



**Pre Conference Edition 1999**

**BONE MARROW TRANSPLANT SCIENTIST'S ASSOCIATION OF AUSTRALASIA**

Annual Scientific Meeting  
Saturday 16 October 1999

Wrest Point Convention Centre, Hobart, Tasmania

**Program**

- 8.30 - 9.15 Annual General Meeting
- 9.30 - 10.00 Chairperson: Dr Annabella Chang  
"The Use of 'Real Time' CD34 Quantitation to Optimize Peripheral Blood Stem Cell Harvests: Experience of The Johns Hopkins Oncology Center & Biometric Imaging"  
Dr Steve Noga
- 10.00 - 10.30 **AMGEN Australia BMTSAA Travel Grant Recipient's Report**  
Dr Cheryl Hutchins  
  
*Presentation of the 1999 AMGEN Australia BMTSAA Travel Grant*
- 10.30 - 11.00 Morning Tea
- 11.00 - 12.30 Chairperson: Dianne Tucker  
**AMRAD Investigator Award Symposium**
- 11.00 - 11.15 Alterations of the T Cell Repertoire Post Allogeneic Stem Cell Transplantation  
L. Barrow, M. Raitakari, R. Brown, J. Gibson, D. E. Joshua
- 11.15 - 11.30 Delayed T Cell Depletion of Matched Unrelated Donor Marrow  
D. Ford, J. Argyle, M. Vowels, R. Lindeman
- 11.30 - 11.45 *Ex Vivo* Purging With Rituximab of Peripheral Blood Stem Cells Collected From Patients With Non-Hodgkin's Lymphoma  
CJ Hutchins, KJ James, JV McAlonan, R Bird & STS Durrant
- 11.45 - 12.00 Peripheral Blood Stem Cell Transplantation - What Do We Infuse?  
K. Jones, D. Tucker, A. Fryga, S. Bol
- 12.00 - 12.15 RT-PCR Detection of Tyrosine Hydroxylase in CD34 Selected Stem Cells from Patients Undergoing Autologous Transplantation for Neuroblastoma  
B.Kramer, G McGowage

- 12.15 - 12.30 Stem Cell Selection and Concomitant T Cell Depletion Using CliniMACS for Allogeneic Transplant  
R Soares Mendes, PK Cannell and RP Herrmann
- 12.30-1.30 Lunch
- 1.30 - 2.15 Chairperson: Gail Lazzaro  
"FDA Regulation of Haemopoietic Stem and Progenitor Cell Products"  
Dr Liana Harvath
- 2.15 - 3.00 "Australian Approach to Stem Cell Regulation"  
Dr Albert Farrugia
- 3.00 - 3.15 Open Forum
- 3.15 - 3.45 Afternoon Tea
- 3.45 - 5.15 Chairperson: Cheryl Hutchins
- 3.45 - 4.00 CD8 Depletion Using T8 Murine Monoclonal Antibody-Coated Dense Nickel Particles: Efficacy of Depletion and Safety in Donor Lymphocyte Infusion  
  
K. Atkinson, E.P. Aleya, C. Canning, H. Houde, R.J. Soiffer, S. Giralt, A. Gee, R. Champlinun
- 4.00 - 4.15 Haematopoietic Stem Cell Transplantation for the Treatment of Systemic Lupus Erythematosus  
J. Ouyang, L.Y. Sun, Y.G. Yang, X.M. S
- 4.15 - 4.30 Peripheral Blood Stem Cell Selection Using the ISOLEX 300i  
R Soares Mendes, PK Cannell and RP Herrmann

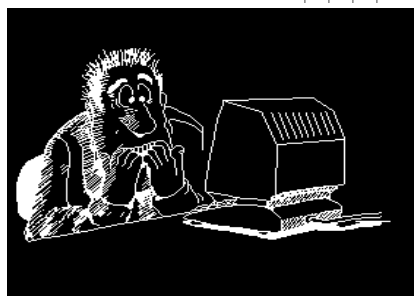
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- 4.30 - 4.45 From Survey to QAP of CD34+ Stem Cell Enumeration  
A Chang and DDF Ma for the BMT Scientists Study Group

