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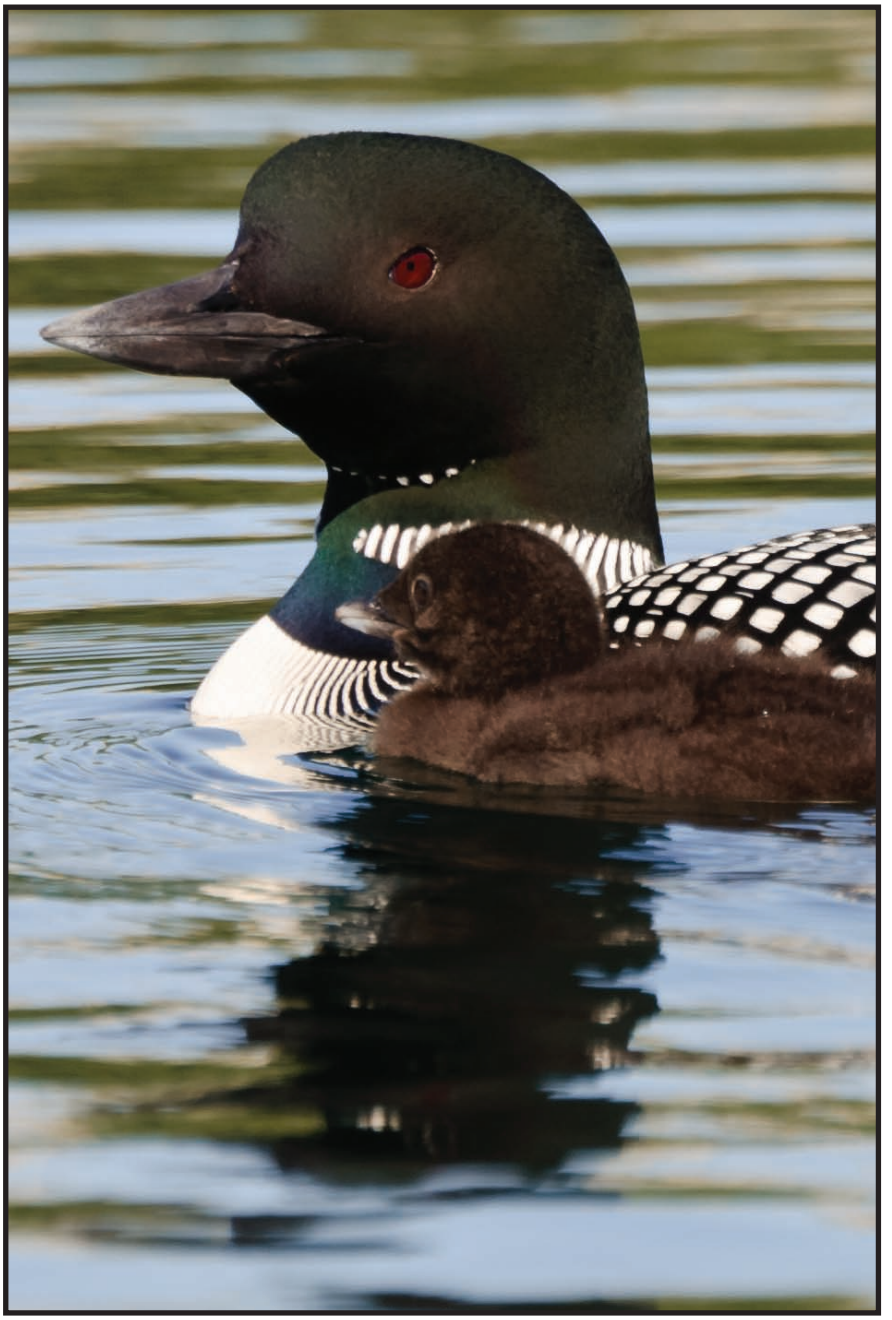

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Internal Medicine Examinations
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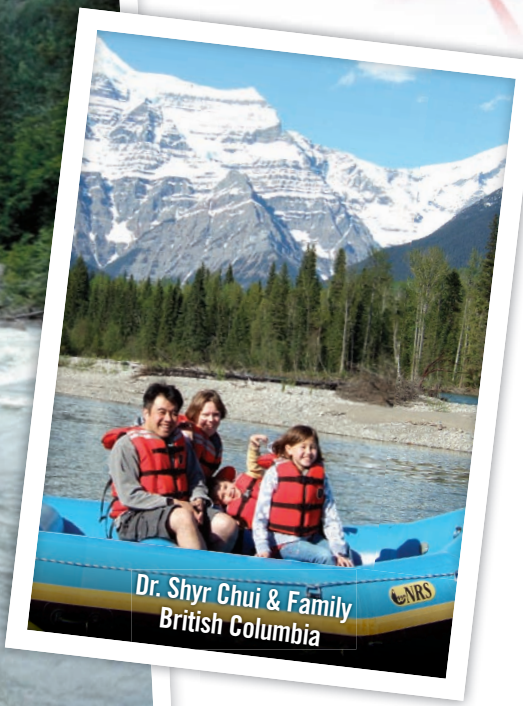

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ABOUT THE COVER

This photo was taken by Michael Vermeer, a 26-year-old amateur photographer. He enjoys being out in nature and loves to share what he discovers through his photography (www.flickr.com/photos/michaelvermeer): "This photo of a common loon and chick was taken on David Lake, July 2010, while on a truly fantastic canoe trip in Killarney Provincial Park, a majestic, mountainous wilderness of sapphire lakes and jack pine ridges. Finding and photographing this pair of loons was a real delight."

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Message from the President

Finlay McAlister MD

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Medical textbooks of 100 years ago were just as big as the textbooks of today; they were just filled with different mistakes.

This quotation, heard during my training, comes to mind whenever I attend a journal club or open the latest issue of a medical journal. The medical literature continues to expand at a dizzying rate; even counting only the highest-quality evidence that should potentially influence practice, 75 randomized trials and 11 meta-analyses are published each day.[1] How much of this evidence will subsequently prove to be wrong?

Two decades ago, how many of us prescribed encainide or flecainide to patients post–myocardial infarction with frequent ventricular ectopy, before the *Cardiac Arrhythmia Suppression Trial* (CAST)[2] proved that these drugs were harmful? A decade ago, how many of us recommended hormone replacement therapy for post-menopausal women to prevent cardiovascular events, before the *Heart and Estrogen/progestin Replacement Study* (HERS)[3] and the *Women's Health Initiative* (WHI)[4] established that there were no such benefits and, indeed, a strong signal of harm? If we think back to just 3 years ago, how many of us routinely prescribed β-blockers for patients undergoing non-cardiac surgery whom we felt had an increased risk of post-operative cardiac complications, before the *Perioperative Ischemic Evaluation* (POISE)[5] demonstrated the potential harms of routine β-blocker use? Health outcomes studies have shown that clinicians modify practice in response to evolving evidence but are quicker to embrace new therapies shown to be beneficial than they are to abandon old therapies once disproven. Even a decade after randomized trials established that vitamin E is not beneficial in preventing cardiac events, more than half of the articles published in the medical literature that discussed vitamin E continued to advocate its use for this purpose.[6]

So where do we go from here? Although a necessary first step, simply teaching critical appraisal skills is not enough – even well-done, high-quality research can provide the wrong answer. While journal clubs can be entertaining academic exercises, few attempt to integrate the lessons from one article with other evidence and clinical expertise to reach a consensus opinion for clinical practice. I believe that *ACP Journal Club and Evidence Updates* (from the *BMJ Group* and *McMaster University*; see http://plus.mcmaster.ca/EvidenceUpdates for information) are definitely a step forward for busy clinicians. They provide brief critical appraisals of recently published articles that have passed methodological quality filters. They also have brief comments from clinicians with content expertise, putting articles into the context of what is already known (or not known) about that topic. I believe these types of resources help us to make sure that our practice is not only evidence based but also consistent with those of our peers, and allow us to optimize the care we provide to our patients. As the half-life of truth for most medical research is somewhere between 45 and 50 years,[7] only our grandchildren will know for sure if the therapies we embrace today will stand the test of time. Until that time, the best we can do is to embrace evidence-based resources that help us keep afloat in the face of the tsunami of literature that floods our inboxes each and every day.

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Finlay McAlister MD

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Les traités de médecine vieux de 100 ans sont tout aussi volumineux que les traités d'aujourd'hui; la seule différence réside dans les erreurs dont ils sont remplis : elles ne sont pas les mêmes que celles qui se retrouvent dans les manuels contemporains.

Cette citation, entendue pendant mes études, me revient à l'esprit lorsque j'assiste à une réunion du club de lecture ou que je feuillette le dernier numéro d'une revue médicale. Les publications médicales se multiplient à un rythme effréné; même si l'on ne tient compte que des données probantes de la meilleure qualité susceptibles d'influer sur la pratique, on dénombre aisément 75 essais cliniques randomisés et 11 métaanalyses publiés chaque jour[1]. Quelle proportion de ces données probantes ne résistera pas à l'épreuve du temps?

