Australia, as well as the Netherlands, Spain, Finland and Sweden and was most likely due to the stricter criteria for blood donation that were introduced around that time.

SECTION 3

How good are the systems for identifying post transfusion hepatitis C in use in Australia?

In Australia, as in other countries, a system called lookback is in place to identify as many recipients as possible who have been exposed to an infection such as HIV, Hepatitis B and Hepatitis C via fresh blood components. The ARCBS HIV lookback program was developed by the organisation and led the world in lookback efforts for the virus. It was used as a model internationally.

Lookback for hepatitis C is a much more complex undertaking due to the greater number of people in the community with Hepatitis C and the greater length of time over which the virus may have been transfused. The lookback program for hepatitis C had to be developed differently in each State and Territory to meet their different policy and legislative requirements. It is important to know that ARCBS pursues every avenue it can in tracing individuals through lookback. However, the process has significant limitations.

There are 2 main types of lookback.

The first is Donor Triggered Lookback. This is where a donor is found to be positive and all their previous donations are traced to try and find all the recipients who received them. These recipients are then tested to see whether they have been infected.

This form of lookback is undertaken by ARCBS on donors who have come back to the ARCBS after hepatitis C screening commenced and have been found to be positive, or who have notified us that they are positive. There are a number of reasons why a donor triggered lookback may not be possible.

Firstly, as a large proportion of blood comes from the 10% of donors who only ever donate once, there are a considerable number of donors whose hepatitis C status is not known to us.

Secondly, even though ARCBS may trace a donation to a particular hospital, the hospitals may not be able to find or link the donation to a particular patient. Why is this? Hospital records may be incomplete or lost or even destroyed. Legislation in different states and territories allows hospitals to destroy records after certain timeframes, varying in each jurisdiction. Patients may have moved and be uncontactable.

Thirdly, doctors may choose not to contact or test patients particularly if they are very elderly or terminally ill.

International experience, including recent research in the UK shows that only about 1/3 of infected recipients can be found using this method.

The second method of lookback is Case Triggered Lookback. This is where an infected recipient is reported to the ARCBS and we conduct an investigation to determine, through testing, if the patient is linked to a hepatitis C positive donor.

There are also significant limitations to this process.

Firstly, and most crucially, many cases are not reported to us as notification to ARCBS is not compulsory. We cannot investigate cases unknown to us.

Secondly, as with finding recipients, donors may also have moved and be uncontactable or may be now deceased and therefore unable to be tested.

Thirdly, in many cases the recipient has received hundreds of blood products and the task of finding and testing all the donors is enormous and often impossible.

In the Australian setting, there are a number of further limitations, which have made the Lookback process even more difficult. These explain why there are differences between states and territories, and why, in addition to the problems already described, there may be a very considerable delay in finding, notifying and testing recipients.

The process involves many stakeholders, donors, recipients, doctors, hospitals, ARCBS and not least of all, Governments. Each state and territory developed their own Lookback program involving these stakeholders and the role of the Red Cross was and remains different in each program. Thus, although ARCBS has a clear role in each jurisdiction it has had to work with the different requirements of each State and Territory Government and within the legal constraints of tracing methods.

The recommendation of a working party reporting to the Commonwealth Diseases Standing Committee of the National Health and Medical Research Council in 1991 was that only 'Recipient (case) triggered lookback' should be undertaken as other forms of lookback were too expensive and inefficient.

It was not until a further application by ARCBS that it was agreed by Health Ministers in December 1994 that donor triggered lookback should be undertaken.

Funding for lookback programs was only formally received from 1995 onwards and thus lookback programs were, by necessity, limited by resources available prior to this time.

So clearly the lookback program can never be complete and there have been limitations to the programs in Australia. ARCBS is concerned that although in our submission we identified 2050 recipients, there are others who have not and cannot currently be found. ARCBS has however, pursued all cases as well as it has been able. That said, the lookback experience in Australia has the same difficulties as experienced in other countries and in fact, commenced well before many other countries, notably the USA which did not decide to commence lookback programs until 1998.

One of the things we have learnt through our management of lookback programs is that one of the initial means of contacting donors (i.e. by letter) was inappropriate and we are sorry for any distress this may have caused. Subsequently our procedures were modified. Presently, where we have to use a letter to contact patients or donors who are likely to be infected with hepatitis C, it is purely for confirmation of identity, inviting them to contact us.

ARCBS does have concern that there are people who may never have been notified. Recently we have completed our own modelling taking into account survival rates of people receiving transfusions, and have estimated a maximum possible number of Australians alive today with transfusion acquired hepatitis C. This is calculated from transfusion of fresh blood products in Australia. Our upper limit of people alive today with transfusion transmitted hepatitis is estimated to be 8764, 25% of these might be expected to have cleared the virus which would result in a figure of 6573 with an ongoing infection.

To this number we need to add the number of people with haemophilia who have hepatitis C. In our written submission we calculated the number of people with haemophilia living with hepatitis C as 1350. We note the estimates from the Haemophilia Foundation Australia, AHCDO and the Commonwealth Department of Health are all somewhat lower than our estimate.

Thus in total we have estimated there to be in the range of 3,500 to 8,000 people living with hepatitis C, as a result of transmission through blood and blood products.

To put these figures into context, in the past twenty years Blood Services in Australia have issued in excess of thirty million blood products.

Canada

The Krever report from Canada has received extensive attention during the various submission. It deserves some attention here with regard to its proper context.

Primarily, the Krever inquiry was instigated to investigate the management of the Canadian Blood Supply with respect to HIV. In relation to HIV Krever made the following comments "The information known … was sufficient for public health officials, regulators and blood bankers in … Australia to take preventive action … it should have prompted a similar response in Canada." A minor focus of the Krever Inquiry was hepatitis C. In relation to hepatitis C, there are major differences between Canada and Australia. The key being that Australia had a much lower incidence rate of post-transfusion hepatitis C than Canada or the US.