- 4.45 - 5.00 Validation of a Stem Cell Washing Procedure Prior to Autologous Transplantation  
N Wiggins, S Ragg, R Lowenthal
- 5.00 - 5.15 Retrospective Analysis of Outcome Following Autologous Haematopoietic Stem Cell Transplantation (HSCT) After Long-Term (≥12) Versus Short-Term (<12 months) Cryopreservation  
RA Harrup, E Tegg, RM Lowenthal
- 5.15 **Presentation of 1999 AMRAD Investigator Award**
- 5.20 Meeting closed



## Editorial

Again members will have wondered if the editor had dropped off the edge of the earth! "What has been happening to the newsletter!" There was simply nothing to report for a Easter newsletter, except one item a member sent in. Thanks Sue, your 'Tech Talk' item appears in this one.

Still the content of this newsletter seems to depend on very few members supporting it.

I have included an article about an English scientist who in the old days would have been called a 'medical technician', when he first started his career. Some of our members may have had a father image senior member of staff when they first started work, especially any of us who trained on the job as trainees. I knew such a man who was a microbiologist.

I meet this Englishman in Seattle some time ago is probably a similar man to some of his junior staff. Because he worked so long in BMT, I thought you might see this as an interesting article. Enjoy.

David Ford

### A man of ideas and questions

***From England to Africa to Seattle, semi-retiring Reg Clift builds legacy of insightful contributions to transplantation***

It was a time of transitions.

Having turned Churchill out of office just the previous year, the British people reversed themselves and once again made him prime minister. The war in Korea raged, and two unknown scientists named Watson and Crick were struggling to describe DNA.

In 1951, 22-year-old Reg Clift was making a transition, too. Discharged from the Royal Air Force and newly married, he and his wife Joyce settled down in Truro, England, where he worked for two years as a technician in charge of the hematology department at the Royal Cornwall Infirmary.

AFTER 30 YEARS of service to the Center,  
Reg Clift has entered semi-retirement.



Things were gray in England, as the economic consequences of World War II dominated every aspect of life. In search of warmth, color and excitement, Clift joined the British Colonial Service in 1953, and the couple moved to Africa.

Little did the two realize that the road to Africa would lead them to Cooperstown, N.Y., and, eventually, Seattle.

Last December, after 30 years as a member of Dr. E. Donnall Thomas' marrow transplant team, Clift stepped down from his full-time duties as a staff scientist in the Clinical Research Division. Though officially retired, he continues to work at the Center, pursuing his research interests on a more flexible schedule.

How Clift came to the Center is a story of fortunate coincidences. His first assignment in Africa was to Nyasaland, now called Malawi. In 1952, this tiny country, smaller than King County, was a 19th century paradise in which few whites had settled and where Africans were among the world's warmest and friendliest. Clift supervised the country's medical laboratory services and had to acquire a range of skills not usually demanded of a technician. Not only did he direct the usual hematology, infectious disease, biochemistry and pathology services (including forensic work), but he also took charge of a production facility that made all rabies and smallpox vaccine used in a group of central African countries, a school for medical technicians and the manufacture of all intravenous fluids used throughout the country.

To accomplish this in the face of endemic malaria, sleeping sickness and epidemics of bubonic plague required a steep learning curve and more than a little sweat. These formative experiences deeply influenced Clift's subsequent life and work.

In 1957, Great Britain embarked on a major political re-organization of its central African colonies, intending to give more security to the settlers of Southern Rhodesia (now Zimbabwe). Not happy with this development, the Clifts transferred to Kenya, arriving in the middle of the Mau Mau war. Clift soon met a brilliant head and neck surgeon, Dr. Peter Clifford, and the two became close friends and working partners. In Africa, cancer of the head and neck is surprisingly common, and because there were no facilities for radiotherapy for thousands of miles, there was strong justification for the use of chemotherapy, which in those days was considered to be dangerous and highly experimental.

The only agents available were nitrogen mustard, busulfan and melphalan. While each of these drugs was dramatically effective in treating the cancers common in Kenya, they did not produce permanent cures. Clift and Clifford used larger and larger doses until stopped by marrow toxicity.