Remontons le temps justement, combien d'entre nous prescrivaient de l'encaïnide ou de la flécaïnide en cas d'ectopie ventriculaire consécutive à un infarctus du myocarde voilà 20 ans, avant que l'étude CAST (*Cardiac Arrhythmia Suppression Trial*)[2] démontre que ces médicaments étaient dangereux? Ne serait-ce qu'il y a 10 ans, combien étions-nous à recommander l'hormonothérapie substitutive après la ménopause afin de prévenir les incidents cardiovasculaires jusqu'à ce que les études HERS (*Heart and Estrogen/progestin Replacement Study*)[3] et WHI (*Women's Health Initiative*)[4] mettent en évidence non seulement l'absence de cet effet bénéfique, mais également de solides faits à propos des risques de ce traitement? Et que dire d'il y a trois ans seulement alors que nombre d'entre nous prescrivaient couramment un bêtabloquant avant une chirurgie de nature autre que cardiaque quand ils estimaient qu'il y avait un risque accru de complications cardiaques postopératoires, jusqu'au moment où l'étude POISE (*Perioperative Ischemic Evaluation*)[5] a illustré les effets néfastes potentiels de cette pratique? Des études sur les résultats cliniques font ressortir la propension des cliniciens à modifier leur pratique en réaction aux données probantes évolutives, plus précisément leur tendance à adopter rapidement les nouveaux traitements dont l'effet bénéfique est démontré et leur lenteur à abandonner les anciens traitements une fois que leur inefficacité est établie. Une décennie après que des essais cliniques comparatifs et randomisés ont déterminé que la vitamine E est inutile dans la prévention des troubles cardiaques, plus de la moitié des articles publiés portant sur la vitamine préconisaient encore son usage dans ce but[6].

Alors, que faire? Chose certaine, nous ne pouvons nous en tenir à l'enseignement de la méthode de l'examen critique qui, bien que nécessaire, ne s'avère pas suffisante, car même la recherche rigoureuse peut errer parfois. Le club de lecture quant à lui peut être un exercice d'apprentissage divertissant, mais il est rare qu'il amalgame les enseignements d'un article, des données probantes d'autres sources et l'expertise clinique afin de promouvoir l'établissement d'une opinion consensuelle qui fera son chemin dans la pratique clinique. Néanmoins, la ressource *ACP Journal Club and Evidence Updates* (fruit de la collaboration entre le *BMJ Group* et *McMaster University*; consulter http://plus.mcmaster.ca/EvidenceUpdates pour plus de renseignements) sera assurément utile au clinicien affairé. Elle offre de brefs examens critiques d'articles de publication récente, retenus après l'évaluation de leur qualité méthodologique. Elle propose également des comptes rendus succincts de cliniciens experts dans le domaine en question, qui examinent les articles dans le contexte du savoir sur le sujet (et de l'incertitude qui règne encore à ce propos). J'estime que de telles ressources non seulement favorisent la pratique fondée sur les données probantes, mais également nous permettent de vérifier que notre pratique est conforme à celle de nos pairs et d'optimiser les services et les soins de santé que nous prodiguons à nos patients. Comme la demi-vie de la véracité de la recherche médicale va de 45 à 50 ans[7] en général, seuls nos petits-enfants sauront vraiment si les traitements que nous choisissons aujourd'hui résisteront à l'épreuve du temps. Ce que nous avons de mieux à faire, c'est de recourir à des ressources fondées sur des données probantes qui nous empêcheront d'être engloutis par la vague de documentation médicale qui déferle sur nous beau temps, mauvais temps.

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Internal Medicine Examinations: Comparative Experiences from Three Countries

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Background

For most clinical trainees, the last milestone in the transition from medical residency to independent practice is obtaining a postgraduate medical certificate or diploma by way of a formal examination. Indisputably, these examinations are known to provoke substantial anxiety and fear among trainees because of the large stakes involved. From 2009 to 2010, I attempted internal medicine examinations in three different countries. Here, I provide an overview of the examinations, a subjective description of my preparation strategies, and a brief narrative of the lessons I learned in an attempt to help demystify the examination process and alleviate some anxiety for other trainees.

Overview

Over the past year, I had the opportunity to sit the internal medicine certification examinations in Canada, the United Kingdom, and the United States.

Canada

The Canadian internal medicine examination is administered by the Royal College of Physicians and Surgeons of Canada, the body that oversees the medical education and certification of specialists in Canada. This examination consists of written and oral components where overall success (or failure) is based on consideration of all components of the examination as a whole. The written component of the examination is composed of multiple-choice questions, mostly presented in the form of case vignettes.[1] On the other hand, the oral component consists of a variety of clinical, bedside, communication, and ethical scenarios. Evaluation of the clinical scenarios is based on a candidate's ability to synthesize the information available and manage the cases appropriately. Physical examination skills are also evaluated with standardized patients and a cardiopulmonary simulator.[1]

United Kingdom

Collectively, the Royal College of Physicians of London, the Royal College of Physicians and Surgeons of Glasgow, and the Royal College of Physicians of Edinburgh share a common diploma in medicine. This diploma examination is divided into three components: part 1, a written paper based on basic and clinical sciences; part 2, two written papers based on medical practice; and part 3, the Practical Assessment for Clinical Examination Skills (PACES). The written components are comparable in format to their Canadian and American counterparts, composed of multiple-choice questions examining a wide range of medical knowledge. However, in contrast to other examinations, the clinical component of the British examination involves real patients with bona fide physical findings. Successful candidates must demonstrate an acceptable examination technique, correctly interpret findings, provide a reasonable diagnosis, and articulate a sound management plan.[2]

United States of America

In the United States, certification in internal medicine is regulated by the American Board of Internal Medicine (ABIM), a board under a larger governing body, the American Board of Medical Specialties. Unlike other certification examinations, the ABIM examination is entirely written and administered over the course of a day at a standardized computer facility.[3] The questions presented are mostly in the format of clinical vignettes. A detailed list of examined topics and frequencies of appearance are freely available.[3]

Overview Summary

Each examination has a different emphasis regarding how candidates should be tested. For example, the British examination has a reputation for placing tremendous importance on the identification of physical signs (common and rare alike), thus sometimes examining obscure knowledge. On the other hand, candidates report that the American examination mostly tests common conditions; however, unlike many other certification examinations, it is completely written. The Canadian examination appears to lie somewhere between the two on this spectrum.

Possible Preparation Strategies

General Strategies

Although the three examinations have obvious differences, there is unquestionably some overlap in the content examined. Along the way, I discovered some useful strategies that helped me prepare for the multiple examinations. It was helpful to seek advice from both authoritative sources (e.g., official examining bodies) and recently successful colleagues.[4] In some cases, authoritative sources have published blueprints,[3] books,[5] or even formal collections of sample examination questions[5] to help applicants prepare. When these were unavailable, I relied on narratives passed down from previous candidates.

Interestingly, in a survey of trainees completing the UK examination, respondents voiced what they felt to be the most (and least) useful preparation aids.[4] A surprising majority of respondents stated that clinical experience was of minimal help in passing the written component of the examination. In contrast, it was strongly expressed that preparatory reading was important; but most also added that reading needed to be specifically examination oriented rather than merely a general reading of

reference texts or journals. All responders also indicated that persistent practice with former or simulated questions was the most effective method of preparation. Moreover, numerous people commented that it was "the only way to pass."[4]

In contrast to the written component, respondents from this same survey overwhelmingly rated clinical experience to be the most important contributor to success for the clinical component of the examination. However, many candidates also emphasized that unguided clinical experience itself was of little help; rather, experience was most rewarding when received in a teaching environment with supportive teachers. The value of participating in specialist attachments and clinics was repeatedly emphasized.[4]

Although the survey discussed above was directed specifically at UK trainees, I suspect that recently successful Canadian and American trainees would likely report similar results if surveyed. When informally polling my peers, there is general agreement that for written examinations, the most important preparation strategy is to repeatedly practice simulated questions and to read examination-focused material. Preparation courses and didactic lectures likely confer little additional benefit.[6] In contrast, for an oral/clinical examination, clinical experience appears crucial, especially when guided by skilled teachers. A wide range of reading is also recommended, including use of reference books, journals, and review manuals.

Available Resources

As discussed above, practising simulated questions is a popular study aid. Perhaps the most widely used example in North America is the In-Training Examination (ITE) developed by the American College of Physicians (ACP). The ITE provides specific feedback to residents and program directors, and also appears to be a useful tool to predict the likelihood of future examination success.[7] Another popular preparation aid is the *Medical Knowledge Self-Assessment Program* (MKSAP), also developed by ACP.[8] Additionally, there are online databases of practice questions available for purchase (e.g., www.onExamination.com by BMJ). I found all these resources to be useful in my own preparation.

Furthermore, there are many general review books available that highlight salient topics in internal medicine. I am aware of two books, in particular, that received largely positive reception among my peers: *Approach to Internal Medicine*, written by a former Canadian trainee,[9] and the *Mayo Clinic Internal Medicine Review*.[10]

To prepare for the oral/clinical examinations, I capitalized on daily clinical encounters at the bedside to practise. Many local physicians helped me polish my presentation skills and examination technique. I also rehearsed approaches to common medical problems and practised physical examination skills with peers. To both these groups, I am incredibly thankful.

