Information technology balancing act: Wealth of information versus increasing time pressures

It now seems that I cannot make it through a single day without marveling at the influence that today's information technology has on the practice of hematology.

In fact, one only needs to look at the incredible number of e-mails that arrive in your inbox each day to appreciate how electronic communication profoundly affects your workday. Many of these e-mails directly relate to patient care and having to deal with these while reviewing laboratory and clinical notes in a number of different data bases can be time-consuming.

The fact that e-mail and clinical data bases can be accessed remotely from your home computer or iphone can be convenient but also indirectly increases the amount of time put into your clinical practice.

Perhaps the most important influence that information technology has had on all of us is as a consequence of the wealth of medical information that is now available on the Internet.

At times, this information can be helpful -- in a pinch, there are few medical queries that cannot be answered quickly with a Google search!

...continued on Page 2
On the other hand, patients and their families have access to all of this information as well.

Not surprisingly, they arrive for clinic appointments with medical information gleaned from Internet searches and frequently present this to the hematologist accompanied by a long list of questions. With an ever increasing number of treatment options, this can lead to a challenging and lengthy discussion.

Agreed, this new process is critical in allowing patients and families to feel that they are very much a part of the decision-making process. However, it can introduce new time pressures for the busy clinician who has allotted one hour for a new patient appointment and 30 minutes for a follow-up.

In this day and age, it is not possible to limit the distribution of inaccurate or outdated medical information which is widespread on Internet websites.

Dealing with alternative and complementary therapies can be especially challenging since scientific data is usually lacking but this often has no influence on the patient's desire to pursue a particular treatment.

One solution to the evolving physician/patient relationship is for the hematologist to be as proactive as possible. Printed and web-based educational material can be prepared, with physician involvement, in order to ensure that accurate disease and treatment information is available for review by the patient and their advocates.

The advantage of web-based material is that it is easier to maintain and update. Unfortunately, this too requires ongoing physician input and that takes time — time that can take a hematologist away from their attempt to answer the inevitable backlog of e-mails!

Dr. Tom Nevill

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**CHS 2011 Research Abstract Competition**

*The CHS 2011 Research Awards* will be presented on **Sunday, Dec. 11, 2011**, at the CHS Annual Reception and Awards Gala held during the **53rd ASH Annual Meeting and Expo**, in San Diego, California.

**Award CATEGORIES:**

- **Residents & Fellows**  
  (Two awards, $3,000 each)

- **PhD and Postdoctoral**  
  (Two awards, $3,000 each)

- **Junior Faculty Award**  
  (One award, $3,000)

- **John H. Crookston Award**  
  (One award, best paper given by a resident, $5,000)

**Applications must submit:**

1. A **LETTER OF REFERENCE**, from your research supervisor.

2. ASH Abstract **APPROVAL LETTER copy**

3. A completed **APPLICATION FORM** — available on the CHS website

[http://www.canadianhematologysociety.org](http://www.canadianhematologysociety.org)

**Please send all applications to:**

The Canadian Hematology Society  
Suite 199, 435 St. Laurent Blvd.  
Ottawa, ON, K1K 2Z8  
Tel: 613-748-9613  
Fax: 613-748-6392  
Email: caq@ca.inter.net

**DEADLINE for submission is October 31, 2011**
A 44-year-old woman presents with a three-month history of fatigue, weight loss, night sweats and increasing abdominal girth.

Physical examination shows pallor and a spleen that was palpable 20 cm below the left costal margin.

CBC showed a hematocrit of 0.24, WBC of 945 x 10^9/l and platelets of 81 x 10^9/L.

Peripheral blood smear is shown here (above).

For the answer:

... See bottom of page 14.
Despite losing his battle with lung cancer in 2001, at the age of only 59 years, former CHS President, Dr. Ken Shumak had by then lived a life of renowned accomplishment and leadership in his field.

"Ken’s many accomplishments and appointments belied his unpretentiousness," his brother, Dr. Steven Shumak, told the Canadian Medical Association Journal for an article shortly after his death.

