Implementation of a Comprehensive Procedural Skills Examination for Internal Medicine Using Simulation
Ma et al.

Perspectives on the Clinician-Scientist Pathway
Desplantie, Filion, and Eisenberg
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Mary Chapin Carpenter has long been one of my favourite singer-songwriters, probably because she is about my age and shares many of my sensibilities. “Songwriting is what I do,” Carpenter has written. “[It’s] how I make sense of things, [and] it’s how I seek connection and make my way through the world.”

Lately I have been listening to The Age of Miracles, the album that Chapin Carpenter released in 2010, three years to the day after her hospitalization for life-threatening pulmonary embolism. Reflecting on her illness, Chapin Carpenter remarked, “It was the most terrifying experience. The health crisis itself was enough to paralyse you, and the subsequent depression that followed was so difficult. They wave goodbye to you at the hospital, and they don’t tell you — or they didn’t tell me — ‘now be aware that the next few months [are] going to be really tough, and it’s not just because you don’t feel well.’ I was completely unprepared for it.”

While the despondency that Carpenter experienced in the wake of her hospitalization is reflected in some of the songs that she included on The Age of Miracles, so too is a tentative sense of buoyancy and hope. The title track concludes as follows:

We think we’re just standing still,
One day we’ll get up that hill.
In the age of miracles,
There’s one on the way.

In our practice and teaching of internal medicine in the 21st century, we are faced with no shortage of seemingly miraculous technologies to use in the service of our patients’ and students’ needs. How William Osler would have marvelled at the “space age” simulation techniques described in Irene Ma and colleagues’ article in this edition of the journal!

It is only through the ongoing medical research achievements of inquiring minds that we and our patients can continue our uphill climb together. The article by Olivier Desplante, Kristian Filion, and Mark Eisenberg identifies a number of barriers confronting bright young people who might otherwise pursue careers as clinician-scientists. Although the subjects of their survey research were fellows in cardiology, the results are generalizable to all branches of internal medicine, and are cause for concern.

Yet, even in this age of medical and scientific miracles, it’s often our inherent biases and stereotypical thinking that contribute most to our sense of “standing still.” Kirsten
Jewell’s insightful essay “Patient Profiling” reminds us of what is most important – and timeless – in the practice of medicine: seeking connection with those who come to us for care. As Jewell points out, the labels and shorthand that we find so useful in distilling and conveying our patients’ stories of illness can distract us from the person behind the problem list. Discovering that human being is what gives meaning to our work, and helping him or her to heal is what frees us from standing still. As the French philosopher and social activist Simone Weil wrote, “The capacity to give one’s attention to a sufferer is a very rare and difficult thing; it is almost a miracle; it is a miracle.

Having seen the end of another calendar year, miracles of other sorts are on the minds of many: the birth of a baby, the liberation of a people, the triumph of light over darkness. We at C J G I M wish our readers peace and contentment, and renewal in the year ahead!
L’exercice de la médecine interne à l’ère des miracles

Donald Farquhar MD SM

Au sujet de l’auteur
Donald Farquhar exerce la médecine interne et la pneumologie à l’Hôpital St. Joseph et au Centre hospitalier universitaire de London (Ontario) et il enseigne à la faculté de médecine Schulich de l’Université Western Ontario. Prière d’adresser la correspondance à Donald.Farquhar@sjhc.london.on.ca.

Mary Chapin Carpenter figure parmi mes auteurs-compositeurs interprètes favoris depuis fort longtemps, peut-être parce qu’elle est de mon âge et que nous avons en commun une certaine vision de la vie. « Écrire des chansons, c’est mon métier », a-t-elle écrit. « [C’est] ainsi que la vie a un sens pour moi [et] c’est ma façon de m’ancrer dans la réalité et de trouver ma place dans le monde. »

Ces temps-ci, j’écoute The Age of Miracles, l’album qu’elle a fait paraître en 2010, trois ans jour pour jour après avoir subi une embolie pulmonaire grave. Elle avouait plus tard que « cette période a été des plus terrifiantes. La maladie d’abord m’a terrassée, puis la dépression est venue m’accabler davantage. À la sortie de l’hôpital, personne ne vous met en garde, à tout le moins personne ne m’a prévenue que les mois à venir seraient difficiles et que ça ne serait pas juste parce que je n’allais pas bien. Je n’étais absolument pas préparée à cela. »

Comme il est vrai que certaines chansons de l’album The Age of Miracles évoquent le découragement dans lequel elle a sombré après son hospitalisation, il est vrai également que d’autres font entendre une note de légèreté et d’espoir. La chanson titre se termine comme suit :

We think we’re just standing still,
(Nous avons l’impression d’être immobiles,)
One day we’ll get up that hill.
(Un jour, nous grimperons sur la colline.)
In the age of miracles,
(En cette ère des miracles,)
There’s one on the way.
(il y en a un qui se prépare.)

Dans l’exercice et l’enseignement de la médecine interne en ce XXIe siècle, nous avons l’embarras du choix devant l’abondance de technologies apparemment toutes plus miraculeuses les unes que les autres à utiliser pour le bien de nos patients ou l’éducation des étudiants. William Osler se serait certainement émerveillé à la vue des techniques de simulation de « l’ère spatiale » dont il est question dans l’article d’Irene Ma et ses collègues qui paraît dans le présent numéro.

C’est avant tout grâce aux percées de la recherche médicale incessante sous l’égide d’esprits curieux et persévérants que nous et nos patients pouvons grimper ensemble. Dans leur article, Olivier Desplante, Kristian Filion et Mark Eisenberg relèvent les obstacles que doivent surmonter les brillants aspirants à la carrière de clinicien chercheur. Bien que leur sondage ait été adressé à des stagiaires en cardiologie, les résultats s’appliquent à toutes les branches de la médecine interne, et ils soulèvent des préoccupations.

Pourtant, à cette époque de miracles médicaux et scientifiques, ce sont notre subjectivité et notre façon de penser stéréotypée qui sont les grands responsables de notre sentiment « d’immobilisme ». L’exposé inspirant de Kirsten Jewel sur le « profilage du patient » souligne l’aspect le plus important – et intemporel – de l’exercice de la médecine : établir un lien avec ceux qui viennent à nous pour se faire soigner. L’auteure le dit bien, les étiquettes et les abréviations dont nous faisons ample usage dans le compte rendu du récit du patient, dans la liste de ses problèmes, peuvent nous faire perdre de vue la personne comme telle. Être conscient que l’être humain est au cœur de ce que nous faisons et tout mettre en œuvre pour qu’il guérisse est le plus sûr moyen de nous libérer du boulet de l’immobilisme.

Une autre année écoulée, et nombreux sont ceux qui espèrent des miracles d’un autre genre : la naissance d’un enfant, la libération d’un peuple, le triomphe de la lumière sur l’obscurantisme. L’équipe de la RCMIG souhaite à ses lecteurs paix et contentement et renouveau en cette année qui commence.
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Implementation of a Comprehensive Procedural Skills Examination for Internal Medicine Using Simulation at the University of Calgary: A Descriptive Report

Irene W. Y. Ma MD MSc, Maria Bacchus MD MSc, Jennifer Glow, Charlene Brass, Liz Fradgley BHSc, Michael Fisher MD MSc, Ghazwan Altabbaa MD, Jeffrey P. Schaefer MSc MD

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Competency in the performance of a number of bedside procedures is an objective of training, set forth by the Royal College of Physicians and Surgeons of Canada. These procedures include venous access including central line placement, lumbar puncture, peripheral arterial catheter insertion, abdominal paracentesis, endotracheal intubation, thoracentesis, and knee arthrocentesis.

The assessment of procedural competence is primarily the responsibility of the Residency Training Program, which is in turn informed by the preceptors who educate and evaluate individual residents during clinical rotations. While this approach has been satisfactory historically, this is no longer the case. Societal expectations around quality and safety of care, resident expectations regarding fairness and due process in assessment procedures, and the profession’s commitment to continued improvement compel us to find new ways to ensure that certified specialists in internal medicine have achieved these expected competencies.

Why Assessments for Competency Have Been Problematic
Assessment of procedural skills has traditionally relied on a logbook-based approach. In this approach, a trainee who had completed the minimum required number of procedures was deemed competent. One major argument against this approach is the lack of validation for a specific recommended number for each procedure. Indeed, what evidence there is suggests that the number needed to attain competency is often much higher than the minimum recommended number based on expert opinion. Thus, the number of times a trainee has performed a procedure is at best only a surrogate marker for competency.

The second traditional approach involves having the supervising physician directly observe trainee performances in the clinical setting. This approach too is fraught with problems. Clinical encounters occur at unpredictable times. Our previous survey suggests that only about half of the central venous catheters insertions were supervised by faculty members. If faculty members cannot reliably be present during procedures, objective assessments are difficult to achieve. Secondly, varied clinical environment precludes standardization of assessments. For instance, how does one rate a trainee who was unsuccessful in placing a central venous catheter in an awake patient with a difficult and complex anatomy, compared with a trainee who successfully performed the procedure in an intubated patient with standard anatomy? Lastly, one may argue that assessments during clinical care may even be potentially harmful. A trainee, aware that his or her performance is being evaluated, may experience performance anxiety, which may negatively impact on patient outcomes. Indeed, attending physicians serving the dual role of both a clinical supervisor and an evaluator may sometimes find themselves in a difficult position.

Thus, we argue that a standardized observed examination using simulation should be the preferred method of bedside procedural skills assessment. Indeed, simulation for technical skills assessment is endorsed by the Accreditation Council for Graduate Medical Education.