Already, some publications from America and England had described autologous marrow transplants. After some rapid instruction in cryopreservation (using bull sperm) from the local veterinary college, Clift and Clifford performed several autologous transplants of their own, and they were reported in the medical press.

In 1960, a noted American hematologist, Dr. Louis Diamond, visited hospitals in Africa on a World Health Organization tour, and at the government hospital in Nairobi, he met with Clift and Clifford. "We had done 20 or 30 marrow transplants by then, and some patients did very well, but not many," Clift recalls. "After listening to our explanation of the protocol, Diamond recommended that I go to study with Dr. Thomas in Cooperstown. I thought it was a great idea, but we just didn't have the resources to do that."

Six months later, Clift received a letter from Thomas, who had heard from Diamond. Thomas invited him to work on a six-month U.S. Public Health Service fellowship in Cooperstown. The

Wellcome Foundation offered Clift a travelling fellowship, and he soon headed for the States.

Following the fellowship, Clift returned to Nairobi, but the encounter with Thomas had been memorable.

"From the time I first met him," Clift says, "I knew there was something special about him and that he was the type of person I wanted to work with."

When Kenya gained independence in 1963, Clift moved to Nigeria, but the political situation deteriorated into civil war by 1966, and the Clifts decided to leave Africa. So Clift contacted Thomas, who by then had moved to Seattle.

Thomas recalls that, at the time, he had no job appropriate for Clift's skills and experience.

"I told him that I didn't have a research position," says Thomas,



"but that I did have a vacant technician position that he could fill until we could work out a better arrangement.

"The next thing I knew, he showed up in Seattle. We found a research associate position at the University of Washington. Of course, it turned out to be one of the best things to happen to the program. He's been an integral part of it ever since."

With no room at the UW, the university's medical school allocated space for Thomas' team in the former Public Health Hospital on Beacon Hill in south Seattle.

"They put us in the oldest building they could find," Clift says.

"The hospital had suffered significant damage in an earthquake two years earlier. We were on the 10th floor, and there was a large crack in one of the walls.

"I asked one of the engineers how they knew the crack didn't go all the way through. The engineer laughed and said that since they didn't have an X-ray machine, there was no way they could tell. Having just escaped from a war-torn locale, it seemed quite familiar to me."

When Clift arrived, Thomas' team including Drs. Rainer Storb, who now heads the Center's Transplantation Biology Program, C. Dean Buckner, now with Response Oncology, Inc. and Robert Epstein, who is now at the University of Oklahoma, were working on the problems of graft-versus-host disease and tissue typing in the dog model.

"There were two periods in the history of marrow transplantation," Clift says. "There were lots of marrow transplants in the 1950s, nearly all of which were spectacularly unsuccessful. No one knew anything about tissue typing. Donors were selected by how healthy they looked. Lots of people died, and many involved in the research recoiled at the results and abandoned this approach. But Dr. Thomas returned to the laboratory work and persevered."

By 1969, the second period began, as the team was ready to attempt marrow transplants in humans once again. Thomas assigned Storb to work on graft versus host disease while Buckner and Clift were to work on patient support.

Storb recalls that Clift was an interesting fellow because he was not an MD or PhD. "He was a technician who had risen by sheer intellectual ability to the highest level," Storb says. "We always considered him a colleague, and he was valued for his thoughtful and critical insight."

Patients with no immune system needed tremendous patient support. With few effective antibiotics, protecting patients from infection proved a major challenge.

"Reg and Dean worked on white cell transfusions," says Storb.

"The idea was to introduce white cells into the patient to fight infection during the period after transplant before the new donor marrow had begun to function.

"With many new antibiotics, that technique isn't used much anymore, except in one situation, in patients with a proven fungal

infection and no granulocytes (white cells). The use of white cells is very effective and is still used today."

Clift and Buckner also adapted laminar airflow technology to create higher air pressure in patients' rooms than in hallways and carry airborne infections away from patients.

To an outsider, Buckner and Clift might have seemed an odd pairing. Buckner had a bold, even brash approach that contrasted sharply with Clift's more staid British style.