**CHS President 1996—1998**

Dr. Ken Shumak was President of the CHS from 1996 to 1998 - transitional years for the national blood system. During his presidency, one of the most important issues facing the CHS, was how the society and its members should be involved in Canada’s new blood system.

"Through the leadership of Dr. Shumak, the society and its members are actively involved," noted incoming president, Dr. Man-Chiu Poon, in his message in the November 1998 issue of this newsletter.

“Several members participate in the National Blood Safety Council (mandated to provide advice to the Health Minister on matters of blood safety) with Dr. Ken Shumak as its chair," states Dr. Poon’s 1998 message.

**Established CHS office**

The present-day public image of the CHS was in very large part, developed and established under Dr. Shumak’s direction and leadership. As president, he established the first, permanent CHS administration office.

Minutes of meetings during his term of leadership, document his oversight of the development of the CHS website.

The minutes also detail his call to members for ideas, suggestions or designs of a logo for the organization.

**CCO President & CEO**

Until just a few months prior to his death, Dr. Shumak was President and Chief Executive Officer of Cancer Care Ontario, where he had presided over a very tumultuous time in the history of the agency, responsible for coordinating cancer treatment in the province.

He handled the very controversial matter of the establishment of the province’s first privately run cancer care clinic.

His announcement of the opening of an after-hours clinic at Toronto-Sunnybrook Regional Cancer Centre on Bayview Avenue in Toronto, operated by Canadian Radiation Oncology Services Ltd., a private company, brought a reaction of furor.
Brave stand
"Ken was the person who had to stare down a lot of people who were against the clinic," said Dr. Tom McGowan, a former cancer agency executive and head of the private clinic at the time of Dr. Shumak’s death.

"The clinic was important for the patients but the true bravery for it rested all with Ken," Dr. McGowan told the Toronto Sun newspaper. "He was the kind of person you would want for your own doctor if you were sick," said Penny Thomsen, then executive director of the Ontario division of the Canadian Cancer Society. "He was very, very smart but he also had wonderful people skills. Anybody who interacted with him considered him a friend."

When the University of Toronto was experimenting with a decentralized approach to teaching – one of the first medical schools in North America to do so – Dr. Shumak was a professor of medicine as well as an associate dean at the University’s medical school.

He chaired the task force that reviewed the medical curriculum at the University of Toronto and then led the introduction of that substantially revised curriculum.

Bio highlights
Highlights of Ken Shumak’s biography:
- University of Toronto, (1965) Hematology, FRCPC
- Professor of Medicine, Laboratory Medicine and Pathobiology, Immunology and Health Administration, University of Toronto
- President and CEO, Cancer Care Ontario
- Associate Dean, Medicine, University of Toronto
- Physician-in-Chief, Women’s College Hospital
- President, Medical Council of Canada
- President, Canadian Hematology Society
- Chair, National Blood Safety Council.

Dr. Shumak testified at the Krever Commission into Canada’s tainted blood scandal.

In 1995 he was recognized by the Canadian Hemophilia Society for advancing the care of patients with inherited bleeding disorders.

Grace and dignity
It was only about seven months prior to his death that Dr. Shumak learned of his own cancer.

“He handled it with ultimate grace and dignity. Dignity is a word which is used a lot in association with Ken." Penny Thomsen told the Toronto Sun newspaper.

Somewhat of a sports enthusiast, Dr. Shumak always had time for golf and baseball.

"He was equally at home in the corporate boardroom, by the bedside, in the research laboratory or at a Blue Jay game," said his brother, Steven.

Even after a 36-hour hospital shift in the early part of his career, it has been said by former colleagues, that he would arrive at home and head straight for the basement for a game of floor hockey with his children.

Dr. Shumak was survived by his wife, Dr. Rene Shumak, three children, Brian, Michael and Marcia, and five grandchildren, Diane, Ethan, Cade, Zachary and Kyriah.

Throughout a career of providing stable and steady leadership in times of great change and unprecedented tumult and controversy, Dr. Shumak has been credited by his peers as never failing to look out for the welfare of patients.
A seven-page survey was mailed out to 313 Canadian Hematologists between August 2009 and January 2010 through a joint initiative of the Hematology Specialty Training Committee and the Canadian Hematology Society in order to assess the nature of practice and satisfaction of Canadian Hematologists.