Assumptions and/or inferences about the Red Cross cannot be drawn from the examination of a different system operating in another jurisdiction. The findings of the Krever Commission and the recent criminal charges against the Canadian Red Cross are not relevant in any way to the Australian situation.

SECTION 4

Litigation

We have great sympathy for those with hepatitis C. We recommend that personal, social and medical support should be provided to anyone with hepatitis C. ARCBS itself is not an organisation which provides support and counselling as a core service and is not funded to do so. It does provide some counselling at the initial interview with a positive donor or recipient and then it refers people to other expert services. In fact it assisted in the setting up of just such a service in NSW - the Traids Service. This Service provides support and advocacy for people with medically acquired HIV/AIDS and hepatitis C. We have detailed in our written submission several areas where we believe there could be changes made which would improve the situation for people with hepatitis C.

As a humanitarian organisation and charity which is dependent on the goodwill of the Australian public ARCBS fully recognises the importance of transparency in all its activities. The question of litigation is therefore difficult and frustrating for us due to the constraints of the legal process in Australia.

It is on the public record (ARCBS Annual Report) that there are legal proceedings against the Society (and other parties including state and territory governments, hospitals etc) in relation to hepatitis C. The Society has denied liability in all these proceedings. Financial exposure to claims relating to events prior to June 30 2000 are subject to commercial and government indemnities and are dealt with under a variety of arrangements. Many of the proceedings have been finalised. We are unable to comment on the specific situation or outcome of any individual case.

There are sometimes confidentiality issues when litigation is resolved and as you would understand confidentiality clauses are standard practice in legal agreements. Given the issues canvassed by this Inquiry regarding discrimination, confidentiality agreements can also act to the benefit of plaintiffs.

Any decisions about specific financial assistance to people who have hepatitis C should be resolved by the whole community, and involve a number of parties including governments and cannot be resolved by ARCBS in isolation.

SECTION 5

What recommendations would you make to address the issues and concerns of this Inquiry?

Importantly, we are focussed on the future and have considered what more could be done to alleviate the problems of those Australians who have contracted hepatitis C through transfusion.

Finally, we have a number of recommendations and suggestions for the committee's consideration. These focus on areas that other submissions have also identified as needing attention, including better medical, social and personal support services, better access to medical treatment, addressing discrimination, improving public education about the disease, and research focussed on hepatitis C, especially in epidemiology.

Recommendation 1
That, as supported by TRAIDS, measures to ensure appropriate personal, medical, and social support services are considered and made available to those suffering complications as a result of post-transfusion hepatitis C;

Recommendation 2
We strongly support the recommendation of the Australian Hepatitis Council in particular regarding the improvement of community education and awareness of hepatitis C and its causes – such initiatives can only curb the discrimination felt and expressed by those living with the disease;

Recommendation 3
We support and recommend expediting consideration of and access to anti-hepatitis C drugs for Australian patients;

Recommendation 4
Those governments facilitate access to recombinant Factor VIII and Factor IX as recommended by the Commonwealth Working Party and by Haemophilia Foundation Australia in its submission. More specifically, we support efforts to enable doctors treating patients with hemophilia to be able to prescribe recombinant Factors VIII or IX where it is the most appropriate product for the patient;

Recommendation 5
We recommend and support research into Hepatitis C including epidemiological studies

Recommendation 6
We recommend and support the timely introduction of a national government-sponsored haemovigilance system in Australia. Such a system linking all hospitals with ARCBS would provide valuable data to detect hepatitis C transmission, other emerging blood borne infectious diseases and other non-infectious complications of blood transfusion. This would ultimately enable us to maximise patient safety and care for the longer term.

We also offer several additional suggestions for the committee's consideration:

Suggestion 1
If the committee wishes to further explore universal lookback, it would be worth focusing on younger patients transfused in the 1980's, or to give consideration to patients who were under a certain age when they were transfused. Unlike the majority of transfusion patients who were quite elderly when transfused, younger patients would be much more likely to be alive today. They may have experienced the burden of (perhaps undiagnosed) disease for a considerable part of their life. They would be likely to both qualify for treatment and be able benefit from treatment once diagnosed.

Suggestion 2
Government consideration for mandatory reporting to ARCBS by medical practitioners or healthcare professionals of suspected transfusion transmitted cases of Hepatitis C to enable more timely tracing and adequate support of those affected.

Suggestion 3
In agreement with many of the submissions, support for an educational program for the medical community about hepatitis C generally, including transfusion acquired hepatitis.

In conclusion, I have spoken about how Australian management and decision making about blood and its safety has been based on knowledge available at the time, and has been in line with best international practice.

Like all in the healthcare system, we strive to reduce risks wherever possible. However, all medical procedures involve risk and there has been, and continues to be risk in blood therapy. Blood is a biological material and it is never possible to say that there are no associated risks; accordingly there is inherently a balance of risks and benefits involved in its use.

The current risk of receiving a hepatitis C infection through blood is less than 1 in 3 million. The choice of accepting this level of risk must be weighed against the possibly life threatening consequences of not receiving a transfusion.

I reiterate that we extend our sympathy to each Australian who has acquired hepatitis C. It is a sad fact that some people have contracted hepatitis C through blood transfusions. We recognise the impact that this disease can have on the person and their family. The heartfelt accounts within the submissions of those affected speak eloquently and we particularly extend our sympathy to those who have or will develop symptoms and complications.

We are committed to continuing to provide services and to working with the Australian and State and Territory Governments to improve options and remedies available to those in need.

ARCBS, clinicians and health authorities have a collective responsibility to understand levels of risk in relation to transfusion therapy so that patients and the community at large can be adequately informed.

We look forward to hearing the findings of this Inquiry, and we would be happy to answer your questions.

Thank you for your time today.