"Dean was a Maoist, the best sort of American revolutionary," recalls Clift. "At first, I had some trouble understanding him because he seemed to favor action in all circumstances, whereas I needed a lot of convincing to do anything at all. He had an enormous influence on me and really changed my outlook on life.

"Don Thomas' genius really was that he could assemble people as disparate as Rainer Storb, Bob Epstein, Dean Buckner and me, and we all worked together."

That assessment is shared by other members of that early transplant team. Storb says the styles of Buckner and Clift effectively complemented each other.

"Reg is less mercurial than Dean," says Storb. "Dean has the ability to convert an idea from the lab into clinical action. That is one of Dean's chief strengths. Reg, on the other hand, is the idea man. He often floated an idea and Dean would say, 'Well, let's do it.'"

Buckner credits Clift with critical thinking, excellent editorial and writing skills and a civilized manner.

"He is always interesting, always brings out interesting aspects of a problem," says Buckner. "He is curious, and he makes people think and work a little harder. Through it all, he maintains style and class. He brought collegiality and gentlemanly behavior to the group. He is always a gentleman."

Thomas attributes Clift's successful integration into the team to the Britisher's personal strengths.

"Reg is always very intellectually stimulating," says Thomas. "He has a keen mind and a tremendous intellect, and his sense of humor with the British penchant for understatement make it a pleasure to work with him."

A story about an early laminar airflow room typifies Clift's humor, says Thomas. One day, a nurse entered the room and exclaimed that she had seen a mouse. Clift, without hesitation, said, "Quick, get a sterile cat."

The first year of working with human patients, 1969, was discouraging for all concerned, says Clift. Success was rarely measured in terms of curing anyone. Usually, it manifested itself in the number of additional weeks patients survived.

Nonetheless, the team persevered, incrementally improving results with each new patient until eventually more survived.

"Most of what we did was not to invent things but adapt them to our use," Clift says.

Over the next decade, Clift lists three developments that produced a profound impact on the program's success.

Besides vulnerability to infections, marrow transplant patients face potential internal bleeding because their new marrow cannot produce enough platelets for clotting. Platelets also are among the last cells to recover.

"One of the most important developments was platelet transfusion," says Clift. "We didn't invent that. The nuts and bolts of platelet transfusion support were worked out in the National Cancer Institute in Bethesda. But we were quick to adopt it and set up our own platelet pheresis unit at a time when most people thought there was no great future in it."

Another necessary advance, says Clift, was the Hickman catheter. Dr. Robert Hickman, a Seattle pediatric nephrologist, designed a tube that could be inserted into the aorta to continuously deliver drugs and remove blood samples.

"You can have no idea how that sort of access revolutionized things," Clift says. "In the old days, you had to stick a needle into a vein every time you wanted to do something for the patient. These patients were black-and-blue from needle sticks, and almost certainly some patients died for lack of a usable vein. So Bob Hickman's development was an enormously influential thing. That was invented here."

Other important developments included cyclosporine and other antibiotics and immunosuppressive agents. Both classes of drugs

made it possible for more patients to survive the most critical post transplant period \_ the time when the new marrow is regaining function.

However, as often as those advances are cited, Clift also points to personal computers as another technological development that proved indispensable. In the past decade, he has assessed transplants for the treatment of acute and chronic myeloid leukemia (AML and CML). He originally followed these diseases by taping charts to a wall.

"When I began working on these databases, we had a small enough number of patients that I could have all the patients with that disease and a certain treatment on the wall on graph paper and I could follow them along. That was 15 years ago.

"Now we've done 8,000 or 9,000 transplants and we've treated 1,500 CML patients and more than 1,000 with AML, and the walls have not grown commensurately. So I became interested in computers. For the past 10 years, I've invested a lot of my time maintaining and using databases that enable me to ask questions about different subsets of patients."

Although medical researchers have used big computers for nearly 30 years, Clift says the ability to download information to desktop computers has made an enormous difference.