Implementation of a Comprehensive Procedural Skills Examination
In 2009, the University of Calgary implemented a simulation-based procedural training curriculum. This academic year...
(2011–2012), we launched our first comprehensive simulation procedural skills formative examination. To do so, seven procedural skills were evaluated in five 20-minute objective structured performance-related examination (OSPRE) stations, with standardized instructions. In this report, we outline briefly the steps taken to implement this examination. In addition, we address lessons learned from challenges we faced and propose future directions.

**Examination Set-Up**

Prior to the implementation of the examination, a comprehensive checklist for each skill station was created, with content validity and standard setting completed through expert panel input. For this task, we gathered six experts for each procedure. Standardized examination instructions were prepared. Material resources were then gathered for the examination; these included appropriate simulators for each technical skill assessed, procedural kits and supplies, replacement parts and fluid, ultrasound machines, assessment forms, and examination instructional materials. Written examiner instruction packages were prepared and distributed to examiners. Information included instructions given to candidates, expectations of the skills evaluated, the scope of the examination, the role of the examiner, the timing and flow of the examination, assessment forms, a description of the simulators, and how to avoid damaging the simulators. In addition, we prepared optional instructional videos for examiners to view on how to troubleshoot simulators. In order to standardize the examination set-up, we photographed each station, showing how the materials and simulators were set up. Material resources needed for each station were packaged in a standardized kit and with contents displayed on a labelled photograph. These photographs, as well as a material checklist, were referenced for each station for the duration of the study.

**Examination Implementation**

Two tracks of procedural skills were evaluated on academic half-days. Twenty minutes were allotted to each skill station except for arterial blood gas sampling, intubation, and knee arthrocentesis. These three skills were combined into one single 20-minute station. Each station had one examiner who had been instructed to fulfill the role of a nursing assistant and to allow candidates to go through each station unchallenged. Two minutes of feedback were given to the candidates by the examiner at the end of each station.

To date, we have run six afternoons of examinations (4 hours each), with 45 residents having completed all seven skills evaluations.

**Table 1. Tips for Running Objective Structured Performance-Related Examinations for Procedural Skills**

| Use valid and reliable assessment tools. |
| Photographs, checklists, and equipment kits assist with the standardization and set-up of stations, but significant human resources are still required. |
| Faculty training is needed on simulator use and evaluations. |
| Funding is critically important for the pilot implementation phase of the examination. |

**Challenges and Barriers**

Station set-up and scheduling, faculty development, simulator care, simulator maintenance, and costs are the biggest challenges in the implementation of these examinations. (Tips for running these examinations are presented in Table 1.) While photographs of equipment and stations assist in standardizing our examination and assisting with equipment set-up, these examinations require significant commitment from the program staff and assistants, who are integral to the success and conduct of the examination. In order to cover the costs of acquiring additional simulators and payment for experts to participate in expert panels for the contribution of content validity to the assessment forms, we obtained support from the Department of Medicine Research Development Fund Competition, which made this work possible.

**Future Directions**

In our next phase, we will evaluate the reliability of the examination and validate each of our developed assessment tools. If shown to be valid and reliable, the role of these procedural examinations in a summative examination can then be considered and explored.

**References**

In recent decades, it has become increasingly difficult to attract medical trainees to the clinician-scientist pathway. Several measures have been undertaken to increase the number of clinician-scientists, but the anticipated results have not been obtained. In many ways, the clinician-scientist can be considered an “endangered species.” To promote this career path, there is increasing interest in some specialties in developing training programs that would encourage medical students to pursue research by increasing their exposure to research early in their training. Our study sought to examine cardiology fellows’ perceptions of the clinician-scientist career path, and their ideas on how to promote it.

Methods

Expedited ethics approval was obtained from the Research Ethics Board of the Faculty of Medicine of McGill University.

We surveyed cardiology fellows of three McGill University teaching hospitals (Jewish General Hospital, Montreal General Hospital, and Royal Victoria Hospital) in 2009. Fellows were contacted by email, and all 19 fellows contacted agreed to participate. Each fellow participated in an individual, semi-structured, face-to-face interview with one of the authors (O.D.). Each interview was 5–15 minutes in duration and consisted of 20–25 open- or closed-ended questions regarding the participant’s research experience and perceptions of the clinician-scientist pathway.

Collected responses were anonymized, and qualitative responses to open-ended questions were grouped to reflect the most significant perceptions. Selected quotations are presented in tabular format to illustrate fellows’ experiences and perceptions of this career choice.

Results

Of the 19 participating fellows, 16 were male. Participant ages ranged from 28 to 34 years, and they were in years 1–3 of fellowship training. Time elapsed since medical school graduation varied from 4 to 11 years. The fellows had a variety of academic backgrounds prior to their medical training: four did not have university degrees, having instead completed a year of preparatory medicine; 10 had bachelor’s degrees; three had master’s degrees; and two had doctoral degrees.

Interest in Research and Pursuing Additional Research Training

Of the 19 fellows, seven were planning to pursue careers as clinician-scientists, eight were not, and four were unsure. Of the seven fellows who were interested in the clinician-scientist career path, five had identified their interest prior to medical school. Only two fellows wished to pursue research degrees during or after their fellowship.

Perceived Barriers to Pursuing the Clinician-Scientist Pathway

Common themes emerged among the perceived barriers to pursuing the clinician-scientist pathway (Table 1). The uncertainty of obtaining a position in an academic centre was a considerable source of anxiety, as were concerns about the difficulty in obtaining funding and a lack of sufficient protected time for research. These perceived issues were identified by both those interested in pursuing careers as a clinician-scientist as well as those not interested in this career path.

When asked to name the single most important barrier to pursuing a career as a clinician-scientist, the most frequently
identified barriers were insufficient protected time, grants, and lack of interest (see Table 1). The former two factors were also perceived as important contributors to the low number of clinician-scientists. However, despite their concerns about protected time, most fellows believed their current schedules permitted some time for research.

Other barriers mentioned were the lack of mentors, the scarcity of resources and positions in academic centres, and the difficulty in finding good ideas for research projects. While mentorship was considered important, there were mixed feelings about the utility of implementing a formal mentorship program (Table 2). However, there was consensus that there was a need to improve the research infrastructure to support trainee research, with a particular need for methodological and statistical support.

The majority of the cardiology fellows believed a
Character traits required to be a successful clinician-scientist

- “You have to be able to think outside the box. You have to like asking questions and to generally want to answer those questions and be good at observing things that happen because research really comes down to asking a good question, and that’s the hardest part to do in research.” (6)
- “You got to be patient; that’s going to be your cup of tea.” (7)
- “I think persistence and being able to work hard with not much gratification for long periods of time and being passionate about what they’re doing.” (9)
- “I think you have to be determined and ambitious and, for the clinical part, you have to make it relevant to your research.” (10)

Should there be a mentorship program?

- “I don’t know if you can assign a mentor, because I think the whole point of a mentor is somebody that you end up meeting … It’s like if you say, is it better to meet somebody at a friend’s place and start to date them solely, or just directly off an Internet single date site, you know? I think you’re both going to meet people, but what’s ultimately better? I think it’s the more natural way.” (5)
- “It’s elective for some people who prefer to have that, and I think it’s a good idea. Outside of that, I don’t think it’s essential for everyone to have a mentor.” (10)
- “It just provides you with a source of information and human experience so … you can have an idea how the future is. I think what most people are afraid of is the unknown. So, if you have somebody who has been going through what you’re thinking of doing, it takes away the fear of the unknown.” (11)

Importance of mentorship

- “I did research with two different people, both of [whom] were clinician-scientists, and [it was] at that point that I realized that’s not what I wanted to do. So, it was important to do it.” (9)
- “It’s worth it because it’s the responsibility of both. One, of the staff to make sure that there are residents from whatever year [who have had] enough opportunities. And the other thing is that there is no excuse for the residents not to have done any research project.” (12)
- “I think that it’s often something that is lacking. We have research supervisors that meet with us once in 3 years, and mine met with me 3 weeks before I graduated, so it didn’t particularly help at that time.” (14)
- “Everything in medicine is exposure. If you’re not exposed to it, you don’t know what you want to do; so you have to be exposed to it.” (18)

What modifications would have facilitated your ability to do research?

- “I have a lot of contacts in epidemiology or just general research [who] have a good access to health; but as far as statistics, I think it’s where I had the least support.” (3)
- “When it comes to research, everything should be improved. I think there isn’t enough focus on resident research. There are not a lot of ideas.” (12)
- “Instead of having a month doing whatever, we could have a month where we’re expected to help the medical students in some capacity.” (13)
- “Often times, we are requested/required to do our statistical analysis and all the research minding ourselves. If we [had] more support staff, that would be helpful.” (14)

Is it harder to do research when you are a clinician?

- “The amount of knowledge that you need to know is literally doubled as a pure researcher or a pure clinician, and we know very well that you cannot survive by being a half-clinician or a half-researcher.” (1)
- “When it comes down to clinical research, I would think [doing research] would be the same [in either clinician-scientists or pure scientists], if not maybe easier, for the clinician-scientist who has access to patients.” (5)
- “I think that if you have the combination of a clinician and someone with a PhD or a master’s in epidemiology or anything else, I think it would help the research project. I don’t think clinicians should make research projects alone because we have one perspective, and I think you definitely need another perspective.” (11)
- “Research is better to be exclusive to non-clinicians because you can’t mix both of them. You can’t balance your personal life with research projects to do.” (17)

*These quotations were obtained during semi-structured interviews with participating fellows. Numbers in parentheses refer to the participant identification number.
discrepancy existed between the income of clinician-scientists and full-time clinicians. Many fellows considered this discrepancy to be an important contributor to the low number of clinician-scientists, and almost half deemed it important in their own decision-making process.