Figure 1: Timeline of key events

Date	Event
1970	Hepatitis B screening started by Australian Red Cross
1975	Existence of NANBH reported internationally
1979	First Australian post transfusion study commences
23 January 1982	Results of first study are published in Lancet
1987	ALT and anti-core testing introduced by Blood banks in USA
01 July 1987	ALT screening introduced in Queensland
23 September 1987	Second Australian post transfusion hepatitis study commences
1987	Decision made by the NBTC not to support routine surrogate testing
1988	Announcement of discovery of hepatitis C
11 August 1989	First anti-hepatitis C virus research tests arrive (1st generation tests)
14 February1990	Commencement of routine 1st generation anti-hepatitis C virus testing by Australian Red Cross
1991	Introduction of 2nd Generation anti- hepatitis C virus testing
1994	Introduction of 3rd Generation anti- hepatitis C virus testing
December 1994	Donor triggered Lookback approved by Australian Health Ministers
1995	Results of the second Australian post transfusion study are published in MJA
1996	Australian Red Cross Blood Service is established
2000	Introduction of NAT testing

ALT	=	Alanine aminotransferase, a liver function test
MJA	=	Medical Journal of Australia
NANBH	=	Non-A, Non-B hepatitis
NAT	=	Nucleic Acid Testing
NBTC	=	National Blood Transfusion Committee

APPENDIX ONE

SUBMISSION TO SENATE INQUIRY
Dr David Rosenfeld

Honourable Members of the Senate,
I am David Rosenfeld, Head of Haematology (the Speciality that looks after the Blood) in South West Sydney. I have worked in the Public Hospital system for 30 years and have been Head of Haematology for over 20 years. We presently serve a population of around 820,000 with approximately 2000 Public Hospital Beds. We run a very busy Clinical Haematology Service which cares for patients with leukaemia, lymphoma, myeloma and many patients with anaemia and I am also responsible for the Hospital Blood Bank, which actually supplies the blood to the patients, after receiving it from Red Cross. Nearly all of the blood diseases that we treat require blood products in some form. The diseases themselves cause deficiencies in the production of blood cells, white cells and platelets and these require replacement. Treatment of these diseases comprises chemotherapy which also stops the production of blood cells. The Haematologists are major users of blood products in the South West Sydney Area Health Service followed closely by Trauma patients, such as motor vehicle accidents and the like. Easy availability of blood products is an essential requirement for the treatment of cancer patients.

To look after and treat these patients and other diseases such as thalassaemia, haemophilia and anaemia, we need to have ready access to a quality blood supply. We need to have confidence in the supply and our patients need to have confidence in the supply and not be overly concerned that they may be getting a product that has been labelled "risky".

Whenever we start patients on a transfusion program or supply a blood product we always explain to them that the product is the safest that it has ever been and that it is extensively tested however, there remains a small risk of infection with known and unknown viruses. This risk continues to diminish all the time. We spend a lot of time discussing these type of risks with patients and if we were to need to cajole patients into accepting blood to save their life, the situation would become untenable.

Supply of blood products is an issue, recent shortages in supply of red cells, platelets and Intragam has led to problems treating our patients, leading to delays in resuscitation, treatment and the obvious increases in morbidity and mortality.

Australia has had the safest blood supply in the world and NSW Red Cross was one of the first to attempt to exclude risk groups from donating blood, which was to prove correct.

By and large, blood is only administered to save life or reduce morbidity. If there were alternatives most of us would certainly use them in its place.

The Red Cross has always to the best of my knowledge supplied the safest product available.

I have also been involved with the "look back programs". This is a very laborious process often without a positive outcome.

I am very concerned that our patients will lose confidence in the quality of our blood products.

Dr. David Rosenfeld, FRACP FRCPA
Head of Haematology SWSAHS

APPENDIX TWO

SUBMISSION TO SENATE INQUIRY
Statement by Paul V. Holland, M.D., April 7, 2004

I have been asked by the Australian Red Cross to state my opinion regarding the issue of whether or not the Australian Red Cross blood program should or should not have implemented nonspecific, so-called surrogate, testing for non-A, non-B viral hepatitis in the late 1980's, before eventual implementation of the specific hepatitis C antibody test in 1990.

My name is Paul Holland. I am a physician, currently licensed to practice medicine in California and New York. I have been involved in the field of blood banking and transfusion medicine for approximately 40 years, beginning with my service at the National Institutes of Health (NIH) in Bethesda, Maryland, where, eventually, I was Director of the Blood Bank Department, from 1974 to 1983, and continuing as the Medical Director and Chief Executive Officer of what is now known as BloodSource, but which was formally known as the Sacramento Medical Foundation Blood Centers, from 1983 until the present. BloodSource is a large, regional, not-for-profit community blood center, collecting over 200,000 units of blood a year and performing serologic tests for antigens and antibodies of hepatitis viruses and retroviruses like HIV, and also performing nucleic acid technology (NAT) testing for genetic material of these same viruses, which may be transmitted by blood transfusions, as well as by other means.

During my time at the NIH, my major research interest was in finding means to reduce the risk of transfusion-associated viral hepatitis, including evaluation of surrogate (or substitute) tests to identify blood donors carrying what we then called "non-A, non-B viral hepatitis." In addition, our studies at the NIH showed that this third type of viral hepatitis could be transmissible by blood transfusions to chimpanzees and to humans but was unrelated to both hepatitis A (infectious hepatitis) and hepatitis B (serum hepatitis), thus the use of the term non-A, non-B hepatitis. I was an investigator and co-author of a number of studies that came out of our research work at NIH on the potential value of screening donors for an elevated alanine amino transferase (ALT) test, as well as antibody to the hepatitis B core antigen (anti-HBc, "anti-core"). Our major findings on the potential value of these two surrogate tests were published in 1981 and 1986, and did show a correlation (association) between an elevated ALT or presence of anti-core in a donor and non-A, non-B hepatitis in recipients followed prospectively for 6-9 months after their multiple transfusions. However, we did not perform a randomized, controlled trial to prove these points. Instead, in 1981 we began routinely to screen all units of blood for ALT and to discard units if the ALT were elevated. We continued to evaluate the risk of transfusion-associated hepatitis over the next three years; we showed that ALT testing failed to decrease the risk of non-A, non-B hepatitis in carefully, prospectively, followed patients.