"In the early days, if you wanted to ask a new question, you had to visit the oracle at Delphi., or another high priest who knew how to operate the mammoth computer, and ask what you wanted to know. After considerable delay, you received an answer, but it often was not what you expected because you had asked the question in the wrong way.

"Now, if I wake up in the middle of the night and say, 'Gee, I wonder if chocolate consumption affects the survival of patients with a certain disease,' I can now sit at my computer and ask that question very easily, although it is a stupid question. However, the most revealing answers sometimes emerge from asking the most stupid questions. All the sensible questions have usually been asked already."

To ensure that Clift can continue asking questions and contribute to the Center's research, the Clinical Research Division has provided him an office in Eklind Hall and a high-speed phone line to his home that will allow him to "telecompute" more easily. Division Director Dr. Fred Appelbaum says Clift's contribution to the division's research in constructing and maintaining the database has been invaluable.

"An important distinction about the work of the transplant program is that much of it has been incremental, carefully building on past successes and failures," Appelbaum says.

"To that end, Reg has been the singular most important individual in determining how we have organized our knowledge base to make it accurate, available and useful."

Looking back, Clift is satisfied knowing that when he began, almost all children diagnosed with leukemia died within a few months. Now, most children survive leukemia.

However, he does not dwell on the past. The 68-year-old researcher has too many unanswered questions he would like to pursue to stop anytime soon.

How much longer he intends to keep working, Clift doesn't know. However, the curiosity that propelled him from a small town in England to Africa and finally to Seattle undoubtedly will keep him going for some time to come.

story "Reprinted by permission, courtesy of Fred Hutchinson Cancer Research Center."

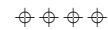


## The Grape Vine

I had an interesting talk to Steve Shaw, the NVE North American products manager. He was visiting Sydney to deliver the Aust. Cord Blood Bank a new design dry shipper that they had

asked to be designed for them. It is smaller than the previous model to make the courier's job easier on the long overseas trips. He was an interesting man with a wealth of experience and knowledge about nitrogen tanks. I wish to share with you. "*The horror story for bone marrow scientists*". As a tank gets older there is more likelihood of a failure of the welding seams. If the seam splits on the internal surface around the bottom and there is a rapid leak of liquid nitrogen into the vacuum space it is possible because of the different gauge of metal thickness between the inner and out skin of the tank that the inner skin is blown inward even before the vacuum safety disk blows. The result is a locked up inventory system that only hacking out with a saw will allow access to. He has seen this happen in the states!!! Obviously he wants us to throw out of our old tanks!

DavidFord



### BONE MARROW TRANSPLANT SCIENTISTS ASSOCIATION OF AUSTRALASIA

*Born to Trevor and Dianne Tucker, Ant.  
Born Saturday 26th June 1999  
Weight 3540g (7 lb 12 oz)*



*Dianne, Trevor and Anthony thank the E  
kindly for their best wishes and flowers -*

*Anthony and Dianne will be in Tasmania  
Scientific meeting.*

Notice is hereby given that the annual general meeting of the Bone Marrow Transplant Scientists' Association of Australasia will be held on Saturday 16<sup>th</sup> October 1999 at the Wrest Point Convention Centre, Hobart, Australia at 8.30 am.

#### AGENDA

1. Welcome to all members
2. Roll call
3. Apologies
4. Registration of proxies
5. Confirmation of the minutes of the Annual General Meeting of The Bone Marrow Transplant Scientists Association of Australasia held on Thursday 16 July 1998 at the Sydney Convention And Exhibition Centre, Sydney, Australia at 11.00 am.
6. President's report
7. Treasurer's report
8. Membership Committee report

9. Ratification of new members
10. Business arising from previous minutes
  - a) NPAAC Guidelines
  - b) Web Page
  - c) Haemopoiesis Meeting
11. Nomination of Chairman for Elections
12. Election of Councillors
13. Appointment of Auditor
14. Committee appointments
15. General business
  - a) ISHAGE
  - b) Newsletter
  - c) BMTSAA meeting 2000

**Tech Talk**  
 Mail Lazzaro  
 Secretary

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Do you remember that some time ago I asked for an opinion on the optimum storage for PBSC without cryopreservation? I chased all around the world asking advice but there was not a lot forthcoming. So I thought I could share my experience - it may spark some discussion.