Discussion
Our study was designed to examine cardiology fellows’ perceptions of the clinician-scientist pathway, and their ideas on how to promote it. We found that few cardiology fellows intended to conduct research in their careers, and even fewer wished to pursue research degrees. When asked to name their personal reservations about pursuing a career as a clinician-scientist, the fellows’ three most-cited issues were the scarcity of grants, positions in academic centres, and protected time.

One barrier to a career as a clinician-scientist appears to be the ability to achieve an adequate work-life balance. A previous survey of established clinician-scientists reported that they believed that they must work evenings and weekends, often to the detriment of their family lives, in order to achieve a satisfactory income and maintain their clinical skills. Another study found that residents shared the belief that clinician-scientists must inevitably take time from their personal lives in order to succeed. In the present study, most fellows agreed that they could make time in their schedules for research; however, the accompanying increase in the difficulty of time-management remained a concern.

Interestingly, although a large majority of fellows believed that there exists a discrepancy between the income of a clinician-scientist and that of a full-time clinician, many found this discrepancy personally unimportant. At the same time, fellows believed that the low number of clinician-scientists could be partially attributed to their lower incomes. Some institutions have recently increased remuneration for research time; however, the remuneration for clinician-scientists remains less than that of full-time clinicians.

Many fellows suggested that mentorship and early exposure to research in the medical curriculum would be helpful. Thus, a structured program with role models early in medical training could help attract new talent to the clinician-scientist pathway. A mentor can be a tremendous resource in guiding a trainee through this pathway. A mentor can provide advice on applying for grants, negotiating protected research time, and, perhaps most importantly, balancing one’s personal life with a clinician-scientist career. The impact of mentorship can continue long after medical school or even fellowship. Most fellows viewed mentorship as a healthy way to learn from experienced clinician-scientists.

One fellow noted that, on occasion, a particular mentor may simply be incompatible with a particular student. Similarly, a previous study observed that even a mentor who is known to be competent and trustworthy will not necessarily satisfy the needs of a junior faculty member. In such cases, the mentee may need to assume much of the responsibility of finding other role models. A structured program that purposefully introduces the student to a number of mentors throughout his training would be a great aid in creating successful mentoring relationships.

Previous studies suggest that many medical students wish to teach and conduct research during their careers; however, the number of clinician-scientists is not increasing. As suggested by the surveyed fellows, medical schools should initiate greater and earlier exposure to research in order to encourage the students to pursue research. Teaching evidence-based medicine, for example, is of great value in increasing the number of clinician-scientists. Medical schools should also encourage and promote participation in research projects outside of the curriculum and the early establishment of mentor-mentee relationships.

The fellows’ perception of the clinician-scientist pathway is generally consistent with the reality described by established clinician-scientists. Both groups share a favourable opinion of mentorship and early exposure to research. They also share concerns about grants and protected time. However, established clinician-scientists are not concerned about the scarcity of academic positions for those interested in this career choice, which was one of the fellows’ most-cited reservations about embarking on a career as a clinician-scientist. If the fellows’ perception of scarcity is not correct, this is an important misconception to correct.

Limitations
Our study has a number of potential limitations. First, our results reflect only the perceptions of fellows in one specialty at a single Canadian university system. The generalizability of our results is therefore unclear. Second, our sample size was modest. For this reason, we qualitatively summarized our data instead of conducting formal statistical analyses. Nonetheless, this qualitative approach allowed for the identification of the major barriers and perceptions of fellows regarding this pathway.

Conclusion
The number of clinician-scientists has decreased substantially in the past decades. Our study was designed to discover how the clinician-scientist pathway is perceived by current cardiology fellows. Our interviews revealed that the perceived
scarcity of protected time, grants, and positions in academic centres were the main factors deterring cardiology fellows from pursuing careers as clinician-scientists. These perceptions must be addressed, particularly the perceived scarcity of academic positions, which may be inconsistent with the reality of the clinician-scientist pathway. Mentorship programs and early exposure to research were suggested as means of promoting the medical trainees to pursue careers as clinician-scientists.

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References
The vast majority of general internal medicine (GIM) programs in Canada have become distinct entities that provide training in additional competencies and leadership above and beyond those required for the specialty of internal medicine. In December 2010, after many years of effort, GIM finally achieved recognition as a distinct subspecialty by the Royal College of Physicians and Surgeons of Canada. A GIM Working Group has finalized the objectives and requirements for a 2-year subspecialty training program in GIM that will follow after the existing 3-year core internal medicine training program. These documents have now been approved by the Royal College.

Starting in 2013, programs will be able to apply to the Royal College to become accredited GIM subspecialty training programs. Undertaking this application process will be an individual program decision. Thus, each university will have the option to offer both a 5-year GIM subspecialty training program and a 4-year internal medicine specialty training program, or to continue with only the existing 4-year internal medicine specialty training program.

GIM subspecialty programs are poised to train physician-leaders who will address the health care challenges of the future, including an aging population, patients with multiple comorbidities and simultaneous health care issues, and the need for health care innovation. This mandate is summarized in the following excerpt from the Objectives of Training in General Internal Medicine (http://rcpsc.medical.org/residency/certification/objectives/gen_internal_medicine_e.pdf; reproduced from the Royal College website with permission).

**General Internists** are prepared to diagnose and manage patients with common and emergency internal medicine conditions, and are able to do so when the individual has multiple conditions and with limited access to other subspecialists. General Internists provide comprehensive care of the adult patient in an integrated fashion as opposed to an organ-centred or disease-centred approach. They are prepared to maintain stability of patients with multisystem disorders over the long-term or during physiological stresses such as during pregnancy or the peri-operative period.

General Internists advocate for their individual patients as well as for all patients within complex healthcare delivery systems, by aiming to optimize and not maximize care, including prevention of other conditions. General Internists recognize that the practice of medicine is tightly linked to the art and science of health care delivery and, by virtue of their pivotal role are uniquely placed to engage in quality improvement, patient safety, and healthcare systems initiatives.

**Frequently Asked Questions**

**What are the objectives of training for the new 2-year GIM program?**

The full GIM program objectives may be found on the Royal College website at http://www.royalcollege.ca/portal/page/portal/rc/credentials/specialty_information. Under “Information by Subspecialty,” select “General Internal Medicine (GIM).”

The medical expert objectives are centred on the pillars of GIM. They include but are not limited to the following:

- Common and emergency internal medicine disorders in the outpatient and inpatient setting, including when there
is limited access to other subspecialists – this includes presentations of illness that are multi-system and undifferentiated; it also includes the ability to independently stabilize critically ill patients

• Internal medicine conditions before, during, and after pregnancy
• Chronic multisystem diseases such as but not limited to diabetes, hypertension, coronary artery disease, chronic obstructive pulmonary disease, dyslipidemia, and chronic kidney disease
• Multiple internal medicine co-morbidities in the perioperative period – both in terms of preoperative risk stratification and management of postoperative problems related to GIM
• Reducing risk factors for disease through application of pharmacological and non-pharmacological preventive measures

Procedural skills in exercise stress testing, ambulatory blood pressure monitoring, Holter monitor interpretation, and mechanical and non-invasive ventilation will be needed by all. Each individual resident may have a different list of additional procedural skills that should be attained. Structure is built into the residency program to allow this flexibility. Defining which procedural skills you need for your practice on an ongoing basis is a key competency to be attained.

Key items being emphasized in other competencies include those needed in the increasingly complex health care system such as handover; inter- and intra-professional collaboration; practice audits and ability to adapt practice; behavioural modification; practice management; patient safety; and knowledge of when to seek assistance.

What are the training requirements in the 2-year GIM program?
The specialty training requirements emphasize that GIM will be a 2-year training program that is planned in a longitudinal fashion with increased graded responsibility over the 2 years, **not** 2 consecutive years with similar content in each year. Key components include 15 blocks of clinical rotations primarily in GIM that may include consultative medicine, perioperative medicine, community GIM, preceptorships, CTU, obstetrical medicine, ambulatory care, and critical care. The other 11 selective blocks can focus on development of clinical skills, scholarly skills, or a combination of both. Flexibility has been built in to allow individual GIM programs to tailor the specific details to their sites.

What certification examination will GIM subspecialty trainees take?
Certification in the subspecialty of GIM will be by written examination, as is the case with all Royal College subspecialties. GIM trainees will take the written examination at the end of their 5th year of training. It is anticipated that the examination will first become available in 2014.

How do I apply for GIM subspecialty training?
Applications for GIM subspecialty training will take place through the CaRMS Medical Subspecialty Match. Information about GIM programs and contact information for GIM program directors can be found on the CaRMS website at http://www.carms.ca/eng/r4_about_intro_e.shtml.

What will happen to certification in the specialty of internal medicine?
No changes in the current path to certification in the specialty of internal medicine are anticipated. The written and oral examinations in internal medicine will continue to be offered to individuals who are completing their 4th year of internal medicine training.

Will every internal medicine program offer a GIM subspecialty program?
Each university will have the option to offer both a five-year GIM subspecialty training program and a four-year internal medicine specialty training program, or to continue with only the existing four-year internal medicine specialty training program.

How can practising general internists (who have completed 4 years of internal medicine training) obtain credentials in the new subspecialty of GIM?
There will be an opportunity for physicians currently practising in GIM to apply for certification through the “Practice Eligibility Route for Subspecialists” (PER-sub). The GIM specialty committee is currently tasked with determining specialty-specific criteria for PER-sub candidates. With this process in the beginning phase, it will likely be a few years before this route is available for general internists. Anyone interested in further information about the PER-sub route to certification should contact the Credentials Unit at persub@royalcollege.ca.