Examination-Specific Strategies

I found that the most useful strategy to prepare for the written portion of the Canadian examination was to practise simulated questions (e.g., from the MKSAP) and to read Canadian and American clinical practice guidelines. For the clinical examination, I was careful to consult reference texts such as *The Rational Clinical Examination*,[11] *Evidence-Based Physical Diagnosis,*[12] and *Clinical Examination*[13] to review the best evidence available for specific examination manoeuvres. I also found it was valuable to acquaint myself with the cardiopulmonary patient simulator at my local institution.

The American examination closely resembled the ITE and MKSAP questions I had practised. It was important for me to review concepts in primary care because these appear in the examination but are not explicitly covered by most Canadian curricula. Reviewing differences in units of measurement for common laboratory values and specific cut-offs for diagnostic tests was helpful (e.g., fasting plasma glucose threshold for the diagnosis of diabetes in mg/dL versus mmol/L).

From the perspective of a Canadian trainee, preparation for the British examination was by far the most difficult for me because I was not able to ask for advice from any peers or teachers. Consequently, I relied on information published by the Royal College and the online community. I practised simulated questions (e.g., from the BMJ database) to prepare for the written paper, and signed-up for an online review course (www.pastest.co.uk) to study for the clinical examination. To pass the clinical examination, it was essential that I used British preparation texts[14] to familiarize myself with some of the rare diseases tested in the United Kingdom but rarely encountered in Canadian training (e.g., Charcot-Marie-Tooth disease, retinitis pigmentosa, pseudoxanthoma elasticum, etc.)

Lessons Learned

Toward the end of my training, I valued clinical experience and patient encounters to help hone my skills and expose personal areas of deficit. In particular, I am grateful to the teachers I had who gave me constructive feedback so that I could improve. I learned that *practice doesn't make perfect* but, rather, *perfect practice makes perfect*. The ability to perform well on these examinations requires the clear articulation of ideas, systematic approaches to common problems, and a confident execution of physical examination techniques, which all come from deliberate practice.

The opportunity to sit multiple examinations was tremendously rewarding for me. Despite the anxiety and fear I may have felt while studying for these examinations, in retrospect, I now appreciate the value of the preparation process. During the year I spent preparing for these examinations, I accumulated a wealth of knowledge, organized approaches to important medical problems, and was able to consolidate the skills that I had acquired during my training. As a result, I believe I have become a better clinician. I think that this is likely the experience of most other colleagues too – and perhaps this is one of the purposes of these examinations.

Acknowledgements

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Pharm-GIM

Evolution of Antithrombotic Prophylaxis in Atrial Fibrillation: From Dead Cows to Dabigatran

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Atrial fibrillation (AF) is a common cardiac condition affecting an estimated 200,000–250,000 Canadians.[1] While some patients with AF can be symptomatic, the most debilitating sequela associated with this rhythm is stroke. It is estimated that nearly 15% of the 50,000 strokes per year in Canada are caused by AF.[1] Specific risk factors for stroke in AF include valvular heart disease, age >75, hypertension, diabetes, heart failure, and previous stroke or transient ischemic attack (TIA).[2] Until recently, only three therapies were considered for AF antithrombotic prophylaxis: warfarin, acetylsalicylic acid (ASA) or combination ASA and clopidogrel.[3] A new treatment option has recently been introduced following the publication of the RE-LY (Randomized Evaluation of Long-Term Anticoagulation Therapy) trial, which compared warfarin to the novel anticoagulant dabigatran.[4] In order to better understand the role of dabigatran, the historical context of the use of warfarin for antithrombotic prophylaxis in AF should be discussed.

The origin of warfarin actually commenced in part on the Alberta prairies in the 1920s.[5] It began with the discovery of cattle dying of internal hemorrhaging after eating improperly cured sweet grass, a condition that became known as sweet grass disease. Many years later it was identified that the substance responsible for the anticoagulant effects of the sweet grass was dicoumarol, the prototype from which warfarin was derived. During the 1950s, the first human trials using warfarin as an oral anticoagulant were conducted. The use of warfarin for antithrombotic prophylaxis in AF was first studied in the Copenhagen AFASAK trial, published in 1989.[6] Since then, at least 18 other trials involving warfarin and AF have been conducted, which have consistently demonstrated superiority over placebo with an average relative risk (RR) reduction in stroke of 64%.[7] Additionally, warfarin has demonstrated superiority over multiple antiplatelet regimens, with an average 37% RR reduction of stroke. The largest and most recent comparison was the Atrial Fibrillation Clopidogrel Trial with Irbesartan for Prevention of Vascular Events (ACTIVE-W) trial, where warfarin was compared to combination ASA plus clopidogrel.[8] Warfarin demonstrated superiority at reducing the primary outcome of stroke, non–central nervous system (CNS) systemic embolism, myocardial infarction (MI), or vascular death by an absolute risk reduction of 1.67% per year (RR 1.44, 95% confidence interval [CI]

1.18–1.76). As such, warfarin has remained the standard of care and "undisputed champion" of AF stroke prevention for more than two decades; however, it is not without its problems. Not all individuals qualify for treatment with warfarin, well known to the general public as "rat poison" (also marketed as a rodent pesticide), due to the high risk of bleeding. It has also been the source of considerable frustration for both patients and clinicians because of its wide inter-patient anticoagulant variability, which requires frequent blood monitoring, and its multiple drug interactions.

Dabigatran

Dabigatran is the new challenger looking to dethrone warfarin as the drug of choice for stroke prevention in AF. Dabigatran was first approved in Canada in 2008 for the prevention of venous thromboembolism (VTE) in patients undergoing hip or knee replacements. In October of 2010, it received a new indication for stroke and systemic embolism prevention in patients with AF. It has a novel mechanism of action, which involves the direct, reversible inhibition of thrombin, an essential factor in one of the final steps of the coagulation cascade.[9] Dabigatran is administered as a prodrug, which undergoes rapid conversion to its active form by serum esterases, and is considered to have an immediate onset of action. Its half-life is between 12 and 17 hours; it therefore requires approximately 60–85 hours to achieve full anticoagulation at steady state. The renal clearance of dabigatran, either as unchanged drug or as glucuronide metabolites, is responsible for 80% of the total drug clearance. Its duration of action is therefore prolonged in chronic kidney disease and is contraindicated in patients with a creatinine clearance (CrCl) <30 mL/min. Dabigatran is not known to be metabolized via the cytochrome P-450 system but is a substrate of P-glycoprotein and may interact with agents that inhibit (amiodarone, clarithromycin, cyclosporine, dronedarone, verapamil) or induce (carbamazepine, rifampin) this drug transporter.[10,11] While limited drug interaction studies have been conducted, its use is contraindicated specifically with any drug that is a strong inhibitor of the P-glycoprotein system.[10] One of the most appealing and important properties of dabigatran is its predictable pharmacokinetic profile, which does not require International Normalized Ratio (INR) monitoring. Although there is no known antidote to reverse its anticoagulant effects, there are limited data suggesting dabigatran is dialyzable.[11]

In September of 2009, the RE-LY study was published.[4] It was a 2-year, randomized, multicentre parallel group comparator trial of two different dosing regimens of blinded dabigatran versus open-label warfarin. The study enrolled 18,113 men (64%) and women with a mean age of 71 and a CHADS2 (congestive heart failure, hypertension, age >75 years, diabetes, and previous stroke/transient ischemic attack) score of 2.1. At baseline, 50% were receiving long-term vitamin K antagonist therapy, 40% were receiving ASA, 20% had a previous stroke or TIA, and 17% had a previous MI. It was designed as a *non-inferiority trial*, and participants were randomized to one of three treatment groups: (1) dabigatran 110 mg twice daily (low dose); (2) dabigatran 150 mg twice daily (high dose); or (3) dose-adjusted warfarin to achieve an INR of 2.0–3.0. To be included, patients had to have documented AF (within the previous 6 months) and at least one risk factor for stroke (e.g., previous stroke or TIA, heart failure, or ≥75 years of age). Patients with valvular AF, recent stroke or hemorrhage, active liver disease, or chronic kidney disease (CrCl <30 mL/min) were excluded. The primary outcome was a composite of stroke (including both ischemic and hemorrhagic) and systemic embolism. The mean percentage of time that patients in the warfarin group were therapeutic over the study period was 64%. Both dosages of dabigatran met the predefined non-inferiority criteria, and the high-dose dabigatran demonstrated superiority over warfarin with an absolute risk reduction of 0.58% per year (Table 1). There was no statistical difference in all-cause mortality between either of the dabigatran groups and warfarin. Myocardial infarction was noted to be statistically significantly higher in the high-dose dabigatran group versus warfarin (absolute risk increase 0.21% per year). With respect to safety, major bleeding was statistically lower in the low-dose dabigatran group versus warfarin (absolute risk increase of 0.65% per year), though there was no statistical difference when compared with the high-dose dabigatran. Life-threatening bleeding and minor bleeding were both lower in the two dabigatran groups compared with warfarin. However, there was a statistically higher rate of gastrointestinal bleeding with the high-dose dabigatran versus warfarin (absolute risk increase of 0.49% per year). The rate of drug discontinuation was higher with both dabigatran groups compared with warfarin, and there was a statistically higher rate of overall treatment discontinuation secondary to serious adverse events in both dabigatran groups versus warfarin. The only adverse effect that was statistically significantly different between groups was dyspepsia, which was approximately 6% higher in both dabigatran groups compared with warfarin.