The patient (a 4 year old male) was to undergo PBSC harvest (Cyco/G-CSF primed) and then proceed to immediate HD Melphalan and PBSCT for neuroblastoma (Stage IV). We stored the product in a Baxter Lifecell flask (4R2110, PL732 plastic, 300 cm<sup>2</sup>) after first adding autologous plasma to achieve a final cell concentration of 1 x 10<sup>8</sup>. The first day of apheresis was stored for a total of 49.5 hours at 4 degrees C in Transfusion Medicine monitored storage. The second day was stored for 25 hours pre reinfusion. Viability at reinfusion was 100 % for both days. The cells were gently agitated after 24 hours storage and returned to 4 degrees C. On the day of reinfusion the cells were brought to RT and again gently mixed.

At apheresis we noted the following :

Total CFU-GM = 50.4 x 10<sup>4</sup>/kg

MNC = 8.9 x 10<sup>8</sup>/kg

CD34 = 2.3 x 10<sup>6</sup>/kg

At reinfusion :

Total CFU-GM = 52.4 x 10<sup>4</sup>/kg

MNC = 8.2 x 10<sup>8</sup>/kg

CD34 = 2.3 x 10<sup>6</sup>/kg

The patient was discharged on Day +31 (23.11.98) . The entire post transplantation course was relatively uncomplicated with early neutrophil engraftment but slow platelet engraftment. I hope this is useful information if ever the question is posed again !! We were happy with the final outcome - processing wise and did not have to add media. There has been some controversy over whether to agitate the cells or not and also the temperature of storage. The agitation question is largely overcome by the dilution with autologous plasma to reduce the concentration of cells in the stored product. The temperature of storage at 4 degrees was largely due to the length of time of storage and local policy.

Sue Carnoutsos



The Fifth International Meeting of ISHAGE was held May 29<sup>th</sup> through June 1<sup>st</sup>, 1999 in Oslo, Norway. After what seemed to be a marathon 34 hour flight (all I wanted to do was lie horizontal and flatten out) wouldn't you know it, my luggage was still travelling around Heathrow terminals whilst its owner was in the land of the Vikings in Oslo. Oh, I forgot to mention, there was a fire at Heathrow, so it was a little hectic. I have to tell you about Oslo Airport! It was elegant, sleek, minimal designer plus! Got the picture? Wonderful woodgrain surfaces, comfortable relaxing colours and everybody looks and is tall, sleek and relaxed, except for the short Australian, Italian looking, crumpled, traveller without her luggage.

A successful Conference is the combination of a great social and educational program and ISHAGE 1999 delivered these aspects. The program covered immunotherapy, T-cells, mobilisation of progenitor cells, the CD34 negative cell, ex-vivo expansion, cord blood and minimal residual disease. Research and laboratory practicalities were discussed and "workshops" provided the opportunity for informal discussion.

The social program provided the opportunity not only to experience Norwegian hospitality but also to meet with colleagues and presenters. The highlights of the conference for me included the uses of T-cells in autologous and allogeneic transplantation, and sailing to a barbequed salmon dinner whilst Icelanders sang Waltzing Matilda.

In summary, the program provided valuable information, possibilities and advances covering the full breadth of haemotherapy and graft engineering.

Nancy Messino.



As most of you who are attending the 1999 conference in Hobart will be arriving on the Friday, Nicole, Beth and I are wondering if anyone would like to join us for a "pre-conference" meal on Friday night. It will be at Rockefeller's restaurant in Morrison St Hobart, down near the waterfront. It has a wide ranging menu, from burgers thru to vegetarian and game meats, and the best desserts in town, all very reasonably priced. Partners welcome of course. If anyone would like to join us, please email me back so I can confirm numbers. Hope to see you in Hobart, Scott Ragg



The 1999 BMTSAA Annual Dinner will be held at "A Splash of Paris" restaurant on the waterfront Elizabeth St Pier complex. Pre-dinner drinks will be served at 7 pm. Cost is \$30 per head and partners are welcome. Vegetarian options have been included on the menu. Drinks will be supplied from one of our kind sponsors. Can those who intend coming to the dinner please email (scott.ragg@utas.edu.au) or fax (03 6226 4894) Scott Ragg so that approximate numbers can be confirmed to the restaurant.