During the same time that I was at NIH, I was the chairman of the oversight committee for a National Heart, Lung and Blood Institute (NHLBI)-sponsored study called, "The Transfusion Transmitted Viruses (TTV) Study," on which Dr. James Mosley was the principal investigator. The TTV Study was a multi-center study, carried out in four cities in the United States, involving over 3,000 patients, half of whom were transfused and half of whom were not. The TTV Study was carried out over five years and resulted in a number of publications, including ones in 1981 and 1984, which showed a correlation between an elevated ALT in donors, as well as the presence of antibody to hepatitis B core antigen in donors, and non-A, non-B hepatitis in recipients. As with the NIH studies, this was not a randomized, controlled trial; plus, this study also tested the donors' blood after transfusion. Much of the blood used in the TTV Study came from those paid for it, so-called "paid donors." Further, the rate of hepatitis (3.2%) in those not transfused in the TTV Study was almost double that found in transfused patients in Australia (1.7%) about the same time.

During the 1980s, I was involved with three committees of the American Association of Blood Banks (AABB), which evaluated the data from the NIH and TTV studies, as well as studies conducted in other parts of the world, on the association between laboratory tests in donors and the potential of non-A, non-B hepatitis in blood transfusion recipients. The first AABB committee, the ad hoc Committee on ALT Testing, was active from 1981 to 1982, and concluded, based on the two American studies, as well as other studies available in the literature, that it was not appropriate at that time to perform ALT screening of blood donors. This national committee included outside (non blood banking) hepatitis and infectious disease experts and became the AABB Transfusion-Transmitted Diseases Committee, of which I was a member from 1982 to 1994. After additional meetings and further evaluations of the available data, the Transfusion-Transmitted Diseases Committee recommended in 1986 that two surrogate tests for non-A, non-B hepatitis, specifically ALT and anti-core, be put into place potentially to reduce the risk of non-A, non-B hepatitis transmission to transfusion recipients. This recommendation was made to the AABB and to its Standards Committee, of which I was then a member and, in fact, chairman, from 1985 to 1989. In the 12th Edition of the (voluntary) Standards of the American Association of Blood Banks, published in 1987 for its institutional members, for the first time there was a requirement to implement, as an "interim measure to attempt to reduce the risk of transfusion associated non-A, non-B hepatitis," anti-core and ALT testing on a sample of blood from each donation, since it appeared that there would be no specific test for non-A, non-B hepatitis forthcoming. This standard to implement surrogate testing by the AABB was adopted for its members despite a lack of specific evidence that such nonspecific testing would be effective and, to the contrary, some evidence that it would not be effective in reducing the risk of transfusion-associated non-A, non-B hepatitis in the United States. There was never a government requirement in the USA for such surrogate testing for non-A, non-B hepatitis due to transfusions.

In sum, I believe, from my work at the National Institutes of Health and on specific blood banking committees in the USA, I am in a unique position to give an opinion on whether or not Australia should have done what America did in instituting surrogate tests for non-A, non-B hepatitis in the late 1980's, before a specific test for hepatitis C was discovered and eventually implemented in both countries in 1990. While it initially appeared in one widely quoted study that the implementation of the surrogate tests for non-A, non-B hepatitis in the United States reduced the risk of hepatitis C virus transmission by transfusions, a subsequent evaluation by the same authors, which was more complete and performed with a more sensitive test for hepatitis C antibody, revealed a negligible impact on the risk of hepatitis C transmission in multiply-transfused patients before implementation of the specific test for hepatitis C carriers in 1990. Further, in a number of countries like Australia, the risk of hepatitis caused by transfusions from the early to the late 1980's decreased, as much or more than in the USA, without implementation of surrogate testing, probably due to the measures put in place to reduce the risk of transmission of the virus of AIDS (HIV). If asked, I would have recommended against institution of surrogate tests for non-A, non-B hepatitis transmission by transfusion in Australia in the 1980's. Even in retrospect, I believe this would have been the correct decision. The risk of transmission of viral hepatitis by transfusions was already much lower in Australia than it was in the United States. Consequently, the application to Australia of just two correlative studies conducted in America, especially when coupled with many studies that came from Europe, which did not show an association between surrogate tests performed on donors and the appearance of non-A, non-B hepatitis in transfusion recipients, was not warranted. Further, unlike Australia, "paid donors" (those who sell their blood for transfusion) are not illegal in the USA even today.

I would like briefly to cover five points regarding the potential impacts of implementation of the surrogate tests ALT and anti-core for detection of individuals infected with non-A, non-B hepatitis who were asymptomatic, without apparent risk factors, and qualified as blood donors. The first point is the relationship between an elevated ALT or reactive anti-core test and resultant hepatitis in transfusion recipients, or not. The second point is the concordance of an elevated ALT and/or anti-core in blood donors with detection of hepatitis C virus antibody when this latter test became available. The third point is the differential impact of the loss of donors in the United States versus Australia, and how their donations of blood would be replaced in each country. The fourth point has to do with what to do with donors found to have a reactive surrogate test. The fifth point is the potential for increased risk with a screening test in place that was non-specific and incapable of identifying the majority of carriers of non-A, non-B hepatitis, while purporting to be effective in reducing such risk.

In analyzing the NIH studies and the TTV Study, there appeared to be about a 30% correlation between an elevated ALT in a donor, or presence of anti-core, and resultant hepatitis in recipients. Again, this was just a correlation – not proof that they were connected. All of these patients were being followed carefully for 6-9 months for evidence of hepatitis but it could not be proven they developed non-A, non-B hepatitis (almost all of which was due to hepatitis C) from the unit of blood that had a reactive test, compared to other units of blood that they received, which did not have an elevated ALT or a reactive anti-core test. Further, it should be noted that 70% or more of the time, when a unit of blood had an elevated ALT or anti-core, hepatitis did not result in the blood transfusion recipient. The latter finding would seem to indicate that the vast majority of individuals who qualified as blood donors but had a reactive surrogate test were not carrying what was eventually identified as the hepatitis C virus, the major cause of non-A, non-B viral hepatitis. In addition, with the high background rate of viral hepatitis (3.2%) in un-transfused but hospitalized patients in the TTV Study, it was not clear that hepatitis identified in transfused patients was actually due to the blood transfusions, and not another, more likely, source.

