



CBMTG Newsletter

Published for the Canadian Bone Marrow Transplant Group

KEYSTONE MEETING CLINICAL HIGHLIGHTS

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The 1996 edition of the Keystone Blood and Marrow Transplant meeting ran from January 15th to January 21st. As always, the action outside the meetings was often more intense or more interesting than that of the official program.

The meeting did not get off to a good start: most people had no idea when the meeting was to actually start. Thereafter the basic science meetings were scheduled later in the evenings, thereby guaranteed to be sparsely attended. Workshops that were well attended often were held in rooms too small to accommodate everyone. Besides these glitches and a couple of off-colour jokes by chairpersons, the meeting covered both old and new ground.

Many of the clinical issues that brought debate and controversy to these meetings in previous years have been settled. Large randomized studies, like those demonstrating the value of autologous BMT for intermediate grade lymphoma or acute leukemia or myeloma have been published. Debate was often muted in these areas. Not so in a couple of other areas.

Following on the heels of Dr.

John Hansen's talks on the excellent results achieved in un-related donor transplants for acute and chronic leukemia, came the stunning (but preliminary) results of haplo-identical transplants from Perugia. Drs. Martelli and Reisner provoked more than a few raised eyebrows in reporting their data on very high CD34 (and severely T-depleted) blood and marrow transplantation, following a variety of radiation, ATG and chemotherapy induction regimens. If reproducible the results were impressive indeed, notwithstanding Dr. Henslee-

This is the first (and last) newsletter to appear only in English. Primarily done to time constraints and the need to get this first Newsletter out quickly after the Keystone meeting.

Subsequent Newsletters will be available both in French and English.

Ceci est le premier (et dernier) bulletin à être publié seulement qu'en anglais. La principale cause est due au manque de temps et ainsi vous faire parvenir la première édition le plus rapidement possible suite à la conférence à Keystone.

Les prochains bulletins seront disponibles en français et en anglais.

Downey's warning of jumping to premature conclusions. (Calgary, Vancouver and now Toronto and Ottawa are to varying degrees going down this road.)

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EDITORIAL

QUO VADIS CBMTG?

H.A. MESSNER, M.D.

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Where are we headed with CBMTG? Are we going anywhere? We all have asked this question on a number of occasions since the idea of a Canadian Bone Marrow Transplant Group was spawned during the Royal College Meeting in 1981. The initial efforts to function as a study group were supported by a modest grant by NCI to meet and develop study protocols. As some of the old-timers will remember the efforts resulted in the preparation of an application for a group grant to sponsor the development of a Canadian BMT registry and to support 4 studies. Unfortunately then the existing enthusiasm for a national study group was dampened by the failure to attract funding. We kept meeting and were successful in organizing the first scientific meeting in 1985. Yet it seemed difficult to engage in more constructive work. This changed somewhat with the advent of transplants using unrelated donors. In order to become eligible to approach NMDP for donors we negotiated with NMDP that Canada would function as a single centre to meet the quota of transplants that had to be performed annually. The formal link established between the Canadian National Coordinating Centre (CNCC) and NMDP served as the model for the now internationally embraced Hub-concept. The need for a common protocol provided the incentive to apply for funding, which was obtained from NHRDP. The study was successfully completed and

published. The united effort of all Canadian Transplant Centres was to a large extent responsible for the continued funding of the Unrelated Marrow Donor Program.

The creation of a more structured group appeared to be necessary to provide the framework for a hopefully effective study group. This realization led to the establishment of CBMTG in its current form and with its current by-laws. At last, we were a structured self appointed interest group --- but as it happened, we were still searching for our role and mission.

The year 1995 changed the status of inertia. We were asked by Health Canada to attend together with professionals involved in the procurement and transplantation of other tissues a National Conference to establish and recommend standards and procedures to minimize the risk associated with transplanted tissues. We recommended to Health Canada to adopt for the practice of a BMT the principles established by the Foundation for Accreditation of Hemato-Cell therapy (FAHCT) as a baseline to ensure standards and to participate in a North America wide accreditation process.

The invitation by Health Canada provided CBMTG with the mandate to advise the Government on BMT related issues. This charge is a challenge for CBMTG and will require a professionally constituted and run organization. This will demand commitment by the executive and will only be possible if many of you are willing to participate in the process. Your current executive would like to start an

information exchange through a newsletter. I invite you to actively participate in the process that should lead to a revision of the existing by-laws, election of an effective executive and active participation of all interested parties. I have a sense that it will be worth the effort.