The results were presented in September 2010 to the International Conference on Residency Education by Dr. Kevin Imrie.

The response rate from English hematologists was 59% and from French hematologists was 48%. Of total respondents, 56% were male. Those involved in academic practice made up 72% of total respondents. Other survey results are summarized in the eight graphs shown below:
Hematology is a varied specialty with the majority of practitioners in academic practice.

Community hematologists are more involved in general internal medicine and solid tumour oncology than academic hematologists, but both participate in teaching and clinical trials.

There is considerable variation in the laboratory component of hematology practice and its ongoing inclusion in training is justified. Most importantly, while trainees are more prepared for hematology practice than they were a decade ago, there remains room for improvement.
CASE:

A 36-year-old previously healthy woman presents with an isolated thrombocytopenia of 6 x 10^9/L and is diagnosed with immune thrombocytopenic purpura.

She is treated with Prednisone 50 mg bid and over the next 10 days, her platelet count normalizes.

The Prednisone is gradually tapered and one month later, while she is still taking 20 mg daily, she develops recurrent severe thrombocytopenia.

She is given 50 g of IV Ig daily for two days and within 5 days, her platelet count normalizes; she proceeds to have an uneventful laparoscopic splenectomy.

Her platelet count remains within the normal range post-operatively and her Prednisone is tapered over the subsequent 6 weeks and stopped.

Six months after her splenectomy, she once again presents with a platelet count of less than 10 x 10^9/L.

This patient has severe and refractory ITP, which in turn represents about one third of adult patients with ITP.

My recommendations are based upon review of the literature and my personal experience, because carefully controlled RCT’s are few and far between for refractory ITP patients. But, a platelet count of less than 10 X 10^9/L almost always requires intervention even for those patients who have no cutaneous evidence of haemostatic impairment.

We no longer look for an accessory spleen since our experience is that removal of an accessory spleen (even if identified by CT) seldom puts the person in remission, because accessory splenic tissue is invariably small. For such a patient, considerations of her age, her wish for future pregnancies, and her previous tolerance to medications are important.

The approach that we would use (in conjunction with my colleague, Dr. Donald Arnold) is to implement a “staircase approach” to treatment. At this point, the physician has considerable discretion concerning therapy and there is art to the intervention, which to a large measure reflects the patient’s response. For example, some patients can be managed by intermittent corticosteroids.

Other patients can respond to intermittent IV IgG, with or without intermittent corticosteroids. During this phase of the patient’s management, which may take three to six months to determine if the patient will respond, the strategy is to always give the least amount of intervention to avoid tachyphylaxis and adverse affects, while attempting to minimize the number of times the patient intersects with the healthcare system.

Unfortunately, most patients with refractory ITP require a higher level of intervention.

John G. Kelton, MD, FRCPC
VP and Dean
Faculty of Health Sciences
McMaster University
than corticosteroids or IV IgG. We typically would next use intermediate doses of danazol, while watching for adverse effects (abnormal liver enzymes) and patient tolerance. Again, a proportion of patients will respond to this treatment with minimal side effects allowing it to be considered for chronic use.

Most patients who have refractory ITP following splenectomy remain relatively refractory and will need to be managed through one of two, or three, different approaches.

Again, depending upon the age, and the patient’s wish to produce offspring, one option is to use immunosuppressants at middle to lower doses. The triple therapy, which we have used, includes azathioprine, mycophenolate, and cyclosporine. The recent introduction of thrombopoietin mimetics offers a safe and well tolerated treatment option which will work in approximately two-thirds of patients.

Currently, both thrombopoietin-like agents are licensed in Canada. As noted, these agents (one parenteral, the other oral) have minimal side effects and have been shown to raise the platelet count and improve the quality of life in most patients.

They have two major drawbacks. The first is the considerable cost of these medications and the second is the observation that they, unlike many other treatments, do not produce a sustained response.