The second point to make is that when the hepatitis C virus antibody test became available, studies were carried out to identify this antibody in otherwise qualified blood donors who did or did not have an elevated ALT or anti-core. In both the U.S. and in Australia, the vast majority of blood donors infected with hepatitis C did not have an elevated ALT or a reactive anti-core. This finding likely accounted for the lack of efficacy of the surrogate tests in reducing the risk of transfusion-transmitted hepatitis C virus in multi-transfused patients in the USA.

The third point is to consider the replacement of discarded blood in the U.S. with implementation of the surrogate tests and the potential loss of donors in Australia if these same tests had been implemented. In each country, by definition, 2.5% of normal people have an elevated ALT level. Their blood would automatically be discarded, along with the blood of those donors with an elevated ALT for any reason, only some of whom were likely infected with the hepatitis C virus. In addition, studies in the U.S. revealed that from 3-5 % of blood donors had a reactive test for anti-core. Thus, in the U.S., it appeared that 6-8% of blood donations would have a reactive anti-core test and/or an elevated ALT and would have to be discarded. However, during that time, the U.S. was already importing hundreds of thousands of units of blood from Europe, to supplement its supply and could import more to make up for losses through the implementation of surrogate tests. Australia did not have the possibility of importing blood from other countries; any loss of donations would have to be made up in Australia, primarily by enlarging the donor pool. It is not clear that Australia could have sustained such an immediate loss of donations and make up for it, certainly without jeopardizing patient safety, especially by replacing deferred regular donors with new, first-time, generally more-at-risk, donors.

The fourth issue regarding implementation of surrogate tests is what to do with donors found to have a reactive anti-core or an elevated ALT. The two surrogate tests, ALT and anti-core, have poor specificity, sub-optimal reproducibility, and no means of being confirmed, especially when found in healthy individuals, without risk factors for hepatitis, who qualify as blood donors. An elevated ALT level is often found in patients with a presumptive diagnosis of viral hepatitis; it helps solidify that diagnosis. Similarly, a reactive anti-core test in an individual with signs and symptoms of viral hepatitis helps determine that the illness in that patient is due to hepatitis B virus. However, a reactive anti-core test, in a normal, healthy individual without risk factors, might be completely non-specific, i.e., due to some innocuous finding, or, even if specific, indicate only prior infection with hepatitis B virus but, in most cases, recovery from, and likely immunity to, it, especially if the test for the hepatitis B surface antigen were not reactive, which generally is present with acute or chronic hepatitis B virus infection. Thus, donors whose blood was discarded because of an elevated ALT or a reactive anti-core test, when sent to their doctors, might or might not have follow-up testing with the same findings. In fact, different assays for ALT and different tests for antibody to core often do not reveal the same findings even when the individual is truly infected with a hepatitis virus. Further, without confirmatory tests to indicate that the elevated ALT and/or reactive core antibody test were due to non-A, non-B hepatitis, donors could be confused and greatly upset when being informed about these non-specific findings. Such donors would not only stop donating, but might tell others similarly not to give blood.

Finally, when a test or tests are implemented to prevent the potential transmission of a transfusion-transmissible virus, such as hepatitis C, some individuals may actually donate blood to get the test, or donate despite having risk factors in the belief that the test would pick them up if their blood were truly infected and, thus, would not cause harm to patients. While we have little direct evidence of this test-seeking behaviour for individuals with viral hepatitis, we and others have seen this behaviour with another test, the test for antibody to HIV, the virus of AIDS. Thus, with a surrogate test or tests in place that would not detect the majority of individuals carrying the hepatitis C virus, those individuals at risk, i.e., carrying the virus, would more likely than not pass the test, have their blood transfused and actually increase risk for transfusion recipients, instead of decreasing it.

In sum, I would have recommended in the 1980's that Australia not adopt surrogate tests to reduce the risk of non-A, non-B hepatitis transmission by transfusions. My opinion is the same today. The two USA studies, which demonstrated a correlation between the surrogate tests in some donors and transfusion hepatitis in a proportion of recipients, were not proof that these tests would be effective. Two other studies in the U.S. that looked at efficacy after implementation did not show efficacy. There was little overlap between an elevated ALT and/or anti-core presence in individuals who were shown to have specific antibodies to hepatitis C virus. Most asymptomatic individuals with hepatitis C virus infection did not have an elevated ALT or a reactive anti-core test, and most post-transfusion hepatitis occurred in patients transfused with blood from donors who had a normal ALT level and no anti-core. Conversely, the vast majority of individuals with an elevated ALT and/or anti-core were not infected with the hepatitis C virus. With the widespread implementation of the two surrogate tests in 1986 and 1987, the loss of donations in the U.S. were, in part, made up by importing more blood from Europe. The option of importing blood from other countries was not available to Australia. What to do with donors, both in the U.S. and in Australia, who had reactive surrogate tests, was problematic. The low specificity, poor reproducibility and lack of confirmatory testing created problems for donors in the U.S., which would have been also present in Australia. Finally, test-seeking by donors, or donations by donors who knew they were at risk but felt a test could identify them if their blood were truly infectious for hepatitis C, would potentially increase the risk of hepatitis C from transfusions for patients - not decrease it. Without proper proof, especially from Australia, that surrogate tests would be effective, it is my view that testing for ALT and anti-core should not have been introduced in the 1980's in Australia, which had an entirely volunteer, unpaid donor base, unlike the USA.