The most promising sign of a renewed interest in CBMTG is the recent development of a multi-centre randomized study to compare conventionally harvested bone marrow allografts with collections of peripheral blood derived progenitor populations. It is refreshing to see that the study design resulted from the intense collaboration of junior members of various transplant teams. In the wake of this effort similar activities have been initiated. Judging from our recent discussions in Keystone it is likely that other studies will follow.

Quo vadis CBMTG? Buoyed by the renewed enthusiasm we have the opportunity to work together and through this effort develop outstanding, research oriented care facilities for patients in need of a blood or marrow derived transplant.

A document entitled "Draft Document Concerning the Regulation of Peripheral Blood Hematopoietic Stem Cell Products Intended for Transplantation or Further Manufacture into Injectable Products" is available from the FDA.

Fax: 1-800-835-4709

or Internet:

CBER_INFO@A1.CBER.FDA.GOV

Executive Members of the CBMTG

- Dr. Hans A. Messner, Chairperson, CBMTG
- Dr. Hans-Georg Klingemann, Vice-President, Allogeneic Marrow Transplantation
- Dr. Armand Keating, Vice-President, Autologous Marrow Transplantation
- Dr. Anne M. Smith, Treasurer
- Dr. Lothar B. Huebsch, Secretary
- Dr. Marlis Schroeder, Chairperson, Canadian Pediatric Bone Marrow Transplant Group
- Dr. Antonio Giulivi, CBMTG Representative on ISHAGE
- Diane Thauvette, Administrative Assistant, Secretary, Layout and Design

Mail articles to:

Diane Thauvette, Ottawa General Hospital, 501 Smyth Road, OTTAWA, Ontario K1H 8L6

Blood Versus Marrow Allogeneic Bone Marrow Transplantation

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D. SIMPSON, M.D.
University of British Columbia,
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C. BREDESON, M.D.
Ottawa General Hospital,
Ottawa, Ontario

Blood progenitor transplants with autologous support is no longer news, being widely adopted and shown to result in long-term sustained hematopoiesis, more rapid engraftment and economic advantages. Allogeneic transplantation using stem cells however is newer, the potential advantages (and disadvantages) more complex.

Considerable experience by Drs. Russell (Nottingham) and Russell (Calgary) and their conclusions, have led others - especially the folks at MD Anderson (Dr. Korbling) - to unilaterally proclaim (based as usual on historical controls, always "properly" selected) stem cells the winner. Well, maybe not. Remember T-cell depletion in CML transplants? Well at least 2 studies that randomize patients to one form of transplant or another are being undertaken. The EBMT study (Schmitz et al) is ongoing, but a better study conducted by the CBMTG and activated in January 1996 is going to put the considerable potential advantages of blood cell transplants to the test.

Organized by the CBMTG and run by the PI's (Drs. Couban, Simpson and Bredeson et al) the study will look for early and late

potential advantages, in terms of engraftment, GVHD, 4-month survival costs and patient and donor quality of life endpoints. The study has not found external support as yet (the NCIC is having its arm twisted by Dr. Messner at present) but a considerable degree of support from within the CBMTG centres has gotten this study underway. It is expected that 180+ adult patients will be randomized in 8 to 10 centres. The priority placed on this study, its uniqueness, and its collaborative nature will be a very good excuse to create an electronic information/database infrastructure for the CBMTG, a work in progress involving a number of the centres and Stem Cell Technologies' software programs.