John G. Kelton, MD, FRCPC
It is somewhat unique amongst lab specialties in that there remains a lot of clinical interaction, not just with hematologists but with all medical and surgical disciplines. I do miss regular contact with patients, though.

What is a typical work week like for you?

I work in a large academic centre and our group divides service work so that we have some protected time to teach, do research, and administrative work. I have a focus in Transfusion Medicine.

When I am not on blood, marrow or flow cytometry service I spend most of my time working on ongoing projects in Transfusion Medicine both for our centre and the other sites in the region.
This involves attending a number of meetings, and working closely with a team; other MD’s, technologists and nursing.

Some weeks a significant amount of time is spent responding to various incidents or adverse events, internal or external to the TML.

Otherwise I teach or am preparing teaching materials, usually on a Transfusion Medicine topic, for residents. I also collaborate with TM colleagues from around the province on various provincial initiatives.

I do end up spending a lot of my time working out of my email in-box and on the phone. When I am on a service week, it’s a nice break to get back to a case-by-case approach, usually working with a resident or medical student signing-out.

On those weeks I try to avoid booking meetings, and let the emails pile up.

**How involved are you in clinical and laboratory research?**

Although I did spend some time doing laboratory research during my hematology and hemopathology residencies I was unable to maintain this once on staff. Fortunately I made some excellent contacts and friends through that experience and now collaborate with scientists from the UBC Centre for Blood Research and Canadian Blood Services.

I am in a great position to help them bridge to the hospital level. Right now our TM lab is participating in three clinical trials. I am very involved with one which is a randomized trial based on technology invented and developed locally. This is one of the most exciting and fulfilling aspects of my job.

**Do you spend any time teaching medical students?**

Aside from time spent teaching at the microscope if they do an elective with us, very little.

**What would you be doing now if hematology and hematopathology had not been an option?**

I’d love to be a professional artist, painting, working flexible hours to spend more time chasing my kids, Euan (9), Isobel (7) and Lily (2).

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**upcoming EVENTS**

- **The Canadian Association of Nurses in Oncology (CANO), 2011 Annual Conference**, will be held September 11—14, 2011, at the World Trade and Convention Centre, Halifax, N. S. For information: [http://www.cano-acio.ca/annual_conference_conference](http://www.cano-acio.ca/annual_conference_conference)

- **The American Society of Hematology (ASH) 53rd Annual Meeting and Exposition**, will be held December 10 – 13, 2011, at the San Diego Convention Centre, San Diego, California. For information: [http://www.hematology.org/Meetings/Annual-Meeting/](http://www.hematology.org/Meetings/Annual-Meeting/)

- **The Canadian Bone Marrow Transplant Group (CBMTG) 17th Biennial Conference**, will be held April 11 – 14, 2012 in Toronto, Ontario. For information: [http://www.cbmtg.org/biennialconference](http://www.cbmtg.org/biennialconference)
INTRODUCTION

Telomeres, the end of linear chromosomes are composed of tandem repeat arrays of (TTAGGG)n nucleotides associated to specialized binding proteins that confer a protective structure at mammalian chromosome ends and regulate their length (reviewed in 1). The major determinants of telomere length between individuals have been shown to be genetic and a fairly wide distribution of average telomere lengths exists between individuals.

Telomere length was demonstrated to shorten with age and in culture with cell division2; a few extremely short telomeres per cell can trigger DNA damage and cell death pathways. Therefore telomere length, when controlled for age and inter-individual variation can attest to the past replicative history of tissues or cells and act as a predicting factor for their remaining proliferative and regenerative capacity3.

Because telomeres represent a significant portion of the genome that may be observed and measured, telomeres have been exploited in the research laboratory as good sensors of genotoxic damage such as that inflicted by reactive oxygen species for example and by genetic instability.

WHY HAS BLOOD BEEN THE TISSUE THE MOST WIDELY TESTED SO FAR?

We are fortunate in the hematology field to remain at the forefront of human telomere basic and clinical research, because of the relative ease and accessibility of blood, stem and progenitor cells, and because of early findings that lymphocytes and progenitor cells are capable of selectively expressing high levels of telomerase.