Updated 2010 Canadian AF Guidelines

In October of 2010, the Canadian Cardiovascular Society (CCS) released

Table 1. Results of the RE-LY Trial

	High-Dose Dabigatran	Warfarin	RR (95% CI)	*p* Value
Primary outcome (% per year)	1.11	1.69	0.66 (0.53–0.82)	<.001
Major bleeding (% per year)	3.11	3.36	0.93 (0.81–1.07)	.31
Drug discontinuation at 2 years (%)	21	17	NR	<.001
Drug discontinuation due to SAE (%)	2.7	1.7	NR	<.001
	Low-Dose Dabigatran	**Warfarin**	**RR (95% CI)**	***p* Value**
Primary outcome (% per year)	1.53	1.69	0.91 (0.74–1.11)	.34
Major bleeding (% per year)	2.71	3.36	0.80 (0.69–0.93)	.003
Drug discontinuation at 2 years (%)	21	17	NR	<.001
Drug discontinuation due to SAE (%)	2.7	1.7	NR	<.001

CI = confidence interval; NR = not reported; RR = relative risk; SAE = serious adverse events.

Source: Data from Connolly et al.[4]

a summary of their updated practice recommendations for the management of AF, with full recommendations to be published in early 2011.[3] These updated recommendations state that dabigatran is the preferred agent over warfarin, except in those at high risk for coronary events, and that a dosage of 150 mg twice daily is preferred over 110 mg twice daily. Notably, Health Canada has approved both strengths of dabigatran, with the 110 mg dosage to be reserved for geriatric patients or patients at increased risk of bleeding.[10] Patients with a CHADS2 score of ≥2 and no coronary artery disease (CAD) are recommended to receive dabigatran or warfarin. For a patient with a CHADS2 score of 1, warfarin or dabigatran is recommended, although ASA is an acceptable alternative if the clinician deems the risks of warfarin or dabigatran outweigh the benefits. Patients with stable CAD and CHADS2 ≥1 are recommended to receive warfarin, due to the observed increased risk of MI with dabigatran in RE-LY. Patients with no risk factors (i.e., CHADS2 score of 0) should receive ASA 75–325 mg daily.

Discussion

So, where should dabigatran fit into our current AF clinical practice? Based on the results of RE-LY and the current CCS guidelines for AF, dabigatran appears to have become the drug of choice in nonvalvular AF. However, one should note that this recommendation is based on one study, and the relative benefit of dabigatran over warfarin in small. Likely the most prohibitive factor to the broad uptake of dabigatran by patients will be its cost. It is currently undergoing the usual process of review prior to being covered by public and private health care insurers, and therefore at this time is not covered by any provincial drug plan. A recent American-based cost-effectiveness analysis concluded that dabigatran is cost-effective despite being more expensive than warfarin as its use results in reduced overall costs for laboratory monitoring.[12] When deciding whether or not to initiate dabigatran, one must consider that it was studied in a select group of patients with nonvalvular AF with normal hepatic and renal functions. It has not yet been studied in patients with valvular AF, with mechanical heart valves, or post-coronary stent implantation. In addition, the bleed risk of dabigatran in combination with ASA or clopidogrel remains unknown, with only 20% and 8%, respectively, being on each agent concurrently during the study. Epidemiological studies of real-world use of dabigatran, with or without concurrent antiplatelet therapy, will be essential to determine if the bleed rate is similar to that seen in RE-LY. In the near future, there will likely be even more antithrombotic agents to select from, such as the direct factor Xa inhibitors rivaroxaban and apixaban, which are being investigated in ongoing trials.

Conclusion

For the past two decades, warfarin has been the standard of care for preventing stroke in patients with AF and known risk factors where the benefit outweighs the risk of bleeding. New therapies have recently emerged including dabigatran, a novel antithrombotic agent that has now been approved in Canada for the prevention of stroke in nonvalvular AF. Based on the results of the RE-LY trial, it has been recommended by CCS as the preferential agent for antithrombotic prophylaxis in nonvalvular AF, except in patients with CAD. The results of RE-LY demonstrated that dabigatran at a dosage of 150 mg twice daily was superior at preventing stroke and systemic emboli as compared with warfarin, with a similar major bleed risk; and that the dosage of 110 mg twice daily was assessed to be non-inferior to warfarin but with a lower rate of major bleeding. Though dabigatran is more expensive than warfarin, its lack of INR monitoring makes it much more desirable to patients and clinicians. Nonetheless, it should not be used in patients with mechanical heart valves, valvular AF, or dual antiplatelet therapy as it has not been studied in those populations. In many ways, dabigatran appears to be superior to warfarin, but will its cost limit its uptake? The impact of dabigatran will be drastically reduced if it does not end up being covered by provincial drug plans. In addition, there is much to be learned from real-world experience with dabigatran to determine if its risk of bleeding is similar to that seen in RE-LY. For now, dabigatran appears poised to become the new champion of AF antithrombotic prophylaxis – we have come a long way from the ill-fated sweet grass disease that affected cattle on Alberta's prairies.

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Une cause inhabituelle d'urgence hypertensive

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Un homme de 59 ans sans antécédent connu consulte à l'urgence pour troubles visuels et céphalée d'installation graduelle depuis une semaine. À son arrivée, les signes vitaux sont stables, outre une pression artérielle mesurée à 200/131 mmHg. L'examen physique et le CT scan cérébral sont normaux, alors qu'au bilan une insuffisance rénale est notée avec une créatinine à 149 µmol/L. Une échographie rénale montre alors une sténose de l'artère rénale gauche avec atrophie corticale asymétrique, et révèle la présence d'une importante dilatation du segment de l'aorte abdominale visualisé. Un anévrisme abdominal de type IV de Crawford s'étendant des niveaux mésentérique à iliaque est confirmé par angioscan, avec compression secondaire de l'artère rénale gauche (Figure 1).

Un traitement pharmacologique avec nitroglycérine, labétalol et clonidine en aigu suivi d'amlodipine et de métoprolol assurera le maintien de la pression artérielle à 130/80 mmHg jusqu'à l'intervention chirurgicale, 2 mois après la présentation. L'évolution post-opératoire sera favorable suite à l'anastomose aortique par prothèse et le pontage de l'artère rénale sans récidive de sténose. Au suivi à 2 ans, le patient gardera de légères séquelles rétiniennes et rénales (créatinine à 122 µmol/L), avec un contrôle adéquat de sa pression artérielle sous monothérapie (métoprolol).

La maladie rénovasculaire est le plus souvent causée par une maladie athérosclérotique ou plus rarement par une dysplasie fibromusculaire, mais des causes extrinsèques de sténose rénale tels que produites par des kystes, tumeurs, hématomes, anévrismes ou autre sont parfois rencontrées. Bien que des conditions comme l'hypertension artérielle et l'anévrisme de l'aorte abdominale soient relativement communes, une crise hypertensive véritable secondaire à un anévrisme reste très peu décrite dans la littérature médicale.

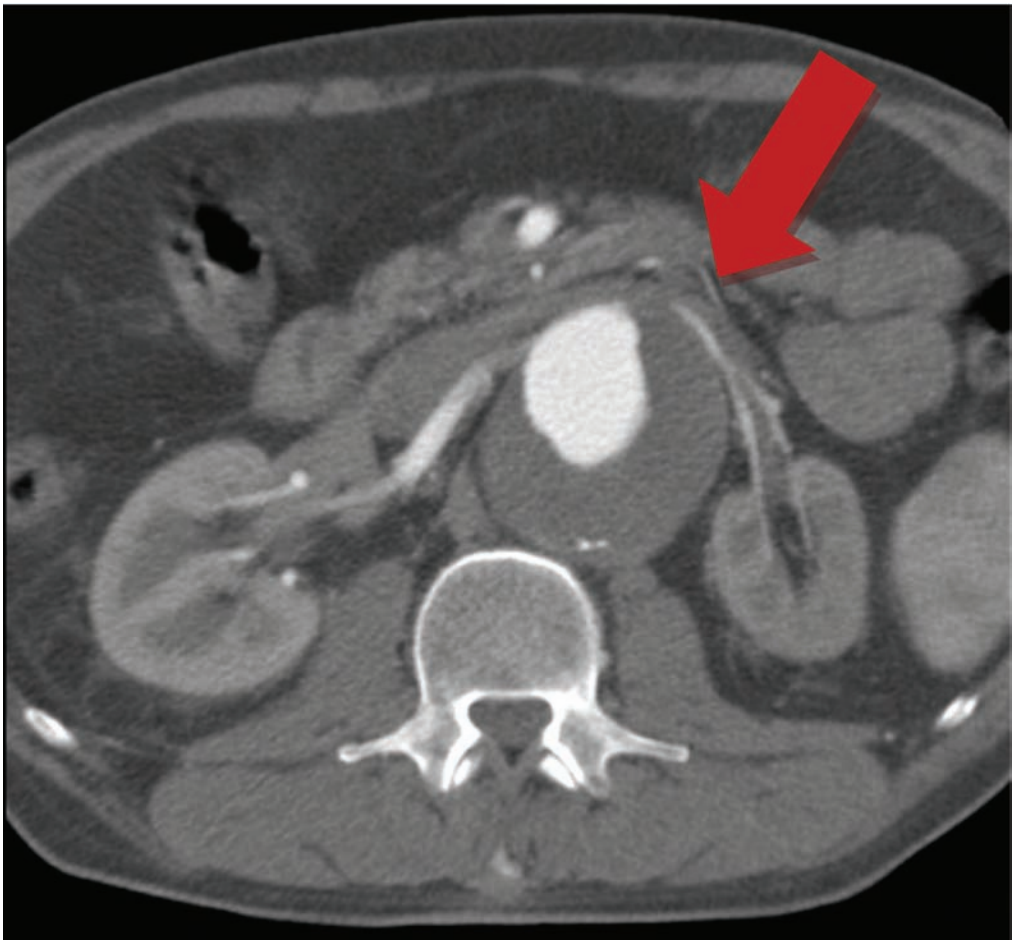

Figure 1. Anévrisme de l'aorte abdominale avant la chirurgie, avec compression de l'artère rénale gauche (*flèche rouge*) (vue transversale).