Some of the Clinical Studies Presented by CBMTG Transplant Centres

*AMERICAN SOCIETY OF HEMATOLOGY,
SEATTLE, DECEMBER 1995*

- HC Fung, NJ Voss, MJ Barnett, RN Fairey, DE Reece, GL Phillips, JD Shepherd, SH Nantel, HJ Sutherland, CL Toze, H-G Klingemann. Low dose thoraco-abdominal irradiation for treatment of advanced chronic graft-versus-host disease.
- VS Reddy, AK Stewart, HM Prince, H Messner, SL Nanji, AP Wild, CM Ruedy, RR Singaraja, P Chu, CM Lutzko, ID Dubé. Gene transfer into human hematopoietic progenitors in long-term marrow cultures (LTMC).
- C Girouard, J Dufresne, K Imrie, M Prince, AK Stewart, A Keating, M. Crump. Mini-BEAM for relapsed or refractory lymphoma prior to autologous bone marrow transplantation (ABMT).
- HC Fung, SH Reece and MJ Barnett. Allogeneic bone marrow transplantation (BMT) for adults with secondary myelodysplastic syndrome (MDS) or secondary acute myelogenous leukemia (AML).
- LC Berkahn, HC Fung, DE Horsman, A Le, SH Nantel, JD Shepherd, CL Toze, HJ Sutherland, H-G Klingemann and MJ Barnett. Allogeneic bone marrow transplantation (BMT) for adults with chronic myeloid leukemia (CML) in accelerated phase (AP).
- HM Prince, M Crump, K Imrie, AK Stewart and A Keating. Long-term event-free survival (EFS) after intensive therapy with Etoposide, Melphalan and autotransplant in patients failing front-line therapy for Hodgkin's disease and non-Hodgkin's lymphoma.
- HM Prince, M Crump, K Imrie, AK Stewart, JM Brandwein, DMC Sutton, JG Scott, S Sutcliffe, R Tsang and A Keating. High dose Etoposide, Melphalan and autologous bone marrow transplant (ABMT) for advanced Hodgkin's disease: Importance of disease status at transplant.
- Y Khaliq, I Bence-Bruckler, C Bredeson, R van der Jagt, S McDiarmid, LB Huebsch. Once daily Ceftriaxone for febrile neutropenia in an outpatient blood and marrow transplant programme.
- DL Forrest, JJ Spinelli, SC Naiman, JH Davis, HC Fung, H-G Klingemann, SH Nantel, KR Schultz, JD Shepherd, HJ Sutherland, CL Toze and MJ Barnett. Second malignant neoplasms after autografting: The Vancouver experience.
- HM Prince, K Imrie, A Keating, PE Goss, AK Stewart and M Crump. Cyclophosphamide, Adriamycin, 5-Fluorouracil (CAF) and G-CSF mobilization achieves high peripheral blood progenitor cell (PBPC) yield which can support multiple cycles of high-dose chemotherapy.

UNDER CONSTRUCTION: A WEB SITE FOR THE CBMTG

By the spring the CBMTG will have its own "*home page*". Dr. Pierre Laneuville and his colleagues at McGill University have taken on the task of building a presence for the CBMTG on the Internet. If you have any thoughts or questions about the services and contents of such a site give Dr. Laneuville a call [tel: (514) 842-1231; fax: (514) 843-1418; E-mail: lanville@rvhmed.lan.mcgill.ca]

UPCOMING MEETING DATES:

For the World Traveler with Deep Pockets and Good Sponsors

- 22nd Annual Meeting of the European Group for Blood and Marrow Transplantation, Vienna [Australia]. March 3-7, 1996
- Clinical and Managed Care Issues in Blood and Marrow Transplantation for Hematologic Diseases, Washington [DC], March 14, 1995
- Blood Cell Transplantation Fourth International Symposium, Adelaide [South Australia]. March 24-27, 1996
- 4th International Symposium on Recent Advances in Hematopoietic Stem Cell Transplantation, San Diego [California]. April 11-13, 1996
- NCIC Clinical Trails Group Annual Meeting of Participants, Toronto [Ontario]. April 12-15, 1996
- American Society of Clinical Oncology, Philadelphia [PA]. May 18-21, 1996
- International Health Economics Association Inaugural Conference, Vancouver [British Columbia]. May 19-23, 1996
- Second Meeting of the European Haematology Association, Paris [France]. May 29-June 1, 1996
- VI. International Conference on Malignant Lymphoma, Lugano [Switzerland]. June 5-8, 1996
- 12th Annual Meeting of the International Society of Technology Assessment in Health Care, San Francisco [California]. June 23-26, 1996
- 25th Annual Meeting of the International Society for Experimental Hematology, New York [New York]. August 23-27, 1996
- 26th Congress of the International Society of Haematology, Singapore. August 25-29, 1996
- International Meeting Haemopoietic Stem Cell Therapy in Autoimmune Diseases, Basel [Switzerland]. September 26-28, 1996
- 1996 Annual Meeting of the Royal College of Physicians and Surgeons of Canada, Halifax [Nova Scotia]. September 26-29, 1996
- Novel Approaches to Blood and Marrow Transplantation, San Diego [California]. October 2-6, 1996
- American Society of Hematology, Orlando [Florida]. December 6-10, 1996