Off the Web

. BLOOD SUPPLY, NEW SCREENING TEST - USA

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A ProMED-mail post  
<<http://www.healthnet.org/programs/promed.html>>

Date: Tue, 9 Mar 1999 16:00:23 GMT-3  
From: GPHIN 6 Mar 1999  
Source: News media, 5 Mar 1999

The nation's blood supply is about to become safer: Blood banks will begin next week phasing in sophisticated new genetic tests designed to wipe out viral infections that occasionally slip into transfusions.

"This is the biggest thing that's happened in blood banking since the HIV test," said James MacPherson of America's Blood Centers, which collects about half the nation's donated blood. The vast majority of transfusions already are infection-free. But the new gene testing, which should encompass all blood transfusions by September, promises to make blood even safer.

That's because the new "nucleic acid testing" can detect tiny amounts of a virus, such as liver-destroying hepatitis C or the AIDS virus, before the blood donor's body has even recognized the infection. Some of the tests can detect as few as 10 copies of a viral gene.

Viral genes spread through blood faster than the immune system begins forming antibodies to fight them, a reaction that may not occur until 20 to 80 days after infection. Today's blood testing depends largely on tests that detect antibodies in an infected donor. So newly infected donors sometimes slip through.

Nucleic acid testing, called NAT by blood banks, promises to close that gap.

It probably will eliminate the few cases of HIV annually caused by donated blood, said Dr. Celso Bianco of the New York Blood Center. And experts estimate it will prevent 84 annual cases of hepatitis C transmission through blood, the majority.

The government hasn't mandated NAT-tested blood yet, because technically it's still experimental: Genetic fingerprinting is commonplace in laboratories, where it's called PCR, for polymerase chain reaction testing. But how to test the entire blood supply raises questions, and blood banks are trying different strategies.

Still, the Food and Drug Administration is strongly encouraging blood banks to quickly begin genetic testing and hospitals to exclusively use NAT-screened blood.

"Everybody with any familiarity with these tests knows this is such an advance ... it would be a terrible mistake not to use it as soon as we can," said Dr. Edward Tabor, FDA's associate blood director. So the FDA is taking the unprecedented step of letting blood banks add NAT to all the other blood safety tests they now perform in a nationwide research project. FDA will monitor the data to decide which NAT method works best.

At first, NAT will hunt hepatitis C and HIV. But eventually, blood banks may test for other contaminants.

The genetic tests also promise that if a brand new virus ever sneaks into the blood supply as AIDS did two decades ago, blood banks could protect Americans much faster, MacPherson said. "This is truly space-age technology," he said. NAT will cost more, about an extra \$6 to \$7 per unit of blood, which will increase hospitals' spending on blood by about 5 percent. Although the FDA is letting blood banks charge for the experimental testing, hospitals can't recover the money from insurers. So some hospitals are questioning if it's worth it. Responded Tabor: "FDA thinks the cost increase will be worth the health benefit."

One of the NAT experiment's biggest questions is whether genetic testing can be performed fast enough. Blood has a limited shelf life, and demand is so great that much is transfused soon after it's donated. But NAT testing takes 48 to 72 hours. That's probably fine for most transfusions of red cells, which last 42 days after donation. But platelets expire in just five days. So hospitals may transfuse platelets that the standard, FDA-approved testing declared infection-free only to learn later that the extra genetic test found a problem. Then they'll have to track down the blood recipient.