APPENDIX FOUR

CURRICULUM VITAE: Dr Brenton Wylie

CURRICULUM VITAE

Name: **BRENTON RUSSELL WYLIE**

Date of Birth: 8 September 1957. Sydney, Australia

Qualifications:

- 1981: MBBS Sydney
- 1988: FRACP (Fellow Royal Australian College of Physicians)
- 1988: FRCPA (Fellow Royal College of Pathologists of Australia)
- 1995: Post Grad. Certificate in Management, Monash Mt Eliza

Current Appointments:

- National Blood Products Manager, Australian Red Cross Blood Service
- Associate Professor of Medicine, University of Sydney

Education:

High School:

- Sydney Boys High School, 1970-5 - Prefect, 1975
- School Certificate, 1973 (8 Advanced Levels)
- Higher School Certificate, 1975 (5 First Levels)

Tertiary:

- Medicine at University of Sydney, 1976-80
- Medical Degree, 1981
- Finance for Senior Executives, Harvard Business School, USA, 1996
- Strategic Executive Program, Monash Mt Eliza, current enrolment

CURRENT APPOINTMENT

National Blood Products Manager

This position is responsible for the overall strategic planning for blood and blood product production for ARCBS. Responsibilities include planning, relationship with CSL, new products including leucodepletion and pathogen inactivation, Rh program and surplus blood products. This position was created in 2003 and reports directly to the Chief Executive Officer of the Australian Red Cross Blood Service.

PREVIOUS APPOINTMENTS

Director, Blood Products and Tissue Banking, Australian Red Cross Blood Service

This position is responsible for the overall strategic planning for production for ARCBS. Responsibilities include planning, relationship with CSL, new products including leucodepletion and pathogen inactivation, coordination of the Australian Bone Marrow Donor Registry (ABMDR) activity, Cord Blood Banking, donor deferral for vCJD, Rh program and surplus blood products. I held this position which was created in 2000 and reported directly to the Chief Executive Officer of the Australian Red Cross Blood Service until 2003.

Director, Australian Red Cross Blood Service – NSW/ACT

This Business Unit of ARCBS was responsible for the collection, preparation and distribution of blood and blood products to hospitals throughout NSW and ACT and also for the provision of plasma to CSL Ltd in Melbourne for fractionation into specialised products which are returned to the Organisation for distribution. There were 30 fixed sites across NSW and ACT with 3 sites being in the Sydney Metropolitan Area. ARCBS-NSW was also and remains the major tissue typing and organ donation co-ordination centre for NSW and ACT. The Business Unit had a total operating budget of $48 000 000 and a staffing of approximately 550 EFTs. The Director of ARCBS NSW/ACT, reported directly to the Chief Executive Officer of the Australian Red Cross Blood Service. I held this position from 1991 until 2000.

WORK HISTORY

1981	Intern Royal Prince Alfred Hospital.
1982-3	RMO (Medical) Royal Prince Alfred Hospital Training in ICU, Casualty, Haematology, Endocrinology, Gastroenterology, Neurology, Cardiology, Nephology and Country Centres (Dubbo and Orange).
1984	Medical Registrar Royal Prince Alfred Hospital, Training in General Medicine, Psychiatry and Rheumatology. This position also involved participating in a roster as the admitting registrar who was responsible for all medical patients in and admitted to the hospital out of hours.
1985-7	Haematology Registrar Royal Prince Alfred Hospital, Training in clinical haematology, haematological pathology, performance of bone marrow aspirates and trephines.
1986	Medical Superintendent (Acting) Royal Prince Alfred Hospital. Responsible for the administration and training of 120 interns RMOs and registrars.
1987	Registrar at the NSW Red Cross Blood Transfusion Service.
1988	Senior Registrar at the NSW Red Cross Blood Transfusion Service.
1989-1991	Assistant Director at the NSW Red Cross Blood Transfusion Service.
1990	Honorary Consultant, Edinburgh and South-East Scotland Blood Transfusion Service.
1991-2000	Director of the Australian Red Cross Blood Service-NSW/ACT
1993	Consultancy for World Health Organisation in Malaysia.
1994	Appointed as a Senior Clinical Lecturer in Medicine, Sydney University.
1997-	Appointed Associate Professor of Medicine, Sydney University.
2000-2003	Director, Blood Products and Tissue Banking, Australian Red Cross Blood Service, Australian Red Cross Blood Service
2003-	National Blood Products Manager, Australian Red Cross Blood Service

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J Wong, J Pink, A Ribeiro, I M Stewart, B R Wylie, C Wright. *'Factor VIIIc Recovery in Blood Collected into CP2D-Adenine and CP2D'*. Abstract, ASBT 1994

J Wong, J Pink, A Ribeiro, I M Stewart, B R Wylie. *'The Effect of Temperature Cycling of Fresh Frozen Plasma (FFP) on Factor VIIIc Recovery'*. Abstract, ASBT 1994

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Andrew R Davis, Anna M Kowalik, Susan L Ismay, Kenneth G Kenrick, Mark G Dean, Brenton R Wylie. *"A Positive Hepatitis C Enzyme Immunoassay Antibody Test in A Low Risk Population: What Does It Mean?"*. Medical Journal of Australia, 1995, 163:7:385.

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Wong, J.M. Pink, M.G. Dean, C.R. Tiley, B.R. Wylie. *"FFP and Platelet Audit of Public Hospital Blood Banks"*. Abstract, ASBT 1996.

Wong, M.G. Dean, M. Ingram, B.R. Wylie. *"Preoperative Autologous Blood Collection - Is It Effective?"*. Abstract, ASBT 1996.

APPENDIX FOUR

CURRICULUM VITAE: Dr David Rosenfeld

CURRICULUM VITAE

NAME: ROSENFELD, David

TEL. NOS:

(02)98285166 OFFICE
(02)98285176 FACSIMILE

DATE OF BIRTH:

21st January, 1950

ACADEMIC QUALIFICATIONS:

MBBS, SYDNEY UNIVERSITY, JANUARY 1974
FRACP, SYDNEY, JULY 1981
FRCPA, SYDNEY, JULY, 1981

Appointed Conjoint Senior Lecturer in the Department of Medicine, South Western Sydney Area Health Service, Clinical School and School of Pathology, Faculty of Medicine University of NSW. 15th March, 1993.