THE CANADIAN ONCOLOGY NURSING CERTIFICATION EXAM:

The Canadian Association of Nurses in Oncology (CANO) is engaging in the exciting process of developing our own oncology nursing certification examination. We hope to receive final approval of our proposal in March 1996 and anticipate the exam will be ready in the fall of 1997. To obtain more information about the exam or to inquire about becoming a CANO member contact your local chapter or the national CANO office at:

111 Peter St., Suite 219
TORONTO, Ontario M5V 2H1
Tel: (416) 596-6565 or Fax: (416) 596-1808

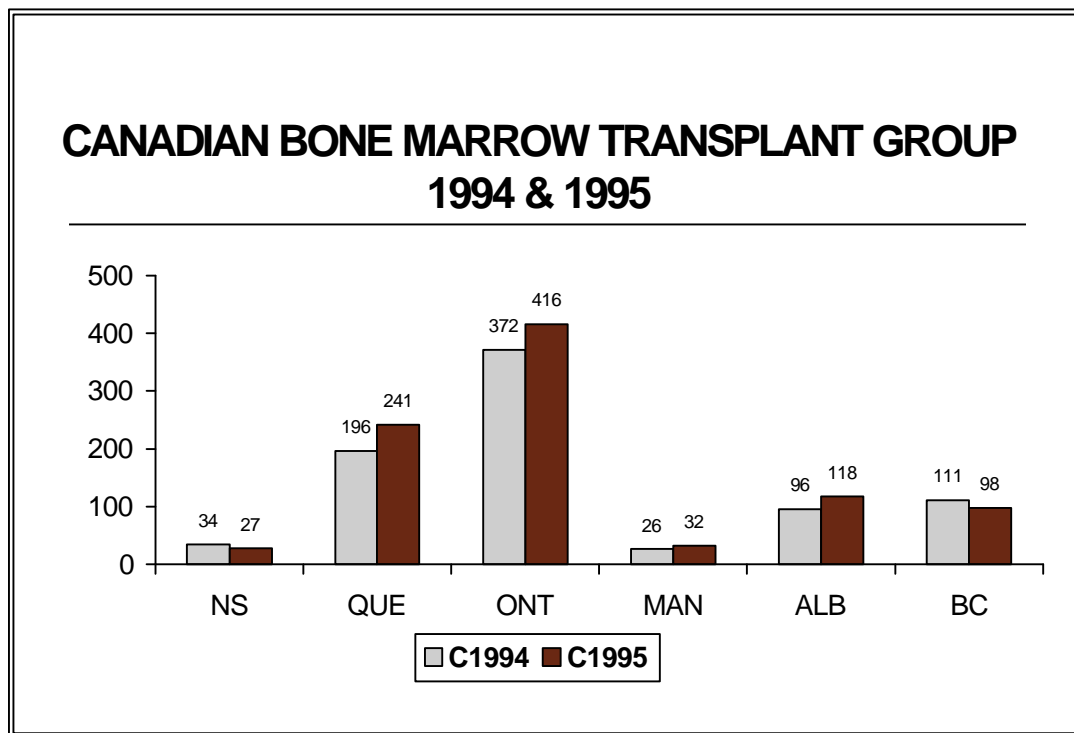
BLOOD AND MARROW TRANSPLANTS IN ONTARIO, 1994 - 6

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Ottawa, Ontario

The Ontario BMT groups maintain a registry which keeps track of information related to a variety of transplant activities

across the province. To give some indication, the transplant groups at the 9 Ontario hospitals performed about 240 autologous transplants in 1995-6 compared to 192 in 1994-5. There were 120 allogeneic related transplants compared to 102 during the same period on the other hand, there were 35

unrelated donor transplants in 1995-6, 10 fewer than the year before. Another 50 transplants each year are being done in Ontario for patients from other provinces. We can expect these trends to continue. With the next newsletter we will provide a summary of BMT activity nation-wide.



TOTALS INCLUDE ALL AUTOLOGOUS, ALLOGENEIC, RELATED AND UNRELATED BONE MARROW AND PERIPHERAL BLOOD TRANSPLANTS

THE CLSG STUDY GROUP

R. VAN DER JAGT, M.D.
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Ottawa, Ontario

The Canadian Leukemia Study Group (CLSG) is a nation-wide clinical trials group interested in pursuing both clinical and basic research in leukemia. Its first study, a phase II study of response-adapted induction therapy for acute

myeloblastic leukemia, was completed in 1995. [ASH - R. van der Jagt Blood 86(10):Suppl 1, 516a, 1995]. A much larger and ambitious phase III study asking the question whether remission consolidation with high-dose Ara-C confers a survival advantage for patients, as compared to 'standard' consolidation as was done in the phase II study is underway.