[Written by: LAURAN NEERGAARD]

Date: 8 Apr 1999  
From: Marjorie P. Pollack [pollackmp@mindspring.com](mailto:pollackmp@mindspring.com)  
Source: American Red Cross, 8 Apr 1999 [edited]

[What's new in this article:

(1) in the one month since the last press release, one unit of HCV positive blood was identified that was negative by standard testing; (note, the original press release mentioned that it expected to prevent 84 cases of HCV annually -- this article doesn't give the denominator for how many units were screened to yield the one positive to see if the estimates of number of cases prevented should be modified)

(2) expected timetable with full implementation of NAT under the IND in all blood centers by June 1999 (earlier release gave Sep 1999 as date)

(3) change-over from unlinked testing to linked testing - MPP]AMERICAN RED CROSS LAUNCHES NEW GENETIC SCREENING TECHNOLOGY The American Red Cross is pioneering the use of an innovative technology that could add an additional layer of safety to the 14 million units of blood components distributed by the Red Cross to hospitals nationwide each year. It is investigating a new genetic test, nucleic acid testing or NAT, for the early detection of transfusion-transmitted viruses, such as HIV and Hepatitis C Virus (HCV), at its National Genome Testing Laboratory in San Diego, Calif. Already the Red Cross' use of NAT has detected the first unit of HCV-infected donor blood that was negative by standard screening tests, thus preventing a probable transmission of the disease. The Red Cross began evaluating NAT under an Investigational New Drug (IND) application approved by the Food and Drug Administration (FDA) in January 1999. Initially it performed unlinked testing, severing the link between the donor and sample, to validate the processes and systems newly created for NAT. Red Cross tested more than 180 000 unlinked samples. Based on favourable test outcomes, the Red Cross began screening blood donations with NAT at the National Genome Testing Laboratory under the FDA-approved IND in early March 1999. It expects to fully implement NAT under the IND in all of its blood centers by June 1999. "While the U.S. blood supply is already safer than it ever has been and current screening tests are very sophisticated, this innovative technology has the potential to enable the detection of dangerous viruses in donors whose own immune systems have not yet recognized the presence of an infectious agent," says Brian McDonough, chief operating officer, American Red Cross Blood Services. "This new screening method is expected to provide more accurate and earlier identification of virally infected blood. "Because NAT looks directly for the genetic material of viruses, either DNA or RNA, the test can detect an infectious agent's presence much earlier than current screening tests. Most available tests detect the antibodies formed as part of the immune response to a virus, often 20 days to 11.5 weeks after infection. NAT may decrease the time after initial donor exposure to when detection is possible. For HIV, this time is usually six to 10 days after exposure, which NAT should reduce by 30 to 50 percent and for HCV, about 41 days, which NAT should shorten by 50 to 98 percent. While the Red Cross' testing of NAT focuses on HIV and HCV, the test can be tailored for future use to screen for other blood-borne pathogens and for newly emerging viruses, bacteria or fungi for which genetic material has been identified. The Red Cross estimates that rates of NAT-reactive donations among those volunteer donors that test negative by currently performed screening tests for HIV and HCV are one per million donations for HIV and one per 100 000 for HCV. Approximately 4 million people annually receive blood or blood products as part of their medical or surgical care in the United States. Gen-Probe Incorporated of San Diego, Calif., developed and manufactures the semi-automated NAT kits used by the Red Cross. Under an agreement with the Red Cross, Gen-Probe and Chiron Corporation of Emeryville, Calif., will provide instruments and NAT kits for the Red Cross testing.

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Nearly 7% of blood donors in Northern California who were randomly tested were found to be positive for a new type of virus, known as TT[transfusion-transmitted] virus. The virus was first identified in 1997 in Japan when researchers found it in 3 of 5 patients who developed hepatitis after blood transfusions. However, it is still not clear if the virus is harmless, or something to be concerned about.

Bernie R Betlach and colleagues at the Sacramento Medical Foundation Center tested a total of 194 samples from volunteer blood donors in a 13-county area of Northern California. The researchers tested 119 healthy volunteers and 75 donors with elevated blood levels of liver enzymes.

"In each group, 6.7% tested positive for TT virus," Betlach told Reuters Health in a telephone interview. All the samples were negative for other viruses checked during routine donor blood screening.

It is possible that the virus may account for some cases of transfusion-associated hepatitis in those cases in which an individual tests negative for any of the known hepatitis viruses, according to Betlach, but more study is needed to find out if this proposed link is true.

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