PROFESSIONAL TRAINING AND EXPERIENCE:

1974 - 1976	Intern, Resident and Medical Registrar at Sydney and Secondment Hospitals
1977 - 1978	Haematology Registrar at Prince of Wales Hospital
1979 – 1981	Haematology Registrar at Royal Prince Alfred Hospital
1982	Appointed Staff Haematologist, Liverpool Hospital
1985	Appointed Senior Staff Haematologist, Head of Haematology
1986 - 1991	Acting Director SWAPS
2002 – to Date	Chair, Medical Staff Council, Liverpool Health Service

ASSOCIATIONS:

- Fellow of the Royal College of Pathologists of Australasia
- Fellow of the Royal Australasian College of Physicians Member of Haematology Society of Australia and New Zealand
- Member of Australasian Society of Blood Transfusion
- Member of NSW Thalassaemia Group
- Member of International Society of Blood Transfusion
- Member of International Society of Haematology
- Member of Australian and New Zealand Apheresis Association
- Member of Clinical Oncology Society of Australia
- Council Member of International Society of Laboratory Haematology

- Member of European Haematology Association
- Member of American Society for Apheresis
- Member of International Society for Apheresis
- Member of Australian Salaried Medical Officers Federation
- Member of Australian Medical Association
- Member of Eastern Suburbs Medical Association
- Member of Medical Staff Councils of: Liverpool, Campbelltown, Camden, Bowral and Fairfield Hospitals

PUBLICATIONS:

"Mantle Zone Lymphoma" - D. Rosenfeld, D. Joshua and H. Kronenberg.
Paper delivered at the Silver Jubilee Meeting of the Royal College of Pathologists of Australasia in Sydney, 1980.

"Treatment of Factor VIII Inhibitor with Plasmapheresis, Immunosuppression and High Dose Human Factor VIII Replacement Complicated by Fatal Myocardial Infarction" - D. Rosenfeld, M. P. Harvey and A. Hackett.
Paper delivered at the joint meeting of the Haematology Society of Australasia and the Australasian Society of Blood Transfusion, Melbourne, 1991.

"Is Microscopy Alive and Well Today?" - D. Crowe and D. Rosenfeld. Paper delivered at the 3rd South Pacific Congress of Medical Laboratory Science, 1991.

"Analytical Performance of a Commercial Erythropoietin Radioimmunoassay Kit and its Clinical Use in Haematology". - V. Kumar and D. Rosenfeld. Paper delivered at the AACB Meeting, 1992.

"Coagulopathy Associated with Massive Blood Transfusion: The Liverpool Hospital Experience. M. P. Harvey, T. Greenfield, D. Rosenfeld. Paper delivered HSA/ASBT
Annual Scientific Meeting, 1994.

"Investigation of the Patient with Anaemia" D. Rosenfeld. Modern Medicine of Australia 37:6. 1994.127-131.

Recombinant Interferon Alpha and Haemolytic Uraemic Syndrome: Cause or Coincidence? M. Harvey, D. Rosenfeld, D. J. Davies ,B. M. Hall. American Journal of Haem. Vol. 26. No. 2. June 1994 152-153.

A New Generation of Haematology Analysers, Evaluation of Cell Dyn 3500: R Watman, L. Vardanega, D. Rosenfeld.
Paper delivered at AIMS Annual Scientific Meeting, Melbourne 1994.

CURRENT POSITION:

Appointed as Staff Clinical Haematologist,	January 1982
Acting Director South Western Area Pathololgy Service	1987 - 1990.
Head of Clinical and Laboratory Haematology and Blood Bank.	1986 to present.
Chairman Liverpool Health Service Medical Staff Council	

GRANTS:

Clive and Vera Ramacciotti Grant for study of "Molecular Rearrangements in Non-Hodgkin's Lymphoma. Clinical and Pathological Correlations".
Drs. M. P. Harvey and D. Rosenfeld.

Bob Pitney Award 1994. Haematology Research and Education Fund.
Dr. David Rosenfeld and Dr. Michael Harvey. "For a study on the Genetic Basis of Non Hodgkin's Lymphoma".

Bob Pitney Award 1994. Haematology Research and Education Fund.
Prof. F. Wong, Annabel Carney, Dr. D. Rosenfeld and Dr. M. Harvey.
"Feasibility Study of PCR Detection of a Thalassaemia Community Screening.

APPENDIX FIVE

CURRICULUM VITAE: Paul V Holland MD

CURRICULUM VITAE

Paul V. Holland, M.D.

Birthdate:	October 29, 1937	
Birthplace:	Toronto, Ontario, Canada	
Family:	Wife, Patricia; four children	
Citizenship:	U.S.A.	
Medical Licenses:	California A-20756	Maryland D-14513 (Inactive)
	New York 174293-1	Pennsylvania 1166E (Inactive)

Current Address:

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Education:	B.A.	University of California at Riverside (Zoology)	1958
	M.D.	University of California at Los Angeles	1962
		Graduate courses in Immunology, Immunochemistry, Genetics and Virology at Foundation for Advanced Education in the Sciences, NIH, Bethesda, Maryland	1963-66
Service in Uniform:		Retired with rank of CO6 from U.S.P.H.S.	1963-83

Positions:

Limnologist - U.S. Fish & Wildlife Service, Brooks Lake, Alaska	1959 (Summer)
Research Fellow - Division of Parasitology, Department of Infectious Diseases, UCLA School of Medicine	1961 (Summer)
Medical Intern - University of California at Los Angeles	1962-63
Staff Associate - Clinical Pathology/Blood Bank, Clinical Center, NIH	1963-66
Assistant Resident in Medicine, UC Hospitals, San Francisco and San Francisco General Hospital	1966-68
Assistant Chief, Blood Bank Department, Clinical Center, NIH	1968-74
Chief, Blood Services Section, Blood Bank Department, Clinical Center, NIH	1972-75
Chief, Blood Bank Department, Clinical Center, NIH	1974-83
Clinical Instructor/Assistant/Associate Clinical Professor in Medicine, George Washington University Medical School and Veterans Hospital, Washington, DC	1969-83
Faculty, Section of Microbiology/Immunology, Graduate School at NIH, The Foundation for Advanced Education in Sciences	1970-83