Twenty-some Canadian centres are participating in the study and of these many are also members of the CBMTG. Clinical laboratory and basic studies and a variety of the leukemias are well along in the planning stages. Further clinical trials are also planned. An electronic database network for exchange of information has been created to support the group's studies.

KEYSTONE MEETING: CLINICAL HIGHLIGHTS

(continued from page 1)

Leukemias are pretty rare. Breast cancer is a whole lot more common, but little light was shed on the utility of high-density therapy in this illness. The NCI is apparently proceeding with an adjuvant study in women with 4-9 node positive breast cancer.

But of greater interest, and like the old days of these meetings when next to no data was available to argue over is the rising enthusiasm of tackling poor-prognosis autoimmune disease with autologous (and even allogeneic) BMT. Possible target illnesses include rheumatoid arthritis, SLE, scleroderma, myasthenia gravis and multiple sclerosis. Combining Dr. van Bekkum (Groningen) mustering what data he could from experimental models, with Dr. Tyndall (Basel) rationalizing the use of high-intensity immunosuppression (TBI, purged autologous BMT), there was considerable interest raised at this symposium. (Several Canadian groups are in the 'talking' phase of Phase I/II studies in this area.) For those who are so inclined, the questions involved in this field will be discussed in Basel in September 1996.

There were a lot of presentations from Drs. Horowitz and Rowlings

for the IBMTR/ABMTR. Many of these studies suffer from methodologic problems inherent to registry data. The EBMT database (presented by Anthony Goldstone) shows a marked recent expansion of transplant activity in Europe in breast cancer and low grade lymphomas. Survival curves unfortunately for both disease continue to look unimpressive, at least in the longer run.

All the registries report a continued shift to blood progenitor cell transplant (there still is no consensus as to what term to use - stem cell, progenitor cell or blood cell transplants). Dr. Korbiling (MD Anderson) presented his institution's 'historical cohort' study comparing blood cell allogeneic transplants with standard marrow transplants. The advantages of blood cells in leading shorter engraftment times will however need to be weighed against other possible advantages (faster immune reconstitution) and disadvantages (occurrence of acute and especially chronic GVHD) of stem cell grafts.

The EBMT study (Schmitz et al) and the CBMTG Study (Couban, Simpson et al) will be needed to settle whether blood cells have significant overall advantages over marrow. Stay tuned.

Outside the meeting rooms, there were often discussions about money, politics and so on. The CBMTG met twice - a business meeting and a scientific session (both timed such as to annoy more than a couple of avid skiers). Discussions about and demonstrations of new database software led to further talk of a national registry and network, as a necessary infrastructure to do some important transplant studies in Canada. (Several ideas are discussed below in this newsletter.)

All in all, there were lots of ideas exchanged and plans conceived. But at 10,000 feet the air is a bit thin, and only time will tell whether a return to reality (and nearer to sea level) will lead to any of the ideas being implemented.

Application for Membership in the CBMTG

The CBMTG is an incorporated organization of bone marrow transplant programs in Canada and of those health professionals who have clinical, educational or research interests in marrow transplantation. Membership is free. To join please fill out the following form and send to:

Dr. L. Huebsch
Secretary, CBMTG
Room 7209
Ottawa General Hospital
501 Smyth Road
OTTAWA, Ontario
K1H 8L6

CBMTG MEMBERSHIP APPLICATION	
SURNAME:	TEL. NO.: (OFFICE): () -
GIVEN NAMES:	FAX NO.: () -
E-MAIL ADDRESS:	
ADDRESS:	
PROGRAM OR UNIVERSITY AFFILIATION:	
PROFESSION: <input type="checkbox"/> PHYSICIAN <input type="checkbox"/> NURSE <input type="checkbox"/> PHARMACIST <input type="checkbox"/> STATISTICIAN <input type="checkbox"/> CLINICAL TRIALS/ DATA COORDINATOR	
MAJOR INTERESTS:	
<input type="checkbox"/> SUBSCRIPTION TO NEWSLETTER	<input type="checkbox"/> RENEWAL