It is an exciting time for GIM with renewed interest for the discipline that is needed for people across the country!
Personal Observation: Intravenous Aminophylline Treatment for Migraine

Michael Kenyon MD, Barry Phillips MD, Christiaan DeWit MBChB

Migraine is a common condition, often affecting young patients and causing disruption in the home and workplace alike. The impact of patients presenting to emergency room services with intractable headache is significant, often tying up space and resources in the tedious wait for a narcotic and sedative “cure.” In Canada alone, 3.2 million adults suffer from migraines, and the condition costs the Canadian economy an estimated $500 million annually. Absenteeism and loss of productivity resulting from migraines cost $20 every second.1

Mills Memorial Hospital is a regional referral centre in Terrace, British Columbia, serving a population of 70,000 people. Between June 2011 and January 2012, 21 patients came to the emergency room (ER) suffering from symptoms compatible with migraine headache as defined by International Headache Society criteria.2 These patients had failed to achieve results from standard outpatient therapy, and the internal medicine service was consulted.

We care for patients in the ER and the intensive care unit (ICU): we also supervise patients undergoing nuclear cardiology testing (stress and dipyridamole methoxyisobutylisonitrile [MIBI]). As such, we have experience in the administration of intravenous (IV) dipyridamole, an arterial vasodilator that can induce a vascular headache in 20% of subjects. Standard therapy for this common side effect is the administration of 50–250 mg (usual dose = 100 mg) of IV aminophylline, given by IV push over a 30– to 60-second period.3,4 This protocol almost always brings about rapid and persistent relief of headache, without significant adverse effects.4

We postulated that the administration of IV aminophylline would be effective in the treatment of the vasodilatory component of spontaneous migraine complex.3–9 Aminophylline is a competitive non-selective phosphodiesterase inhibitor and adenosine antagonist. It has been shown in dipyridamole (Persantine) MIBI studies that dipyridamole administration inhibits adenosine deaminase in red-cell membranes, increasing blood levels of adenosine. This induces coronary vasodilation through a low-affinity interaction with the A2a receptor. The antidote, aminophylline, preferentially binds to this receptor, displacing adenosine and curtailing its effect.3,4

Aminophylline has traditionally and principally been used as an intravenously or orally administered bronchodilator in asthmatics. Caution in its use should be observed in patients with active peptic ulceration, a low seizure threshold, hypokalemia, tachyarrhythmias, and acute congestive heart failure (CHF). It is contraindicated in acute porphyria and in patients with a sensitivity to methylxanthine products.10,11

In keeping with our practice in the cardiodiagnostic laboratory, we monitored the electrocardiograms (ECGs) and blood pressures of all patients during the administration of this drug. For safety, all treatments were administered in a monitored setting to patients under direct observation in the ER by nursing and physician staff.4

Often, migraine patients presenting to the ER have tried various standard therapies, including antiemetics, analgesics, caffeine/ergot preparations, triptans, beta blockers, acetaminophen-codeine preparations, and nonsteroidal anti-inflammatory agents. It is common for these patients to receive parenteral narcotics and antiemetics and be cared for in a dark, quiet room for several hours in an otherwise-busy ER.12

Methods

We report 21 cases observed over a 7-month period; all of these patients attended the ER. Each patient met the International Headache Society criteria for migraine headache2 and had failed standard outpatient therapy with conventional treatments. All

About the Authors

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underwent a complete history and physical examination and had an appropriate laboratory profile performed. We explained the rationale of aminophylline treatment and our experience with it as a safe, readily available treatment for dipyridamole-induced vascular headache in our most medically frail cardiac patients. All gave informed consent to this modest dose of a safe and well-known therapeutic agent, albeit for the unlabelled indication of spontaneous migraine outside of the Nuclear Medicine Laboratory.

**Results and Discussion**

Aminophylline is a cheap, genericized, readily available medication with known pharmacokinetic properties. It has not been studied as an IV therapy for refractory migraine. An extensive literature review on Google, Medline, and PubMed confirmed this. (We did get interesting “hits” for its use in post-lumbar puncture headache and in “myocardial migraine.”) In this observation of 21 patients, aminophylline proved to be a highly effective intervention. After the completion of a 20-minute infusion of aminophylline, 17 of 21 patients had a substantial or complete relief of their headache and were fit for discharge from the ED, two were felt to have treatment failure, and two had partial relief. We noted that patients with localizing symptoms and signs did well uniformly. (Our sample size was small, but this was also something more objective to measure.)

As this was an observational study, it did not incorporate formal long-term follow-up interviews with this patient group; however, we have not been made aware of any subsequent adverse outcome by our family or ER doctors or at follow-up chart reviews (computerized, regional), and there is an impression that there is reduced “rebound effect” compared with several other standard therapies.

We believe our experience with this inexpensive, safe, and easily accessible medication offers promise for a formal randomized double-blind trial in a sizable cohort of migraine patients. Oral and suppository routes for aminophylline therapy for migraine might also be explored. We hope that this approach might afford prompt relief of symptoms for a difficult-to-treat condition, and may allow early and safe discharge from congested ERs. We feel that a randomized, double-blind, controlled trial is indicated, with the approval of our local ethics board.

**References**


**Appendix: Case Reports**

**Case 1**

S.M. was a 40-year-old female migraineur of many years. On her 3rd day of “usual, severe migraine,” and unresponsive to a range of standard therapies, she experienced a rapid, significant (80–90%) relief of the headache with 100 mg aminophylline IV over 20 minutes. The relief was dramatic and rapid, with nausea and photophobia completely cured immediately before the infusion was finished. There were no side effects. She was able to return to work immediately post-treatment.

She subsequently had a second episode, identically relieved by the same treatment, except that the aminophylline was infused over 10 minutes. Once again, she was able to return to work, unlike with other treatments she has tried in the past. She has also observed that the frequency of episodes has diminished after these treatments, as compared to previous experience (no “rebound” phenomenon).

**Case 2**

P.L. was a 52-year-old female homemaker with frequent hemiplegic migraine, complex migraine; she was a frequent recipient of narcotics. Presenting with a hemiplegic episode lasting > 6 hours, accompanied by dysarthria, photophobia, phonophobia, and paresthesia affecting the right side, she was
given 100 mg aminophylline IV over 2 minutes with complete relief of her symptoms within 10 minutes, but she experienced tremor and tachycardia.

She has subsequently had far fewer visits to the ER. She has not experienced side effects when given 100 mg aminophylline in a mini-bag IV over 20 minutes. She has usually asked for aminophylline treatment specifically and has not required narcotics again (>5 months).

Case 3
W.O. was a 44-year-old female homemaker who presented with status migrainosus, semi-continuous clusters over 35 days. She had right-sided ptosis, dysesthesia in the right side of her face, shoulder/arm, and foot, photophobia, and severe headache. Computed tomography (CT) showed a right parietal cavernous hemangioma that was felt to be unrelated to her symptoms and signs, and she was screened by neurology and neuro-ophthalmology in Vancouver, who did not find any structural disease. Most standard migraine therapy had been tried and failed.

She received 100 mg of aminophylline and experienced almost total relief by 20 minutes. A second dose of 100 mg was given with complete relief. The patient had been seen in ER several times in the previous 6 months with headache/migraine. For 4 months since treatment, she has not required ER treatment again. She has had one visit with the visiting neurology service as an outpatient at the 3-month mark.

Case 4
S.B., a 19-year-old female telephone operator, presented with 5 hours’ left retro-orbital headache, facial dysesthesia, and a “leaden” left leg that made her feel “off-balance.” She has had complete relief on two separate ER visits with aminophylline 100 mg IV infusion over 20 minutes.

Case 5
P.H., a 65-year-old female teacher, took early retirement because of migraines. She was allergic to narcotics, took standard migraine therapy, including ergot, and had a long history with neurology with a multi-faceted treatment approach, including onabotulinumtoxinA (Botox), etc. She presented to the ER with one of her usual refractory migraines for approximately 24 hours, despite all usual standard therapy. Usually the migraine lasted 4–5 days. Headache pain was 10/10, and she complained of photophobia, phonophobia, emesis, and incapacitation. She was given 100 mg aminophylline over 20 minutes.

Details from the case notes are as follows: “Apart from feeling slightly jittery at the end of the 20 minutes, there were no other side-effects. At the 5-minute mark her nausea disappeared, at the 10-minute mark her headache was down from 10/10 to 1/10, and at the 20 minute, mark she had no further visual disturbance. She says this is the best she has felt this far into a migraine in her life. She was discharged after removal of her IV. Her usual pattern is two episodes a month, but she has had only one episode in 2 months since treatment.” (Again, there seems to be no “rebound.”)

Case 6
K.C. was a 32-year-old female with a 2-year history of headache following two motor vehicle accidents. Her father had ocular migraine. The patient had had extensive neurological review and treatment at headache clinics. Her headache was thought to be multifactorial – mainly post-traumatic. She has rarely experienced auras.

On this occasion, there was peri-orbital pain, photophobia, phonophobia, nausea, and pain in her neck and shoulders. Her headache had lasted 72 hours. She had tried several therapies without relief, including anti-inflammatories and narcotics. She was nervous to take any more narcotics because she did her own childcare without support. Both the patient and physician were doubtful that there would be benefit.

Surprisingly, after a 20-minute 100 mg aminophylline infusion IV, the patient had an 80% response. She was able to drive home and do her own childcare and go to work. There were no side effects (importantly for her, no sedation). On a second occasion, this treatment was less effective.

Case 7
M.S., a 31-year-old First Nations female with a strong background history of migraine, presented with left arm and leg weakness following a night of heavy alcohol intake, and marked left-sided hyperesthesia, and pain, including headache and marked nausea.

The reflexes on the left were somewhat brisk despite a history of <12 hours of deficit. The patient had normal CT scans, with and without contrast, of the brain. There was no history of seizure or loss of consciousness. General internal medicine consult was requested as the patient had significant hemiparesis, was unable to stand or even turn herself over in bed, and the two radiologists could not agree as to whether or not there was any ischemia on the CT scan. It was felt that the hyperesthesia and brisk reflexes were more consistent with migraine. The patient had never previously experienced hemiplegic migraine.