Project Officer, Study on HBsAg Subtyping Reagents with Dr. K. Madalinski, National Institute of Hygiene, Warsaw, Poland	1976-78
Clinical Associate Professor of Pathology, School of Medicine, Uniformed Services University of Health Sciences, Bethesda, MD and Georgetown University School of Medicine, Washington, DC	1977-83
Medical Director/Chief Executive Officer, BloodSource, Sacramento, CA	1983-Present
Clinical Professor of Medicine, Department of Internal Medicine, Division of Hematology/Oncology, University of California at Davis School of Medicine	1984-Present

Memberships:

American Association of Blood Banks
American Society of Hematology
Foundation for Advanced Education in the Sciences, NIH (Board of Directors 1981-83)
California Blood Bank Society
American Society for Histocompatibility and Immunogenetics
International Society of Blood Transfusion
Sierra Sacramento Valley Medical Society
California Medical Association

Awards and Honors:

Israel Levin Scholar in Medicine, UCLA Medical School	1959-60
Diplomate, American Board of Internal Medicine	1969
USPHS Commendation Medal	1971
Diplomate, Blood Banking, American Board of Pathology	1973
Visiting Scientist, Immunopathology Laboratory, National Institute of Hygiene, Warsaw, Poland	1974 (6 mos.)
USPHS Meritorious Service Medal	1979
Zoutendyk Medal, SA Institute for Medical Research	1988
WHO Expert Committee on Quality Assurance in Blood Banking	1991
Bernice Hemphill (Outstanding Administrator) Award, AABB	1993
Emily Cooley Memorial Award, AABB	1994
John Elliott Memorial Award, AABB	1997
Upton-Hemphill Award, CBBS	1998
Honorary Editor-in-Chief, Chinese Journal of Blood Transfusion	2001

Committees:

Immunohematology Training-American Society of Hematology	1971-72
Policy Board for the VA Cooperative Study of Hepatitis Prevention	1970-75
Hepatitis Studies, Blood Resources Branch, NHLBI, NIH	1971-83
TTVS Contract Review Committee, NHLBI, NIH (Chairman)	1975-81
Hepatitis and Vaccine Studies, NIAID, NIH	1971-83
Technical Seminar Program, AABB	1971-75
Immunohematology Section, ASCP Training Institute (Instructor, Director)	1971-72
ASCP Workshop on Hepatitis B Antigen Testing	1973-75
Scientific Section Coordinating Committee, AABB	1975-77,1980-85

Committees (continued)

Committee for Protection of Human Subjects, ARC	1975-83
Ad hoc Committee for Hepatitis Testing, AABB	1976-77
Quality Assurance Committee, Clinical Center, NIH	1976-83
Medical Board, NIH	1972-73, 1975-76,1983
NIH Hepatitis Coordinating Committee (and Subcommittee)	1973-83
Technical Manual Committee, AABB	1974-81
Scientific Council, American Red Cross Blood Program	1980-84
External Affairs Committee, AABB	1981-83
Ad hoc Committees on ALT Testing, AABB	1981-82
Transfusion Transmitted Diseases Committee, AABB (Chairman 1989-94)	1982-94
Standards Committee, AABB (Chairman 1985-89; Vice Chair 1984-85)	1983-89
Ad hoc Committee on AIDS Related Issues and Scientific Program Committee, CBBS	1984-88
Transfusion Committees: UCDMC, Sutter Hospitals, Mercy Hospitals, Enloe Hospital	1984-Present
Transfusion Safety Study Committee, NHLBI (Chairman)	1984-94
Sacramento-El Dorado Medical Society Committees (Media/Library/Liability)	1986-89
Renal Transplant Programmatic Subcommittee (current Chairman) UCD/Sutter Hospitals	1984-94
Nominating Committee and Committee to Revise the Circular of Information, AABB	1987-88
Advisory Board, Air Lifeline	1986-99
Board of Directors, Golden State Donor Services	1987-Present
NCCLS Advisory Committee	1987-95
Membership (Chairman) and Research Committees, National Marrow Donor Program	1988-92
Donor Recruitment Committee, National Marrow Donor Program	1988-95
Ad hoc Committee on AIDS, National Heart, Lung and Blood Institute, NIH	1992-99
Ad hoc Committee on ICL, AABB	1992-93
Ad hoc Committee on Donor Incentives, AABB	1992-93
Ad hoc FDA Liaison Committee	1990-94
Press Oversight Committee, AABB	1994-98
FDA Evaluation Work Group	1994-Present
BCC Executive Committee	1995-02
Viral Activation Transfusion Study (VATS) Steering Committee	1995-02
Medtronics Advisory Board	1996-99
Shiloov Technologies Advisory Board	1997-00
Gen-Probe Advisory Committee	1996-00
AABB Recovered Plasma Task Force	2000-Present
AABB Awards Committee	1998-02
Southeast Tissue Alliance Medical Advisory Committee	1999-Present

Miscellaneous:

Transfusion (Journal of AABB) Associate Editor	1977-81
Transfusion Editorial Board	1982-Present
Editor, Annual Hepatitis Bibliography of the Hepatitis Scientific Memorandum	1972-81
Editorial Board, Italian Journal of Gastroenterology	1981-99
Course Director, Immunohematology and Blood Transfusion, Graduate Program of FAES, NIH	1970-83
International Society of Blood Transfusion (ISBT) Council Member	1994-98
International Society of Blood Transfusion (ISBT) President	2000-2002
Editorial Board, Journal of Viral Hepatitis	1994-2003
Board of Associate Editors, Viral Hepatitis Reviews	1995-Present
Editorial Review Board, Journal of Intravenous Nursing	1998-1999
Editorial Board, Blood Banking & Transfusion Medicine	2003-Present
Journal of Blood Banks & Transfusion Society of Turkey	

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Paul V. Holland, M.D.

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