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Setting Up a Simulation-Based Procedural Curriculum for Internal Medicine Residency Programs: What Are the Basic Ingredients Needed?

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Technical expertise in the performance of seven bedside medical procedures is a specific objective of training in internal medicine, as mandated by the Royal College of Physicians and Surgeons of Canada.[1] These procedures are central venous catheter insertion, lumbar puncture, peripheral arterial catheter insertion, abdominal paracentesis, endotracheal intubation, thoracentesis, and knee joint aspiration.[1] While trainee competency in the performance of procedures is a clear expectation, how to teach and assess procedural skills is left to the discretion of individual programs.

The Case for a Simulation-Based Procedural Curriculum

Although no guidelines are in place for the implementation of a procedural curriculum, increasing attention has been placed on simulation as an educational tool, for a number of reasons. First, clinical opportunities for learning may be decreasing as patients become increasingly reluctant to allow trainees to practise procedures on them.[2] By today's standards, where patient safety is of paramount importance, the traditional "see one, do one, teach one" model whereby learning is done on patients is no longer acceptable. Second, increasing research supports the value of using simulation for teaching procedures, with positive outcomes including improved learner confidence, performance, and fewer clinical complications.[3–5] Simply put, simulation-based procedural education *works*. It works because it allows for experiential learning and provides trainees with an opportunity for deliberate practice.[6] As such, simulation is increasingly recognized as a useful educational tool. Indeed, the most recent program requirements for graduate medical education in internal medicine issued by the Accreditation Council for Graduate Medical Education, effective July 2009, stipulate that training institutions must provide residents with access to training using simulation.[7] For a program seeking to set up a simulation-based procedural curriculum (SBPC), what are the necessary basic ingredients?

Basic Ingredients for Success in Setting Up an SBPC

Learner Buy-In

Assessing the needs of learners is an important first step in the set-up of an SBPC. A needs assessment, often in the form of a survey, can help identify gaps in the current procedural curriculum, assist in the preparation of a blueprint for the proposed curriculum, and allow an educator to estimate the degree of learners' commitment to the process. Furthermore, learning is more likely to lead to a change in practice and behaviour when a needs assessment has been performed.[8]

Material Resources

After conducting a needs assessment, an educator then needs to gather material resources. Those needed for an SBPC include simulator equipment, procedural kits, secured storage, and adequate space for teaching. Simulator equipment can be costly. (Please contact the author for information on materials and costs.) In budgeting for simulator equipment, educators should take into account how many task-trainers are needed at any given time, the costs of replacement parts in order to maintain a sustainable curriculum over time, and potential cost-cutting measures. Because other departments, such as surgery, emergency medicine, anesthesia, etc., teach many of the same procedures as internal medicine, a potential way to cut costs includes interdepartmental equipment sharing. In addition, some simulators used for high-fidelity simulation, if available, can also be used to teach orotracheal intubation. Departmental support and commitment to providing start-up and maintenance costs are key to the program's success.

Importance of a Champion and Avoiding the "Simulator-in-the-Closet Syndrome"

The implementation of an SBPC requires procedural teachers. One report estimated that a program requires one full-time equivalent (FTE) faculty member, with time commitments divided between four clinical faculty members and a full-time medical educator.[9] These educators not only need to have expertise in medical procedures but also need to be familiar with the simulator equipment. For example, in supervising a trainee who is having difficulty with a lumbar puncture procedure on a patient at the bedside, an attending physician may target the potential source of learner difficulty to one or more of the following causes: wrong entry site, wrong angle of insertion, patient factors such as obesity or osteophytes, needle obstruction secondary to blood clot, etc. A trainee who is having difficulty with a lumbar puncture on a simulator, on the other hand, has similar potential sources of difficulty, in addition to simulator factors such as improper simulator set-up, leakage of simulator tubing, etc. Knowledge of the equipment will not only facilitate trainee learning but also help to avoid simulator damage. For example, the use of a scalpel and dilator on the central venous catheter mannequins is not recommended. Faculty development is important in order to ensure that procedural teachers are familiar with the simulator equipment.

A simulator faculty champion is critical to the success of the program.[10] A champion is needed to coordinate various aspects of the program: curriculum implementation and integration, faculty development, and simulator maintenance. Without due attention to these aspects of an

SBPC, programs run the risk of "simulator-in-a-closet syndrome," whereby simulators are purchased but are not appropriately put to use because of a lack of attention to these critical aspects.

Running Your First Session

After gaining familiarity with the simulators, running your first procedural teaching session can still be a daunting task. Some understanding of what constitutes an optimal teaching session may assist educators in delivering a successful teaching session. First, class size matters. For optimal teaching, one teacher should probably teach no more than four learners.[11] Second, ensure that adequate time is given for the learners to practise and for the instructors to provide feedback to the learners. Repetitive practice and feedback are key features identified to lead to effective learning.[12] What constitutes adequate time varies depending on learner background experience and the nature of the procedure itself. For example, at the University of Calgary, a central venous catheterization teaching session has one instructor for every two to four learners, and sessions are done in a 3–4 hour block. Procedures such as arterial blood gas sampling and knee arthrocentesis, on the other hand, can be taught in a session of shorter duration. Third, whenever possible, aim to individualize training.[12] Clarification of trainees' personal learning objectives prior to the session can help avoid an awkward teaching session whereby one trainee has performed the procedure multiple times and is simply interested in refining his or her techniques, while another trainee has never even observed the procedure. Fourth, build in mechanisms for program evaluation. Constructive comments from learners are vital for program improvement and curriculum modification.

Program Maintenance

Once a few sessions are up and running, educators should work on integrating teaching sessions into the curriculum, another feature shown to lead to effective learning.[12] Teaching should become a part of a learner's normal training schedule, rather than an optional activity. If budget allows, a program administrative assistant will greatly help in the day-to-day aspects of curriculum implementation such as scheduling, simulator set-up and take-down, and inspection of simulators for damage and replacement. However, a program may still flourish without an assistant, provided a champion oversees these seemingly small but crucial aspects of an SBPC.

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Idiopathic Hemophagocytic Lymphohistiocytosis: A Potentially Fatal Cause of Fever of Unknown Origin

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Case Report

A 59-year-old East Asian female presented with a 2-month history of fever (over 39°C) and chills without obvious cause. She was taking losartan for treatment of hypertension but no other medications. She was a non-smoker and had no risk factors for tuberculosis or human immunodeficiency virus (HIV). She had no recent travel history. Screening for breast, cervical, and colon cancers was up to date. On examination, she had a temperature of 38.9°C. She had no lymphadenopathy or organomegaly, and no inflammatory synovitis or rash. The remainder of her examination was normal. Laboratory findings revealed a hemoglobin level of 104 g/L (normal 115–165 g/L), a white blood cell count (WBC) of 2.5 × 10^9/L (neutrophils 1.4 × 10^9/L), and a platelet count of 116 × 10^9/L (normal 150–400 × 10^9/L); an alanine transaminase (ALT) level of 204 IU/L (normal <31 IU/L), an aspartate transaminase (AST) level of 158 IU/L (normal <31 IU/L), a bilirubin level of 13 µmol/L (normal <20 µmol/L), an International Normalized Ratio (INR) of 1.02, an l-lactate dehydrogenase (LDH) level of 753 IU/L (normal 100–250 IU/L), and a serum haptoglobin level of 0.2 g/L (normal 0.3–2 g/L). Her creatinine was 77 µmol/L (normal 44–106 µmol/L), fibrinogen 2.39 g/L (normal >2 g/L), and erythrocyte sedimentation rate (ESR) 12 mm/h (0–20 mm/h). Her serum ferritin was >10,000 µg/L (normal 20–400 µg/L), and her triglycerides were 6.6 mmol/L (normal <1.7 mmol/L). Results of a workup for connective tissue disease, including antinuclear antibodies (ANA), double-stranded deoxyribonucleic acid (dsDNA), rheumatoid factor, C3, C4, cytoplasmic-staining antineutrophil cytoplasmic antibody (cANCA), and perinuclear-staining ANCA (pANCA), were negative. Blood and urine cultures were negative for bacteria and fungi. Test results for hepatitis A, B, and C, HIV, herpes simplex, Epstein-Barr virus, cytomegalovirus (CMV), Lyme disease, leptospirosis, *Coxiella, Bartonella, Brucella*, and malaria were negative. She was continuously febrile, with temperatures exceeding 38.5°C over the next 16 days in hospital. A bone marrow biopsy showed tri-lineage hematopoiesis with normal cytogenetics and flow cytometry. A gallium scan revealed increased activity in the right proximal humerus, which on magnetic resonance imaging (MRI) was felt to represent active hematopoietic marrow. Her abdominal sonogram, computed tomography scan of the abdomen, and MRI of the abdomen revealed a 1.5 cm liver hemangioma and 1 cm simple cyst in the tail of the pancreas. A transthoracic echocardiogram was normal. Infectious disease and hematology consultations were obtained, but no diagnosis was reached. She remained febrile, and her pancytopenia worsened.