At this point, 100 mg aminophylline was given IV infusion over 20 minutes. At the 5-minute mark, the nausea disappeared. At the 10-minute mark, the headache had gone from 8/10 to
0/10. At the 20-minute mark, she could move her left foot and left hand. By 30 minutes, she could stand and had the full use of her left hand. There was mild numbness in the left fourth and fifth fingers. At one hour, the patient was completely back to normal and was discharged.

**Case 8**

M.S., a 45-year-old male, reported a migraine for the previous 3 days. He was uncertain if he could complete his work shift (he was a nurse). He was experiencing a moderate bifrontal headache, nausea, photophobia, and slight tinnitus. He was given aminophylline 100 mg IV over 10 minutes. All symptoms disappeared in 8 minutes, just prior to the completion of the infusion. There was no change in his pulse or blood pressure prior to or upon completion of the infusion.

**Case 9**

J.D., a 35-year-old female with a long history of migraine events, presented with a 2-day history of headache, pain behind the right eye, and severe photophobia but no nausea. She had taken ketorolac tromethamine (Toradol) 2 hours earlier, but her headache was still severe. She was given 100 mg of aminophylline IV over 10 minutes. Headache and photobia were gone 5 minutes into the infusion.

**Case 10**

T.C. was a 23-year-old First Nations female with a history of migraine. She presented to the ER with blurred vision, tingling fingers, vomiting, and a bitemporal throbbing headache. Aminophylline IV was given over 20 minutes, and the symptoms abolished 12 minutes into the infusion.

**Case 11**

K.O. was a 22-year-old normotensive female who was also 34 weeks pregnant, with no proteinuria. Over 24 hours, she had an 8/10, throbbing headache with severe photophobia, dizziness, and scotomata. There was no meningism and no focal deficit, and she was afebrile and having a normal pregnancy.

She was not able to take ergot (definitively contraindicated in pregnancy – in the product monograph), and triptans were relatively contra-indicated in this patient (see Olesen C, Steffensen FH, Sorensen HT, et al. Pregnancy outcome following prescription for sumatriptan. Headache 2000;40:20–24).

She had already had a significant quantity of narcotics, to the point that obesity and related respiratory issues were becoming a concern. She also had severe nausea and emesis. The patient was referred to one of us by the obstetrician who had already done a head CT (because of a suspected subarachnoid bleed), which was normal. Options were limited. The obstetrician felt that all usual, acceptable therapies had been explored, and that the patient’s ongoing nausea, anorexia, emesis, and excessive analgesic requirements were starting to pose a threat to feto-maternal well-being.

Aminophylline is category “C” in pregnancy (no adequate human studies – no proven teratogenicity). The drug is (historically) used for asthma in pregnancy, but has been supplanted by more effective new medications. The obstetrician and patient agreed to her receiving a treatment of aminophylline 100 mg infused by IV over 20 minutes. The patient’s nausea was gone by 5 minutes, and her headache and photophobia were gone by 20 minutes.

The patient had originally arrived incapacitated from a neighbouring town by ambulance for a head CT based on the persistence and severity of her neurological symptoms. Her condition was felt to pose a threat to the health of both mother and fetus. The patient went home direct with her own family 1 hour after treatment. No recurrence was noted at follow-up.

**Case 12**

T.D. was a 42-year-old female with a history of migraines. She presented with a 2-day history of headache with nausea, weakness, and vertigo. Paresthesia in the right arm, neck, and leg was followed by numbness for about 4 hours and 30 minutes. Power, tone, and reflexes were normal. Her CT was normal. The patient was given 100 mg aminophylline IV over 20 minutes and experienced complete relief.

**Case 13**

M.B. was a 46-year-old man who presented after 48 hours of a pounding headache with photophobia, nausea, and vomiting. Usually the patient responded to rizatriptan (Maxalt), but not this time. This migraine also did not have the usual aura. The patient was dysarthric.

He was given 100 mg aminophylline IV over 20 minutes. The patient had some relief at 12 minutes but relapsed with movement. This case was considered an aminophylline failure.

**Case 14**

S.C. was a 40-year-old 40 First Nations female with a history of migraine. She presented to the ER with headache of 8 hours’ duration. She had pain on moving her head, nausea, and photophobia. She was given 100 mg IV aminophylline over 10 minutes, and the headache was gone 8 minutes into the infusion. There was no change in blood pressure or pulse prior to and at the completion of the infusion.
Case 15

H.W. was a 56-year-old First Nations female. She had a severe cardiomyopathy. This patient was receiving nuclear simulated stress testing with dipyridamole, but she already had a bifrontal headache for 2 days prior to the testing. Dipyridamole was infused over 4 minutes as per the usual nuclear medicine protocol, and she developed an additional occipital headache of some severity. Aminophylline 100 mg IV push was given over 1 minute, and both headaches completely resolved 90 seconds later. The improvement was sustained. Photophobia and nausea also resolved along with the headache.

Case 16

C.S. was a 24-year-old female with a history of migraine for years. She had been in bed at home with a severe headache for 24 hours, photophobia, and nausea. As treatment, 100 mg of IV aminophylline was given over 10 minutes. All symptoms resolved 7 minutes into the infusion.

Case 17

R.P. was a 42-year-old First Nations female with a history of migraine and sciatic leg pain for years. She presented with a migraine of 3 days’ duration after a few days of a head cold and possible “sinus pain.” The patient tried self-medication with acetaminophen with no benefit. She did experience vomiting and photophobia.

She indicated she usually needed a narcotic injection of meperidine, which would relieve the sciatic pain as well. Because of that statement, we felt she might be a narcotic seeker. We (the nurses, emergency physician, and internal medicine consultant) were all surprised when the headache and photophobia and nausea disappeared immediately after 100 mg of aminophylline was infused over 10 minutes. Immediate relief occurred just as the infusion was finished. There was some delay in starting the aminophylline infusion, and normal saline was infused over 40 minutes.

To start, there was no significant relief of symptoms, and then the aminophylline was infused over the 10 minutes with the complete relief of migraine symptoms. The patient did not then want a narcotic injection and was discharged.

Case 18

T.S., a 57-year-old male, presented in the ER with a 3-day history of a severe right-sided headache mainly behind the right eye, which he self-diagnosed as a sinus infection. He asked an emergency physician for a CT scan of the sinuses, which demonstrated some slight mucosal thickening but no blockage. He asked for and had received 50 mg of prednisone and also received the antibiotic ceftriaxone for 3 days. He still had the severe headache and was slightly nauseated. He indicated that a few years prior in the United States, he had received similar treatment and that had cured his sinus headache after several days. This time there was no fever, and his white cell count was just at the upper limit of normal even considering he was taking prednisone (which can raise the white cell neutrophil count itself). It was mentioned that we were using the old drug aminophylline for some headaches, particularly migraine, and he wanted to try it even though he felt this was not a migraine and he had no history of migraine except for a prior history of recurrent severe sinusitis lasting several days. He was familiar with aminophylline as he had used it decades ago for asthma attacks. Thus, 100 mg of aminophylline was infused over 10 minutes and partial relief was obtained within 10 minutes.

Two thirds of the headache was gone but one third remained. He felt so much better that he wanted to be discharged and go back to work. Prednisone was discontinued, and it was also suggested that antibiotics be discontinued in 3 more days. We feel this headache might have been a migraine rather than a sinus infection.

Case 19

C.Z. was a 33-year-old female with long history of migraines that were now occurring almost monthly. She presented to the ER with a headache for 24 hours. Pain was a 9 out of 10 in severity. She would not look at the examiner and wanted complete darkness because of photophobia. She was severely nauseated. She kept her eyes closed and her head was flexed, with her hands holding a cold cloth on her forehead. Aminophylline 100 mg was given over 10 minutes with partial relief of all symptoms. She stated that the headache was 50% relieved in 10 minutes and perhaps two thirds gone 10 minutes after that. She still had slight but lesser nausea. She was given ativan 1 mg sublingually and 1 mg to take at home. She was, after the aminophylline, given maxeran 10 mg. She was happy to go home less than 1 hour after arrival. She left by taxi as she had arrived by taxi and the symptoms had been too severe for her to drive.

Case 20

K.S. was a 44-year-old female. This patient had experienced repetitive migraines for a long time, and for years she had attended the ER for injections of the narcotic meperidine (Demerol) and the antiemetic dimenhydrinate (Gravol) if her migraine was prolonged. This headache was right frontal and “pounding,” and pain was mainly behind the right eye but was also generalized somewhat and throbbing. She was vomiting...
and had severe photophobia. Aminophylline was given, 100 mg over 10 minutes, and after the infusion the pain behind the right eye was immediately relieved; but she still felt nauseated and had only a one third relief of the headache and wanted the demerol and gravol. She left with her husband.

Case 21
C.B. was a female with a history of migraine. She presented with a severe (8/10) right-sided headache, accompanied by nausea, photophobia, dizziness, left facial and right arm dysesthesias, whose onset occurred during a morning yoga class. It was not her usual migraine. There were some scotomata at onset. These were worse by afternoon, and she was referred by her general practitioner from a neighbouring town by ambulance for CT scanning of the brain, which was normal. She was referred to one of us for review.

She received 100 mg of aminophylline IV over 20 minutes. The nausea relieved within 8 minutes, and photophobia was gone within 20 minutes. By 1 hour, she was completely back to normal and walked out of the ER saying, “It’s a miracle!”

World Health Day Focuses on Hypertension

Each year on April 7, the World Health Organization (WHO) focuses on a major health issue to celebrate World Health Day. Hypertension was selected for 2013 (http://www.who.int/world-health-day/en/).