In contrast, in most other somatic cells, telomerase levels are undetectable. Telomerase is the protein/RNA holo-enzyme complex responsible for telomere repeat processive addition (reviewed in 4).

The selective expression supports the high proliferative potential and demand put upon cell types within the blood and hematopoietic compartments but is unable to prevent loss of telomere repeats altogether.

For these key reasons, the majority of telomere length data accumulated and published to date are from nucleated blood cells, which provide useful definitions of what may be considered the normal range of telomere length in the majority of individuals.

... continued on Page 13
**MINI REVIEW**

**How is telomere length measured? What are the challenges?**

Most major methods to measure telomere length are technically challenging and require specialized equipment\(^5\). They are however becoming more widely applied and accessible for clinical investigations and soon to general medicine\(^6\).

Direct quantitative hybridization to telomere nucleotide repeats (by Flow-FISH) and quantitative amplification of telomere repeats by polymerase chain reaction relative to a single copy gene (by TS ratio Q-PCR) have been the methods of choice in the hematology field.

It is important to consider that the type of assay used influences greatly the level of resolution that can be achieved (i.e. what is the sample input into the assay and what variability is inherent in the assay); this is in part because telomere lengths differ between cell types within the sample or can be impacted differentially by disease, which may be masked when testing DNA extracted from whole blood or total white blood cells. Further tissue complexity, cell type heterogeneity and disease type all influence what may be interpreted from these measurements.

**What are the impacts of short telomeres on the hematopoietic system? How short is “short”?**

First of all, “short” telomeres have thus far been defined in comparison to an age matched cohort of healthy individuals, and defined as the lower range of normal distribution or well below the normal range. Between different labs, methods and publications, this can be a lower percentile or quartile value; generally speaking telomere lengths within the boundaries of these lower values are considered short, and these completely outside the normal range extremely short.

At the level of the cell, a few very short telomeres have been shown to lead to cellular senescence (in fibroblasts), and in the case of hematopoietic cells to lead to cell death by triggering apoptotic pathways. As a consequence short telomeres in hematopoietic cells are associated with limited proliferative potential and cell loss.

This loss in turn increases the proliferative pressures on remaining cells, increasing their turnover so as to compensate and maintain homeostasis. This can become particularly taxing for cell types that must maintain sustained proliferative potential and function over a lifetime, such as hematopoietic stem and progenitor cells.

Defective telomere maintenance can add further pressure on the system and lead to bone marrow failure \(^2\) often accompanied with increased genetic instability with the potential to result in the selection of abnormal clones with leukemic potential (defective telomere maintenance has been seen in a small proportion of acute myeloid leukemia cases).

**Short telomeres in hematopoietic disorders: are short telomeres the cause or a consequence?**

Although in some cases this remains a “chicken or egg” debate, there are now clear examples that support one or the other possibility: short telomeres are the consequence of increased proliferation or damage, or an inherent genetic defect is responsible for short telomeres and ensuing complications.

In acquired aplastic anemia, in recovery after hematopoietic stem cell transplantation, enhanced proliferative pressures on the hematopoietic stem cell compartment are associated with accelerated leukocyte telomere shortening\(^8,9\).
Short telomeres are also seen in hematologic neoplasia, an observation common with the great majority of cancers, whether of hematopoietic origin or not. Short telomeres were initially thought to be a mere consequence of hyper-proliferation and tumor clonal expansion, but more recent findings indicate they may also be the trigger to genetic instability and the selection of cells with abnormal properties.

Cancer cells also express telomerase in over 90% of cases, an essential pre-requisite for transformation. This allows cells to keep dividing and maintain telomeres, albeit short. The value of telomere length measurements from samples where the great majority of cells are of tumor origin is limited to address suspected telomerase deficiency or in the study of biological processes. However they may be useful in categorizing disease or to assess treatment response.

Dyskeratosis congenita was the first disease clearly associated with hematopoietic failure demonstrated to be caused by compromised telomere maintenance due to mutations in telomerase components.