On readmission to hospital 1 month later, she was febrile and complained of nausea and vomiting. She was clinically jaundiced. Blood work revealed a hemoglobin of 70 g/L, a WBC of 0.8 × 10^9/L, a platelet count of 18 × $10^9$9/L, an LDH level of 3,465 IU/L, an ALT level of 108 IU/L, an AST level of 393 IU/L, an alkaline phosphatase (ALP) level of 1,620 IU/L (normal 40–120 IU/L), and a bilirubin level of 75 µmol/L. Her ferritin was >70,000 µg/L, fibrinogen 0.81 g/L, and triglycerides 9.62 mmol/L. Her blood film did not show fragmented red cells. An abdominal sonogram was normal; in particular, there was no evidence of extra- or intrahepatic obstruction. A lumbar puncture revealed a high protein level (501 mg/L), with a normal cell count and glucose level. Cerebrospinal fluid cultures were negative for bacteria. Upon re-investigation, no infectious, malignant, or rheumatologic disorders were identified. A repeat bone marrow biopsy showed evidence of hemophagocytosis. A diagnosis of idiopathic hemophagocytic lymphohistiocytosis (HLH) was made based on established diagnostic criteria (Table 1).

She was treated with dexamethasone (10 mg/m^2), etoposide twice weekly (150 mg/m^2) for the first 2 weeks (then once weekly), and cyclosporine to keep trough levels at 200 µg/L. She received two doses of intrathecal methotrexate, as well as acyclovir, co-trimoxazole (Septra), and fluconazole prophylaxis. Her fevers subsided shortly after the initiation of chemotherapy, and her laboratory parameters began to normalize. During her 4th week of chemotherapy, she developed intra-abdominal sepsis secondary to neutropenic enterocolitis, and she required a subtotal colectomy. A biopsy of her large bowel showed evidence of hemophagocytosis suggesting progressive HLH. She passed away in the intensive care unit shortly thereafter from intra-abdominal sepsis and *Pseudomonas/Klebsiella* bacteremia.

Discussion

HLH is not a single disease but, rather, a clinical syndrome encountered in a variety of underlying conditions (see below). A characteristic hyperinflammatory phenotype results in macrophage phagocytosis of normal tissue. Initial signs and symptoms of HLH often mimic other disease processes, and the diagnosis of HLH is often made late in the course of the disease. HLH can manifest initially as fever of unknown origin (FUO) in any patient population and can rapidly progress to overwhelming sepsis and death. Despite improved treatment modalities, the mortality rate of HLH approaches 50% in adults.[1] Therefore, a high index of suspicion is required to establish prompt diagnosis.

HLH is diagnosed in an estimated 1.2 children per million per year, but no data exist on its incidence in adults.[2] HLH is either primary (inherited) or secondary to infections, malignancies, or autoimmune diseases.[3]

Table 1. Diagnostic Guidelines for Hemophagocytic Lymphohistiocytosis

Major Criteria (5 of 8 Required)	Initial Presentation*	Readmission*
Fever	Yes	Yes
Splenomegaly	No	No
Cytopenias (affecting 2 of 3 lineages): • Hemoglobin <90 g/L • Neutrophils <1.0 × 10^9/L • Platelets <100 × 10^9/L	Variable	Yes
Hypertriglyceridemia and/or hypofibrinogenemia: • Fasting triglycerides >3.0 mmol/L • Fibrinogen <1.5 g/L	High triglycerides	Yes to both
Hemophagocytosis†: • Bone marrow, spleen, or lymph nodes • No evidence of malignancy	No	Yes
Ferritin >500 µg/L	Yes	Yes
Low or absent NK-cell activity	Not done	Not done
Soluble CD25 (i.e., soluble IL-2 receptor) >2,400 U/mL	Not done	Not done
Supportive Evidence		
Lumbar puncture: • Pleocytosis (mononuclear) • High protein	Not done	High protein
Chronic hepatitis on liver biopsy	Not done	Not done
Associated Findings		
Cerebromeningeal symptoms	No	No
Lymph node enlargement	No	No
Jaundice	No	Yes
Hepatic enzyme abnormalities	Yes	Yes
Hyponatremia	No	Yes

IL = interleukin; NK = natural killer.

*The second and third columns demonstrate our patient's clinical and laboratory criteria at the time of initial presentation (September 2009) and readmission (October 2009).

†If hemophagocytosis is not proven at the time of presentation, further search for hemophagocytosis is encouraged. If the bone marrow specimen is inconclusive, material may be obtained from other organs. Serial marrow aspirates over time may also be helpful.

Source: Adapted from Henter et al.[4]

Clinical presentations of primary and secondary HLH are usually indistinguishable. Macrophage activation syndrome (MAS) also shares many of the clinical features of HLH. This syndrome occurs in patients with juvenile rheumatoid arthritis and systemic lupus erythematosus, and some consider it an acquired form of HLH.[3]

All symptoms and signs of HLH can be explained by high concentrations of inflammatory cytokines and organ infiltration by activated lymphocytes and histiocytes. Fever is induced by interleukin-1, and pancytopenia is the consequence of high levels of tumour necrosis factor (TNF) α and interferon gamma. TNF-α inhibits lipoprotein lipase, thus leading to elevated triglyceride levels. Activated macrophages secrete not only ferritin but also plasminogen activator, which results in high plasmin levels and hyperfibrinolysis. Hepatosplenomegaly, increased liver enzymes, and neurological symptoms are the consequence of organ infiltration by activated lymphocytes and histiocytes.[3]

Guidelines by the Histiocyte Society have contributed significantly to the improvement of diagnosis in HLH (see Table 1).[4] The pathological finding in the bone marrow is histiocytic hyperplasia with prominent phagocytosis of mature and immature hematopoietic elements. Hemophagocytosis is not an obligatory feature and treatment should not be delayed if hemophagocytosis is absent on bone marrow examination. Nearly 20% of cases require more than one bone marrow biopsy to demonstrate this phenomenon.[5]

The progression of organomegaly and cytopenias in an immunocompetent febrile patient should alert the physician that this could be an unusual inflammatory response such as that seen in HLH.[3] Patients should be screened for an underlying infection, malignancy, and autoimmune disease. Appropriate therapy for HLH should not be withheld until one of these triggers is identified. Treatment of the underlying cause is important, but this alone will not reverse the uncontrolled inflammation of HLH.[3]

Without treatment, the uncontrolled inflammation of HLH leads to sustained neutropenia and death from infection or multiorgan failure. With treatment, a 3-year mortality rate of 50% has been reported for acquired cases in children, and the prognosis in adults seems to be worse.[1] The treatment regimen currently used is designed to control T-cell activation (steroids, cyclosporine, etoposide) and macrophage activation (etoposide). A second aim is to kill pathogen-infected antigen-presenting cells to remove the stimulus for the ongoing activation of cytotoxic cells.[3] HLH treatment protocol was created in 1994 by the HLH Study Group of the Histiocyte Society, and a revised protocol was published in 2004.[6] Patients who survive the initial protocol may undergo allogeneic stem cell transplantation, which has a 3-year survival rate in children of 64% with most deaths occurring in the first year after transplantation.[7]

Summary

HLH should be considered in the differential diagnosis of FUO. HLH is a rare condition that carries a high mortality rate if not recognized early. Effective treatment does exist. A high index of suspicion is required to diagnose HLH as ferritin, fibrinogen, and triglycerides are not part of the standard FUO algorithm. Lymph node and bone marrow biopsies are often initially negative in HLH, and the absence of hemophagocytosis is usually the reason for the erroneous exclusion of HLH.[3]

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Correspondence

Letter from the Specialty Committee in Internal Medicine

This is an exciting time for general internal medicine (GIM) as we ride the recognition roller coaster. Ever since the Canadian Society of Internal Medicine (CSIM) was founded in the 1980s, there has been a desire to establish a Royal College specialty in the field. Numerous proposals have been developed for GIM training paths by both CSIM and the Specialty Committee in Internal Medicine (SCIM). Surveys have been completed to establish the practice parameters of GIM, both in Canada and in other countries. Regular plenary sessions have been held at CSIM annual meetings. In recent years, Sharon Card from Saskatoon has been a prime mover of this process, leading a task force and chairing the program director group. Sixteen universities have appointed individuals to act as program directors for GIM programs, and eight have 2-year programs.