Slightly more than half of heart disease and stroke is attributed to increased blood pressure (BP >115/70 mm Hg), with about half of BP-related disease occurring in those with increased but still normal BP. Thus, about 9.4 million deaths per year are caused by increased BP, which is also the leading risk for disability worldwide.1 WHO wants to focus global attention on the causes and adverse outcomes of hypertension, encouraging people to have healthy behaviours and regular BP checks, and to motivate governments to create healthy environments that prevent hypertension.

Although Canada has a lower prevalence of hypertension and higher rates of diagnosis, treatment, and control than are seen in most countries (and thus a lower disease burden from hypertension), still much work needs to be done. A Hypertension Framework was created to guide national efforts for prevention and control, and CSIM has joined a coalition of national health care and scientific organizations (Canadian Hypertension Advisory Committee) to help implement the Hypertension Framework.2

Medical specialists can play important roles. As clinicians, we can both educate other health care professionals in best practices and lead by example to ensure our patients are systematically screened for hypertension and that those with hypertension are optimally managed. We can also focus efforts on documented clinical care “gaps.” Currently, about one in three adult Canadians with hypertension are “uncontrolled” – more often systolic than diastolic BP and more often older women than men. Lack of awareness of having hypertension is most common in the young adult, with men more likely to be undiagnosed than women. Also, most vascular risks apart from BP are not well controlled in people with hypertension.

The Hypertension Advisory Committee, recognizing that up to 80% of hypertension is caused by obesity and unhealthy diets, has prioritized the development of healthy eating policy statements that, if implemented, could markedly prevent and control much of hypertension and also reduce health care costs. CSIM has been actively supporting healthy public policy statements, and individual members can play important roles in advocating for the implementation of these policies. This is particularly important as current federal and provincial governments are predominantly relying on the food industry to voluntary self-regulate, despite the long-term and consistent failure of that industry to do so in a manner that promotes public health. It is time for a paradigm shift to prioritize the health of Canadians by ensuring we have a healthy environment both for ourselves and future generations. Internists can help lead this important change.

Norm Campbell MD

References
Medical Dreams and Academic Pressure: The Terror of Indecision

Ben J. Wilson MD

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As I write this, it is November, a time when PGY4 residents in general internal medicine (GIM) must make weighty decisions about whether to pursue additional clinical or research training before setting off into independent clinical practice. Such questions pre-suppose answers to deeper questions: What is our underlying personal medical mission? How can we launch ourselves into a program or career aligned with our sense of purpose? Too often the passion associated with initial medical career decisions can become dimmed by the academic culture that defines residency training programs. Consideration of the next steps in our career paths and the consequences of our decisions can be associated with significant anxiety.

In the context of this “terror of indecision,” it is helpful to understand that the PGY4 resident in GIM is faced with three options: (1) complete a 5th year of residency in GIM (relevant for the 10 Canadian GIM programs without a mandatory or offered 5th year); (2) pursue a graduate degree, or (3) begin clinical practice. Clearly articulating the seemingly obvious can be reassuring: “a problem clearly stated is a problem half solved.”

The potential utility of a 5th year of GIM residency is resident specific (Table 1). Although additional experience as a resident could be useful in particular situations, the value of an additional “general” year might be called into question by the majority of non-community-bound residents. Despite this, there is mounting pressure from academia to complete a 5th year. Current trends in academic medicine – longer training, narrower and deeper sub-specialization, additional credentials, and “added value” – create substantial pressure to extend training, irrespective of tangible benefit.

Further, the recent decision by the Royal College of Physicians and Surgeons of Canada (RCPSC) to recognize the subspecialty status of GIM favours the completion of a 5th year, in that subspecialty certification necessitates the completion of an accredited two-year GIM training program. It can be argued, however, that the benefits of this new recognition itself are still unclear. Aside from the prestige associated with the new subspecialty designation, concrete benefits remain to be seen. It is altogether imaginable that such recognition may be a prelude to eventual increases in GIM-specific fee codes. But regardless of any future advantages offered by subspecialty recognition, the pursuit of a 5th year of clinical GIM training is difficult to justify for many residents.

Pursuit of a graduate degree offers GIM residents a second option, and in many cases is a necessary step for those who aspire to careers as researchers, administrators, and, increasingly, medical educators. An appropriately tailored program, conscientiously selected for the acquisition of specific skills or out of a genuine interest in a field, can prepare the incumbent to innovate and conduct high-quality research. Graduate work is a clear and logical choice for this subset of GIM residents. For others, however, academic pressure itself can be a powerful influence in deciding to pursue a graduate degree.

Graduate work has become a near-universal requirement for general internists who wish to practise in university settings. Indeed, pursuit of a master’s degree in medical education,
clinical epidemiology, public health, or public policy has effectively become the default pathway for many who aspire to an academic career. Consequently, residents may experience undue pressure to pursue advanced degrees. Many residents find this pressure overwhelming and ultimately might pursue programs by virtue of their novelty or perceived added value rather than from their own intrinsic interest.

In this context, many residents struggle with indecision when confronted with the trifurcation of the 5th postgraduate year. In many cases, this indecision stems from the fact that – as a consequence of the indoctrination that inevitably results from spending thousands of hours immersed in a culture as influential and pervasive as academia – residents may have lost sight of the dreams and inspirations that drove their career choices in the first place. Residents may come to perceive academic medicine not as one way of medical practice, but perhaps as the only way. The critical questions then become: How do we reconnect with our original medical dreams? and How can we best align our immediate training opportunities with them?

Answers may lie in a combination of targeted experience, mentorship, and reflection. Exposure to a wide range of medical subspecialties and practice settings is critical. Diverse experiences allow residents to appreciate the respective merits and drawbacks of various practice settings, and may help to reawaken dormant medical dreams. Because formal training is finite and practice opportunities can be time sensitive, residents need to be shrewd when deciding how to invest their valuable time and effort in these experiences. Careful reflection on innate strengths and interests will help to pare the surfeit of possible experiences into a manageable number. Once identified, electives, clinics, shadowing, and, depending on stage of training, locum opportunities, can be arranged to allow more in-depth appraisal of each area of interest.

Mentors can facilitate this process and empower residents to make better, more genuine decisions. Emotionally intelligent mentors will have the ability to elicit and clarify a trainee’s strengths and interests. By asking the right questions, they can guide residents to consider previously unexplored areas and develop new insights. Good mentors can help residents to identify the experiences that will enable them to draw comparisons among training and career opportunities. In addition, mentors often have the personal connections to facilitate these targeted, high-yield experiences.

Such targeted experiences, reflection, and mentoring can be useful strategies to assist us when we face these times of indecision. It is also important to recognize that this choice is but one in a long series of decisions that ultimately define careers and lives. When viewed in this light, the consequences of any one decision seem less momentous. The medical life cycle is, after all, long and dynamic, offering many opportunities to shift direction and reinvent.

The ultimate goal of these decisions is a meaningful, engaged, and enjoyable medical career. Making the decisions necessary to create such a career hinges on an understanding of one’s core values and medical dreams. Given the pressures and expectations of academia, it is easy to lose sight of these values and dreams. We must avoid the temptation to make decisions based on convenience and the appeasement of the system. We must acknowledge that success is unique to individuals and not to systems. Such realizations will help inform decisions that will keep us on the path to a more authentic and inspired career.

### Table 1. Considerations Regarding a 5th Postgraduate Year in General Internal Medicine

<table>
<thead>
<tr>
<th>Considerations</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Create a clinical niche and/or acquire a particular (e.g., procedural) skill</td>
<td>Useful in community setting. May not practise acquired skills in academic centres where subspecialists traditionally monopolize procedures.</td>
</tr>
<tr>
<td>Gain additional experience before independent practice</td>
<td>Relevant in an era of restricted resident duty hours. Learning yield as a 1st-year attending physician likely outweighs that of an additional supervised postgraduate year.</td>
</tr>
<tr>
<td>Defer career decisions if uncertain about future</td>
<td></td>
</tr>
</tbody>
</table>
In medicine, we use profiling every day to help us make clinical decisions. What is the first thing we are taught to write on every admission note, progress report, and discharge summary? The Patient Profile, or Identifying Information. “Ms. Jewell is a 24-year-old female.” But, in an attempt to be thorough, other information is also often included here: “Ms. Jewell is a 24-year-old, white, intravenous drug user (IVDU) female living in a shelter.” Suddenly, with just a few added words, we have a lot more information from which to frame our initial assessment of the patient’s presenting history. We have also placed this patient into a box, one that may carry significant stigma and may negatively affect the patient’s care. Would you approach a patient with the same history differently if the profile read, “Ms. Jewell is a 24-year-old female, Caucasian medical student presenting from home with her boyfriend”?

Labelling our patients is generally accepted in medicine as it helps us to organize our thoughts and prioritize our differential diagnoses; but how do patients feel about the labels applied to their name?

Let me tell you about T.M. Ms. M is a 29-year-old white female IVDU and high-school dropout, with Addison’s disease, and type 1 diabetes, living in an apartment with her father. That’s the short story. The long story is much more interesting, if you have the time.

I met this young woman on the medicine ward during my first rotation of clerkship. Her history with the medical system was much longer than my 2 weeks on the wards, beginning at the age of 8 when she was diagnosed with type 1 diabetes after presenting to the emergency room in a diabetic coma. Over the next few years, she was seen at the diabetic clinic at SickKids Hospital in Toronto frequently: between once every 6 months to as often as every 2 weeks when her sugars were hard to control. She had multiple seizures due to hypoglycemia and also multiple admissions for diabetic ketoacidosis (DKA).

At the age of 14, she was diagnosed with Addison’s disease, which helped explain some of her uncontrolled blood sugars. It was at this admission that she first felt blamed by the medical system for her condition. She says she was accused of trying to commit suicide and put on a Form 1 at the time. When asked why, she figures it was because she was “a teenager.” You know, just another troubled kid, from a troubled home. A label.