First identified were mutations in the essential telomerase components dyskerin DKC1, then TERT, TERC and later with telomere sheltering proteins (TIN2) for the majority of cases. Although the disease penetrance and symptoms do vary, unifying features include extremely short telomeres, most strikingly in children. Similar mutations and observations have been made in subsets of patients with other types of bone marrow failure etiologies, raising tremendous interest related to molecules involved in telomere biology and their potential implications in hematopoietic disorders.

Still many more questions remain to be asked and answered in the context of telomere biology and hematopoietic disorders. Areas of interest include graft versus host disease, chronic autoimmune conditions and metabolic disorders to cite just a few.

No doubt the future for studies on telomeres and hematology is bright!

ACKNOWLEDGEMENT
I would like to thank Dr. Pete-Lansdorp for helpful comments regarding this mini-review.

Dr. Geraldine Aubert

REFERENCES
DR. NOEL BUSKARD, a former President of the CHS, died unexpectedly Saturday, July 16th in Vancouver, British Columbia at the age of 71.

He will be greatly missed by his colleagues in the hematology community.

A clinical professor emeritus at UBC’s Faculty of Medicine’s hematology division, he retired in 2005 after 27 years in the department and the Vancouver General Hospital, where he was a staunch advocate of patients’ rights.

Dr. Buskard was an excellent teacher and was recognized by numerous awards.

Born in Ottawa, he attended Queen's University in Kingston, Ontario. His first career was in the Canadian Navy. He is survived by sisters Janet McDiarmid and Ruth Krupka, and children Sarah Smythe, John, Adam, James, Felicity, Verity-Claire and Andrew.

OPPORTUNITIES

Thrombosis Fellowships - Up to 3 positions

Applications are encouraged from MDs who have completed or who will complete General Internal Medicine, Respirology and/or Hematology training. Foreign medical graduates with equivalent qualifications are eligible.

Applicants may apply to one of three training streams:
1.) Clinical Fellowship, one-year—To consolidate expertise in thrombosis.
2.) Clinical and Research Fellowship, 2-3 years (to become a clinician investigator in thrombosis (Fellows enroll in the Master’s of Clinical Epidemiology Program at the University of Ottawa).
3.) Clinical and Education Fellowship, 2-3 years (to become a clinician educator in Thrombosis. (Fellows enroll in a Master’s in Education).

The Thrombosis Program of the University of Ottawa Division of Hematology is an active, academic, tertiary care subspecialty service.

To apply, please contact:
nlanglois@ohri.ca

Details are available on the CHS website.

Thrombosis Fellowship 2012-2013
Jewish General Hospital, McGill University, Montreal, Quebec

The JGH Thrombosis Program is currently accepting applications for a one year fellowship (July 1, 2012 - June 30, 2013) to acquire and consolidate expertise in Thrombosis. Specific areas of clinical activity include the Thrombosis Clinic, Anticoagulation Clinic and In-patient Thrombosis Consultation Service.

Our Thrombosis Program also encompasses a broad range of research activities that relate to diagnosis, risk factors and treatment of venous and arterial thromboembolic disease.

For information contact Dr. Susan Kahn, susan.kahn@mcgill.ca
Membership Matters

The Canadian Hematology Society has represented all physicians and scientists with an interest in the discipline in Canada since its founding in 1971. Our society now has over 300 members.

Membership is open to physicians engaged in the practice of clinical or laboratory hematology in Canada and to any persons doing scholarly research in hematology in Canada.

In appropriate cases, the requirement for a university degree or other qualifications may be waived if in the opinion of the Executive Committee the candidate is making significant continuing contributions to science.

We also welcome residents and fellows in approved university training programs in hematology or hematological pathology.

Non-members may be invited to become Honorary Members of the Corporation by virtue of their outstanding contributions to any discipline which is of importance to hematology.

CHS members are reminded ...

to please remit your 2011 Annual Dues. Your $75. annual dues payment may be made online at the CHS website: www.canadianhematologysociety.org

Or mailed to:
Canadian Hematology Society, 199-435 St. Laurent Blvd., Ottawa, Ontario K1K 2Z8

Please provide the following information with your payment:

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2011 Membership Renewal: Canadian Hematology Society