The Committee of Specialties has now approved SCIM's application for subspecialty status for GIM. The Royal College Council unanimously approved the application on December 17, 2010. The next step includes the creation of a working group tasked with, among other things, the establishment of objectives, training requirements, evaluation processes, accreditation standards, and the process for recognition of specialists currently practising GIM.

The second major initiative from the committee is the development of much more detailed objectives of training than exist at present, focusing on both areas of knowledge and skills as well as levels of competency. Bruce Fisher, Darryl Rolfson, and Vijay Daniels (University of Alberta); Tom Maniatis (McGill University); and Adam Peets (University of British Columbia) have made major contributions to their development, and these are now being considered by the college for approval.

Brian O'Brien MD
Chair, SCIM

Letter to the Editor

Dear Editor:

After reading Dr. Finlay McAlister's e-newsletter about the Canadian Society of Internal Medicine, I thought I should write you.

I have always thought that the practice of general internal medicine requires a particular state of mind. This state of mind results in an interest in people, not only in their diseases, and a thorough comprehensive assessment of the whole person.

I work at St. Clare's Mercy Hospital in St. John's, Newfoundland, where we have a number of first-class physicians who practise general internal medicine. Some of them practise a subspecialty in addition to general internal medicine and practise both with a high degree of skill. Their in-patient and emergency room practice is general, and their outpatient practice mostly subspecialty. Some others practice general internal medicine with emphasis on a particular problem, for example, diabetes or asthma.

In any group of general internists with such a practice almost the whole field of medicine can be efficiently covered, and I feel sure this is the way of the future if we can persuade trainees that this is a good way of life. It is, however, a difficult way of life, and our internists are almost always on service. However, the delivery of medical care in internal medicine by subspecialists who do not practice general medicine is extremely expensive and not always in the best interest of the patient.

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Canadian Cardiovascular Outcomes Research Team: Lessons Learned

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Background

The Canadian Cardiovascular Outcomes Research Team (CCORT) was created in 2001 through a $4.6 million 5-year Canadian Institutes of Health Research (CIHR) Interdisciplinary Health Research Teams grant and a $1 million grant from the Heart and Stroke Foundation of Canada. Funding was renewed in 2006 for an additional 5 years (2006–2011) through a $4.2 million CIHR Team Grant in Cardiovascular Outcomes Research. CCORT involves over 30 investigators from six Canadian provinces (Nova Scotia, New Brunswick, Quebec, Ontario, Alberta, and British Columbia) working together, over the past decade, on research aimed at measuring and improving the quality of cardiac care. CCORT has generated over 155 peer-reviewed publications and provided funding to over 50 students (summer students to postdoctoral fellows) from across Canada to pursue training in cardiovascular (CV) outcomes research. CCORT's national coordinating centre has been located at the Institute for Clinical Evaluative Sciences (ICES), in Toronto, Ontario since its inception.

Rationale for Team-Based Research

Historically, medical research involved small studies conducted by solitary scientists or small teams working in isolation in a local laboratory. Today's complex research questions, in contrast, often involve large-scale, multi-site studies and require multidisciplinary research teams with diverse professional and technical skill sets. These teams, enabled by technology, collaborate across time and space, as they address local as well as global health issues.

The creation of CIHR was motivated, in part, by a vision of health research where scientists working in four pillars of research (biomedical; clinical; health systems services; social, cultural, environmental, and population health) collaborate to bring research from "bench-to-bedside-to-community," in order to improve the health of Canadians as well as the quality and sustainability of the Canadian health care system. An additional mandate of CIHR's multidisciplinary teams, including CCORT, involves active engagement in knowledge translation (KT) activities to translate research findings into improvements in health for Canadians.

While collaborative research is a highly desirable outcome for funding bodies, and team-based approaches can provide the capacity required for complex areas of study,[1] the practical reality of doing team-based research and KT can involve many challenges. Over the past decade, CCORT has undertaken a number of large and complex research studies. These studies, including the development of a national CV atlas and the completion of two cluster randomized trials on the effectiveness of health care report cards, provided valuable experience; hopefully, sharing our experience will assist others embarking on team-based research initiatives.

CCORT Canadian Cardiovascular Atlas

The objective of the CCORT Canadian Cardiovascular Atlas project was to create a comprehensive "report card" on the patterns of CV health and care delivery in Canada. Building on prior work completed in Ontario, the CCORT Atlas project, launched in 2002, addressed topics ranging from geographical variations in the burden of cardiac risk factors and disease to variations in survival rates following acute myocardial infarction (AMI) and cardiac surgery. Published as a series of 24 peer-reviewed articles in the *Canadian Journal of Cardiology* from 2003 to 2005, the atlas was compiled as a book in 2006, and freely distributed, in print form and electronically, via CCORT's website where it has been downloaded over 50,000 times.[2,3]

The CCORT Atlas proved to be an ideal team-based project as it required a large group of clinician researchers with expertise spanning the spectrum of CV medicine, from primary care to acute hospital-based care to chronic and end-of-life care for heart failure. It also leveraged the combined knowledge of the team, engaging investigators with different skill sets and insights to address CV-related issues facing Canadians. With in-depth knowledge of their local systems and data, investigators were also able to identify and interpret findings relevant to their respective regions and the country as a whole. Some 50 authors contributed to the CCORT Atlas, coordinated by an editorial team composed of me (University of Toronto), Louise Pilote (McGill), William Ghali (University of Calgary), all members of the Canadian Society of Internal Medicine (CSIM), and Susan Brien, a senior research coordinator at ICES. The group managed to overcome many barriers (from gaining access to provincial data sets and ensuring consistency of variables and algorithms, to meeting publication deadlines along with clinical and other professional commitments) during this mammoth project. The findings from the Atlas project have been used by many organizations throughout Canada to improve the quality of health care delivery.

Lessons Learned

A key lesson learned from the CCORT Atlas project involves selecting the "right" types of research projects, that is, those that address an important, novel question that are of appropriate scale and complexity to warrant a team-based approach. The CCORT Atlas was an excellent team project due to its size, scope, and complexity. It required the combined efforts of the entire team, and actually helped the team members to "gel" as they worked together to plan the articles, assemble data sets, conduct analyses, and put pen to paper. It also provided all team investigators with an opportunity to lead an important area of study, as part of a first-ever project, resulting in many peer-reviewed publications.

As noted, KT is part of CIHR's mandate; however, at the beginning of CCORT, little guidance was provided in terms of the types of activities that were expected. Even today, the science of KT remains in its infancy; few proven strategies exist for effective translation and the timely incorporation of clinical evidence within routine care. Despite this, we made a concerted effort to embed KT within all CCORT research activities. For the CCORT Atlas, in particular,

we established a process of preparing media releases, sharing PowerPoint slide collections and, eventually, the complete set of articles via our website, and conducting multiple presentations and workshops at local and national meetings, all of which helped increase awareness and maximize the impact of the Atlas project.

Population-Based, Cluster Randomized Trials: AFFECT and EFFECT

CCORT also conducted two large population-based, cluster randomized trials designed to evaluate the "real-world effectiveness" of hospital report cards for improving care – a controversial topic in the medical field.

In the Administrative Data Feedback for Effective Cardiac Treatment (AFFECT) study, 76 hospitals in Quebec were randomized to receive either rapid or delayed feedback in the form of a confidential report card on their performance on a set of AMI quality indicators, measured using linked administrative databases. The results showed that the confidential report cards had no measurable impact on any of the indicators included.[4] The study, published in *Journal of the American Medical Association* in 2005, was described as an important contribution to the science of quality improvement in an accompanying editorial.[5]

In the Enhanced Feedback for Effective Cardiac Treatment (EFFECT) study, 86 participating hospital corporations in Ontario were randomized to either early (January 2004) or delayed (September 2005) feedback of a publicly released report card on a set of 18 CCORT/Canadian Cardiovascular Society AMI and congestive heart failure (CHF) process-of-care quality indicators, derived from chart review.[6,7] Initial results for the early-feedback hospitals released at a press conference in January 2004 attracted widespread media coverage and reached an estimated audience of over *12 million Canadians* (via the media and the web).[8–10] A survey of participating hospitals, conducted that summer, found widespread awareness of the study's findings, with more than half of early-feedback hospitals (as well as several in the delayed feedback "control" arm of the study) engaging in initiatives to improve the quality of cardiac care provided. Although the study failed to reach its composite primary end point, several positive secondary outcomes were achieved including lower 30-day and 1-year mortality rates in patients with AMI and lower 1-year mortality rates in patients with CHF with reduced ejection fraction.[8] Key findings included the observations that 24% of early-feedback hospitals changed their policies to allow emergency physicians to give fibrinolytic drugs directly to appropriate patients rather than waiting for a specialist to make the decision, and that "door-to-needle" times for fibrinolytic therapy were significantly faster in hospitals where this was a routine policy.[8]

Lessons Learned

AFFECT and EFFECT, both landmark studies, demonstrated that it is possible to study important health policy questions using scientifically rigorous designs. As well, the EFFECT study reflected the benefits of a multi-disciplinary team engaged in KT research along with key stakeholders in the health care system, including the Canadian Cardiovascular Society (involved in the design and endorsement of the AMI/CHF quality indicators), CIHR and the Heart and Stroke Foundation of Canada (involved in organizing and co-hosting the EFFECT press conference), and the Ontario Hospital Association (a key partner in disseminating the results to participating hospitals before and after the press conference).