Well, this troubled kid had multiple other admissions to hospital in high school for her chronic health conditions, but did quite well and managed to finish grade 12. She enjoyed English classes in high school and used to write frequently; however, she gave this up when her health declined midway through the second semester of grade 13. At that time she became very ill and was hospitalized for 3 months. She never graduated from high school. Another label.

Around this time, T.M. began experiencing chronic pain, which she attributes to the diabetes. She found it very difficult to control, even with fentanyl patches, hydromorphone, and oxycontin. Opioid addiction soon became a problem, and she admits to boiling her fentanyl patches and crushing her medications to inject in an attempt to self-medicate. She denies injecting other illicit drugs; however, the knowledge of this practice was enough to earn her the label “IVDU” when she was admitted to our team.

That’s a label that bothers T.M. In her many interactions with the health care system, what frustrates her most is feeling judged. She knows people must think of her as “white trash” and a “difficult patient.” She feels like the doctors that treat her have made up their mind about who she is before they even peer through the curtains and say, “Hello.” And, with so many different doctors on the scene, she doesn’t feel she has the time to change their minds. And, isn’t this the truth? We rarely walk into a patient’s room without any preconceptions, as we spend the majority of our time talking about patients’ cases behind closed doors, handing over information from one health care professional to the next. In T.M.’s case, despite her serious chronic health issues, what gets mentioned first when presenting her story is the fact she is an IV drug user, often without any mention that she struggles with chronic pain. She senses that she is not trusted, and consequently believes that
her opinions about her health are not given full consideration, that she is not truly being listened to. Accordingly, she places less faith in treatments the doctors suggest to her, and may be less compliant with the treatment plan, which perpetuates the cycle of distrust.

Ultimately, the fact that she injects may be important to her care. And not every patient can be trusted – some stereotypes hold true. But is it worth jeopardizing the physician-patient communication lines just so we can say, “I told you so?”

Medicine is a place for respect, privacy, and confidentiality, but it is no place for political correctness. Personal details that may be regarded as irrelevant in the typical job interview, details such as age, sex, ethnicity, religion, income, sexual practices, and drug habits, become undeniably pertinent to the physician in a medical history. However, we need to be careful how we present this information to others involved in a patient’s care. Is the term we are using correct for the situation? Does it need further explanation or clarification? Is it relevant to the patient’s care in this specific instance, or is it just interesting or “sensational”? While we don’t always know which facts are relevant at the start, we can ask ourselves whether it is important enough to be included in the first 10 words out of our mouths about a patient, or perhaps it can make its way onto the list of co-morbidities a little further down. And, when it is our turn to see a patient, regardless of what labels are placed on her, regardless of how those labels prejudice our assessment, regardless of how many times we have seen someone in a similar situation, it is our duty to listen to the patient and treat her with respect.
Calcific Pericarditis

Ben J. Wilson MD

An 84-year-old woman presented to the emergency department with progressive shortness of breath, orthopnea, paroxysmal nocturnal dyspnea, and fatigue. She had a past history of atrial fibrillation and was taking digoxin. Clinical examination revealed normal vital signs, 6 cm of jugular venous distension with Kussmaul’s sign, a pericardial knock, and pedal edema. An electrocardiogram showed only nonspecific T-wave changes, consistent with digitalis effect. Her troponin levels were normal. Chest radiographs (Figures 1 and 2) show significant pericardial calcification. An echocardiogram showed her left ventricle to be small and hyperdynamic: left heart failure was attributed to right heart dysfunction from pericardial constriction. She denied a history of previous pericarditis, pericardial infection, radiation, trauma, surgical instrumentation, tuberculosis, cancer, connective tissue disease, or asbestos exposure. Her condition was deemed idiopathic.

Radiographic evidence of pericardial calcification is present in 27% of surgically confirmed cases of constrictive pericarditis.¹ The distribution of the calcium has reported etiological significance, with a thick and shaggy appearance being more common with pericardial tuberculosis.² Today, constrictive pericarditis is most often secondary to mediastinal irradiation, chronic idiopathic constrictive pericarditis, and post-intrapericardial instrumentation.³

References

About the Author
Ben Wilson is a PGY4 resident in general internal medicine at the University of Alberta, in Edmonton, Alberta. Correspondence may be directed to Ben.wilson@albertahealthservices.ca.

Figure 1. Frontal chest radiograph demonstrating prominent pericardial calcification. Calcification is most evident surrounding the right atrium and inferior cardiac border.

Figure 2. Lateral chest radiograph demonstrating marked anteroinferior pericardial calcification.
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Canadian Society of Internal Medicine
Annual Scientific Meetings

October 2–5, 2013
Toronto, Ontario

October 1–4, 2014
Calgary, Alberta

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Dr. David Sackett received the Lifelong Achievement Award at the McMaster University Day in Geriatric Medicine on November 28, 2012. This award, sponsored by the Division of Geriatric Medicine and the Regional Geriatric Program, is presented annually at the Division’s Geriatric Education Day. The recipient is an individual who exemplifies qualities of leadership and integrity, and is regarded as inspirational, forward-thinking, committed to lifelong learning, and a selfless contributor to the building of caring communities. Eligible candidates will have lived or worked within the regions of the Hamilton, Niagara, Haldimand, Brant, and Waterloo/Wellington Local Health Integrated Networks, and are 65 years of age or older.

Dr. Ernesto L. Schiffrin has been awarded the Queen Elizabeth II Diamond Jubilee Medal in recognition of his rank as an appointee to the Order of Canada and his contributions to McGill University. This new commemorative medal is awarded to distinguished citizens who have made significant contributions to Canadian society. The medal presentation ceremony was held on Monday, February 18, 2013, in Montreal.

In addition, Dr. Schiffrin assumed the presidency of the International Society of Hypertension (ISH) at a special ceremony in Sydney, Australia, in October 2012. Dr. Schiffrin, an internist and physician-in-chief at the Jewish General Hospital, is professor and vice-chair (research) of the Department of Medicine at McGill University, and director of the Hypertension and Vascular Research Unit at the Lady Davis Institute for Medical Research. On October 12, 2012, the Honourable Gary Goodyear, federal minister of state for science and technology, speaking at the University of Toronto, reported on the outcome of Canada Research Chairs program, including the renewal of Dr. Schiffrin’s Tier I Canada Research Chair in Hypertension and Vascular Research from January 2013 to December 2019, valued at $1,400,000. Dr. Schiffrin is a fellow of the Royal Society of Canada, a recipient of the 2007 Irvine Page-Alva Bradley Lifetime Achievement Award of the High Blood Pressure Research Council of the American Heart Association and the 2010 Bjorn Folkow Award of the European Society of Hypertension, and a member of the Order of Canada. In 2011, he received the American Heart Association’s 2011 Excellence Award for Research in Hypertension.
Patient Selection Criteria

THERAPEUTIC CLASSIFICATION: Vasopressin V1-receptor Antagonist

INDICATIONS AND CLINICAL USE
SAMSCA® (tolvaptan) is indicated for the treatment of clinically important, non-hypovolemic hyponatremia, e.g., serum sodium <130 mEq/L, or symptomatic hyponatremia. SAMSCA should be limited to use by physicians experienced in the management of clinically important hyponatremia.

SAMSCA has not been studied in patients with serious neurological symptoms requiring urgent correction of serum sodium. Patients requiring urgent intervention to raise serum sodium to treat serious neurological symptoms associated with hyponatremia should not be treated with SAMSCA. It has not been established that raising serum sodium with SAMSCA provides symptomatic benefit to patients or improvement of clinical outcomes.

CONTRAINDICATIONS
SAMSCA (tolvaptan) is contraindicated in the following conditions: hypovolemic hyponatremia, urgent need to raise serum sodium acutely, inability of the patient to sense or appropriately respond to thirst, concomitant use of strong CYP 3A inhibitors, e.g., ketoconazole, clarithromycin, ritonavir, saquinavir, nefazodone, anuric patients, in patients who are hypersensitive to this drug or to any ingredient in the formulation. For a complete listing, see DOSAGE FORMS, COMPOSITION AND PACKAGING in the Product Monograph.

SPECIAL POPULATIONS
(see full listing in Supplemental Product Information section)

Pregnant Women: There are no adequate and well controlled trials of SAMSCA use in pregnant women. In animal trials, clcf palpate, brachymelia, microphalpnea, skeletal malformations, decreased fetal weight, delayed fetal ossification, and embryo-fetal death occurred. SAMSCA should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Women: It is not known whether SAMSCA is secreted into human milk. The presence of tolvaptan has been observed in the milk of lactating rats. Because many drugs are secreted into human milk and because of the potential for serious adverse reactions in nursing infants from SAMSCA, a decision should be made whether to discontinue nursing or the administration of tolvaptan, taking into consideration the importance of SAMSCA to the mother.

Pediatrics (≤18 years of age): Safety and effectiveness of SAMSCA in pediatric patients have not been established.

Geriatrics (≥65 years of age): Of the total number of hyponatremic patients treated with SAMSCA in clinical trials, 42% were 65 and over, while 19% were 75 and over. No overall differences in safety or effectiveness were observed between older patients and younger ones. Other reported clinical experience has also not identified differences in responses between the elderly and younger patients, however, greater sensitivity of some older individuals cannot be ruled out. Increasing age has not been associated with tolvaptan plasma concentrations.

Hepatic Impairment: Moderate and severe hepatic impairment do not affect exposure to tolvaptan to a clinically relevant extent. No dose adjustment of tolvaptan is necessary.

Renal Impairment: Exposure and response to tolvaptan are similar in patients with a creatinine clearance 10-79 mL/min and in patients without renal impairment. No dose adjustment is necessary. Exposure and response to tolvaptan in patients with a creatinine clearance <10 mL/min or in patients on chronic dialysis have not been studied. Note that no benefit can be expected in patients who are anuric.

Heart Failure: The exposure to tolvaptan in patients with heart failure is not clinically relevantly increased. No dose adjustment is necessary.

Safety Information

WARNINGS AND PRECAUTIONS
SAMSCA (tolvaptan) should be initiated, or re-initiated, only in hospital where serum sodium can be monitored closely by physicians experienced in the management of clinically important hyponatremia. Too rapid correction of hyponatremia, e.g., >12 mEq/L/24 hours, can cause osmotic demyelination which may result in dysthria, mutism, dysphagia, lethargy, affective changes, spastic quadriparesis, seizures, coma or death. None of the patients in the controlled clinical trials with tolvaptan exhibited evidence of osmotic demyelination syndrome or related neurological sequelae, but such complications have been reported following too rapid correction of serum sodium. There is no experience with concomitant use of SAMSCA and hypertonic saline. Concomitant use with hypertonic saline is not recommended.

Dehydration: SAMSCA therapy induces copious aquaresis, which is normally partially offset by fluid intake. Dehydration and hypovolemia can occur, especially in potentially volume-depleted patients receiving diuretics or those who are fluid reduced. In multiple-dose, placebo-controlled trials in which 607 hyponatremic patients were treated with tolvaptan, the incidence of dehydration was 3.3% for tolvaptan and 1.5% for placebo-treated patients. In patients receiving SAMSCA who develop medically significant signs or symptoms of hypovolemia, interrupt or discontinue SAMSCA therapy and provide supportive care with careful management of vital signs, fluid balance and electrolytes. Fluid restriction during therapy with SAMSCA may increase the risk of dehydration and hypovolemia. Patients receiving SAMSCA should continue ingestion of fluid in response to thirst.

Contraindicated: While the overall risk of hemorrhage was similar to placebo in the total population studied to date, in patients with cardiac studied in hyponatremia trials, gastrointestinal bleeding was reported in 6 of 63 (10%) tolvaptan-treated patients and 1 of 57 (2%) placebo-treated patients.

Laboratory Findings: Treatment with tolvaptan may be associated with a modest increase in serum potassium.

ADVERSE REACTIONS
(see full listing in Supplemental Product Information section)

Adverse Drug Reaction Overview: Overall, over 4,000 patients have been treated with multiple doses of SAMSCA (tolvaptan) in placebo-controlled or open-label clinical trials. Approximately 150 patients who had hyponatremia and approximately 219 of these hyponatremic patients were treated with tolvaptan for 6 months or more. About 223 patients with hyponatremia received tolvaptan in pivotal trials dedicated to evaluate its effects in the treatment of hyponatremia. Other patients with hyponatremia were evaluated in chronic heart failure trials. The most common adverse reactions, at an incidence >5% more than placebo, as seen in two 30-day, double-blind, placebo-controlled hyponatremia trials in which tolvaptan was administered in titrated doses of 15 mg to 60 mg daily. These were thirst, dry mouth, and polyuria or polydipsia. Consistent with the known mechanism of action of the drug, in these trials, 10% (23/223) of tolvaptan-treated patients discontinued treatment because of an adverse event, compared to 12% (26/220) of placebo-treated patients, with no individual adverse reactions resulting in discontinuation of trial medication at an incidence >1% in tolvaptan-treated patients.

Clinical Trial Adverse Drug Reactions: Because clinical trials are conducted under very specific conditions the adverse reaction rates observed in the clinical trials may not reflect the rates observed in practice and should not be compared to the rates in the clinical trials of another drug. Adverse drug reaction information from clinical trials is useful for identifying drug-related adverse events and for approximating rates.

In multiple-dose, placebo-controlled trials, 607 hyponatremic patients (serum sodium <135 mEq/L) were treated with SAMSCA, whether in hyponatremic trials or in those that evaluated patients with heart failure. The mean age of these patients was 62 years, with 70% of patients male, and 82% Caucasian. One hundred eighty-nine (189) tolvaptan-treated patients had a serum sodium <130 mEq/L, and 52 patients had a serum sodium <125 mEq/L. Hyponatremia was attributed to cirrhosis in 17% of patients, heart failure in 68% and SIADH/other in 16%. Of these patients, 223 were treated with the recommended dose titration, i.e., 15 mg OD titrated to 60 mg as needed to raise serum sodium.

Table 1 lists the adverse reactions reported in tolvaptan-treated patients with hyponatremia (serum sodium <135 mEq/L) at a rate at least 2% greater than placebo-treated patients in two 30-day, double-blind, placebo-controlled trials. In these trials, 223 patients were exposed to tolvaptan, starting at a dose of 15 mg once daily, titrated to 30 and 60 mg, as needed to raise serum sodium. Adverse events resulting in death in these trials were 6% in tolvaptan-treated patients and 6% in placebo-treated patients.

Table 1: Adverse Reactions (>2% more than placebo) in Tolvaptan-Treated Patients in Double-Blind, Placebo-Controlled Hyponatremia Trials

<table>
<thead>
<tr>
<th>System Organ Class</th>
<th>MedDRA Preferred Term</th>
<th>Tolvaptan (n=223)</th>
<th>Placebo (n=220)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastrointestinal Disorders</td>
<td>Dry mouth</td>
<td>28 (13)</td>
<td>9 (4)</td>
</tr>
<tr>
<td></td>
<td>Constipation</td>
<td>16 (7)</td>
<td>4 (2)</td>
</tr>
<tr>
<td>General Disorders and Administration Site Conditions</td>
<td>Thirst</td>
<td>35 (16)</td>
<td>11 (5)</td>
</tr>
<tr>
<td></td>
<td>Asthenia</td>
<td>19 (9)</td>
<td>9 (4)</td>
</tr>
<tr>
<td></td>
<td>Pyrexia</td>
<td>9 (4)</td>
<td>2 (1)</td>
</tr>
<tr>
<td>Metabolism and Nutrition Disorders</td>
<td>Hyperglycemia</td>
<td>14 (6)</td>
<td>2 (1)</td>
</tr>
<tr>
<td></td>
<td>Anorexia</td>
<td>8 (4)</td>
<td>2 (1)</td>
</tr>
<tr>
<td>Renal and Urinary Disorders</td>
<td>Pollakiuria or polyuria</td>
<td>25 (11)</td>
<td>7 (3)</td>
</tr>
</tbody>
</table>

The following terms are subclassified under the referenced DRG in Table 1:
- polydipsia, "diabetes insipidus", nephrogenic diabetes insipidus, "urate output increased", uricosuria, urgency, nocturia.
In a subgroup of patients with hyponatremia (n=475, serum sodium <135 mEq/L) enrolled in a double-blind, placebo-controlled trial (mean duration of treatment was 9 months) of patients with worsening heart failure, the following adverse reactions occurred in tolvaptan-treated patients at a rate of at least 2% greater than placebo: mortality (42 tolvaptan, 36 placebo), nausea (21 tolvaptan, 16 placebo), diarrhea (10 tolvaptan, 2 placebo), dry mouth (9 tolvaptan, 2 placebo), and polyuria or polypnea (4 tolvaptan, 1 placebo).

To report an adverse event, contact the medical info line at 1-877-341-9245 or write to: Otsuka Canada Pharmaceutical Inc., 2250 Alfred Blvd, Saint-Laurent, Quebec H4S 2C9

DRUG INTERACTIONS
(see full listing in Supplemental Product Information section)

Overview: SAMSCA (tolvaptan) is a CYP 3A substrate and does not appear to have clinically meaningful activity. In vitro trials indicated that tolvaptan was extensively metabolized by the cytochrome P450 isoenzyme CYP 3A4/5 and formed many metabolites. The metabolism of most tolvaptan metabolites is also mediated by CYP 3A4/5. There have been no trials performed to determine the potential interaction of tolvaptan with alcohol.

DRUG-FOOD INTERACTIONS
(see full listing of other interactions in Supplemental Product Information section)

Grapefruit Juice: Co-administration of grapefruit juice and SAMSCA results in a 1.8-fold increase in serum tolvaptan levels. Hence, grapefruit juice should be avoided in patients receiving SAMSCA.

For management of suspected drug overdose, consult the regional Poison Control Centre.

Study References

Supplemental Product Information

SPECIAL POPULATIONS
• PREGNANT WOMEN: In embryofetal development trials, pregnant rats and rabbits received tolvaptan during organogenesis. Both received to 162 mg/kg, which is greater than the maximum recommended dose for human use based on plasma concentrations. In rats, tolvaptan did not cross the placenta. In rabbits, tolvaptan was found in the milk of nursing females. Studies in pregnant rabbits indicated that tolvaptan was extensively metabolized by the cytochrome P450 isoenzyme CYP 3A4/5 and formed many metabolites. The metabolism of most tolvaptan metabolites is also mediated by CYP 3A4/5. There have been no trials performed to determine the potential interaction of tolvaptan with alcohol.

Adverse Drug Reactions: The most common adverse events reported with SAMSCA treatment regardless of causality were thirst, polyuria, nausea, vomiting, abdominal pain, diarrhea, dyspepsia, vaginitis, vaginal pain, increased serum alkaline phosphatase, increased serum creatinine, worsening heart failure, the following adverse reactions occurred in tolvaptan-treated patients at a rate of at least 2% greater than placebo: mortality (42 tolvaptan, 36 placebo), nausea (21 tolvaptan, 16 placebo), diarrhea (10 tolvaptan, 2 placebo), dry mouth (9 tolvaptan, 2 placebo), and polyuria or polypnea (4 tolvaptan, 1 placebo).

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