The EFFECT study demonstrated, for researchers, the benefits of working with larger, more established organizations to translate research into practice. We were able to disseminate our research findings much more effectively by working with larger well-established organizations as opposed to trying to disseminate our research by ourselves alone.

The CCORT website (www.ccort.ca) has also proven to be a very effective KT vehicle as it allows us to publish additional supplementary material (hospital record cards, quality indicator measurement guides, interactive web-based maps, CHF mortality risk model, PowerPoint slides, etc.) to complement material published in traditional peer-reviewed journals. The website received more than 17,000 unique visitors this past year alone.

Conclusion

In summary, CCORT effectively used a team-based research model, incorporating KT, to improve the quality of cardiac care in Canada through innovative health systems and population health research. In recognition of its impact, CCORT was chosen as the recipient of the 2005 CIHR National Knowledge Translation award, and the EFFECT study paper, published in *Journal of the American Medical Association*, was chosen as the 2010 Article of the Year by the CIHR Institute of Health Services and Policy Research.[8]

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A Trip to East Africa – The Circle Is Complete

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Malaria, tuberculosis (TB), syphilis, various parasitic infections, and amoebic liver abscesses preoccupied my mind during my 5 undergraduate years in India. My career then took me to the Caribbean, northern Newfoundland, and New Brunswick. The years have flown by, in a productive and rewarding career practising internal medicine and intensive care. More recently, a role in medical education has been very fulfilling. Several short assignments in South America and India as a volunteer physician have allowed me to maintain a broad interest in international medicine.

Life, they say, comes full circle. This became clear when I found myself yearning to reacquire my forgotten knowledge of tropical medicine. Extensive research outlined some of the following possibilities for study:

- The London School of Tropical Medicine and Hygiene – January to March
- The Liverpool School of Tropical Medicine – February to May
- Gorgas Diploma Course, Peru – January to April
- Institute of Tropical Medicine, Berlin – September to December

While considering these options, I, inadvertently came across the following announcement: "2010 East African Short Course in Tropical Medicine (Oct–Nov)," organized by the London School of Tropical Medicine in Tanzania and Uganda. My inner voice exclaimed, "What a capital idea, a tropical medicine course in the tropics!" I signed on without delay.

The 6-week course was given at the Kilimanjaro Christian Medical College (KCMC) in Moshi, Tanzania, and at Makerere University and Mulago Hospital in Kampala, Uganda. The course consisted of classroom studies, laboratory medicine, workshops, in-patient and outpatient work, field trips, and special projects. Weeks 1–3 took place at KCMC:

- Week 1, basic epidemiology and clinical assessment
- Week 2, diagnostic parasitology/community survey
- Week 3, special topics – dermatology, neurology, sexually transmitted infections

These 3 weeks were extremely enjoyable, a wonderful introduction to tropical diseases. The instructors were very well informed, having worked for many years in Africa. It was refreshing to have patients at hand to illustrate these diseases. This correlation with reality in this resource-poor environment was striking. The emphasis was on practical learning, tailored to local medical conditions. Soon we were taught to rely on the history and physical examination; when the diagnosis was still uncertain, the emphasis reverted to syndromic management.

KCMC is a large 450-bed hospital serving as a referral centre for 11 million people. The course emphasis was largely on communicable diseases. With modernization, non-communicable diseases will soon become more common. For instance, it is estimated that the prevalence of diabetes in Africa will increase by 250% in the next 20 years. The burden of human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS), and its devastating toll on human suffering and health care budgets, has impeded the introduction of modern-day health care technology such as dialysis. This essential service is still non-existent. The health care challenges are daunting amidst grinding poverty, a lack of

Small child at a refugee camp in northern Uganda.

Children at a refugee camp in Uganda.

Patients wait in a community HIV clinic in Uganda.

A newborn brought to the HIV clinic for testing.

adequate health care resources, and the population ravaged by HIV/AIDS. But hope was not found wanting. The incidence and prevalence of HIV is coming under control. Well-trained local physicians are dedicated to the task of public health education. Plans are under way to expand existing programs and create new ones. There are exciting possibilities for collaboration and co-operation between Canadian institutions and the Tanzanian health care system. It is still possible to do pioneering work in KCMC, for example, introducing a dialysis and plasmapheresis program. Young children should not have to die of potentially reversible conditions, such as Guillain-Barré syndrome.

The student body for this course was composed of 30 physicians, of whom half were from Europe and North America and half from Tanzania and Uganda. It was a diverse group, but we soon gelled together. Extracurricular activities on weekends included safaris, trips to the beach, and visits to traditional markets. Networking opportunities were invaluable, and I made long-term friendships.

The second 3 weeks was spent at the Makerere University and Mulago Hospital:

- Week 4, student-selected study – leishmaniasis/trypanosomiasis, schistosomiasis/leprosy, malaria, migrant health (refugee camps), and HIV/AIDS
- Week 5, TB diagnostics/HIV
- Week 6, public health/HIV/Uganda Virus Research Institute

The 3 weeks of study in Uganda were intense. I was fortunate to go the Rakai Health Center where the first case of HIV/AIDS in Africa was described in 1982. This outstanding facility is run by a Canadian, Dr. Stephen Reynolds, representing both John Hopkins and the National Institutes of Health. This outpatient facility provides free medication and management for over 7,000 patients with HIV. It is also the epicentre of HIV research. The ground-breaking trial demonstrating a 62% reduction in HIV seroconversion in HIV-negative males with circumcision was conducted here. Circumcision of 40–50 males aged 14–49 is carried out daily. Field trips bring diagnostic tests and medications to remote villages: the dedication and enthusiasm of local staff are inspiring. It was time well spent.

The final 2 weeks (5 and 6) were spent doing clinical work both in outpatient and in-patient settings. We were also treated to talks by world authorities on HIV/AIDS. A new research study named the POP/ART Trial was introduced to us. Current World Health Organization guidelines for treatment with antiretroviral medications include all patients with a CD4 count of 350 or less. The POP/ART study soon to launch will randomize HIV-positive patients for treatment regardless of the CD4 count. This makes intuitive sense when one realizes that we are currently telling patients, "Yes, you are infected, but we are going to treat you sometime in the future." Other compelling data for early treatment are that a significant number of patients die after coming to medical attention, or while undergoing preliminary workup. In fact, mortality in the first month after diagnosis is 30 deaths per 100 patient years. Sixty-seven percent of deaths due to AIDS occur in the first 3 months, mainly due to late presentations and opportunistic infections. Early treatment, if proven to be useful, would have its own set of challenges in health care delivery in such a resource-poor setting. This study could have far-reaching implications.

As the dean of medicine of Makerere University, Dr. Harriet Mayanja-Kizza, aptly stated, "TB is grand dame of infectious disease; slow, subtle, at times quiescent and other times omnipresent." The combination of HIV/AIDS and TB is lethal. TB accounts for 21% of all AIDS deaths. The prevalence of unrecognized TB at the time of AIDS screening is about 19%. Exciting new studies have demonstrated that 6 months of isoniazid (INH) prophylaxis can afford protection from TB even in an endemic environment. A recent study from Botswana showed that a 36-month isoniazid prophylaxis regime could have beneficial effects.

> *A hunter in pursuit of an elephant does not stop to throw stones at birds.*
>
> – Old African saying

Our patient work consisted of attending HIV/AIDS clinics at the International Infectious Disease Institute and MJAP, in Kampala. Daily case loads averaged 350 HIV patients per clinic. The cases on the infectious diseases ward were 80% AIDS related. I observed more cases of meningitis (*Cryptococcus*, TB, bacterial and fungal) in the short weeks I was in Africa than I had done in my 25 years of practice. What struck me most was the resignation and acceptance of the inevitable by patients and their families. Despite the absolute horror and extreme anguish, patients and their families suffered silently and with a dignity that defied all levels of understanding. Nature has dealt a cruel blow to the young and the innocent, and the devastation is there for all to see. There are 1.2 million orphans in Uganda alone.

Other so-called neglected tropical diseases were also reviewed. Two cases of *Trypanosoma gambiense* and *T. rhodesiense* – both of which are found in Uganda and which cause distinct clinical syndromes – were presented. *T. rhodesiense* presents with an acute illness, sometimes fulminant, leading to multiple organ failure and early death. *T. gambiense* can be asymptomatic in the early phase. Later invasion of the nervous system leads to personality changes, focal signs, somnolence (sleeping sickness), coma, and death.

Malaria continues to be a major health problem, but its prevalence and incidence is decreasing. We saw two cases of cerebral malaria, both in adolescents.

Another startling statistic is the fact that more African children die of neonatal syphilis than of neonatal HIV/AIDS. The fact this could be prevented with a single course of penicillin is noteworthy.

The 6 weeks came and went very quickly. Despite all the hardship I had witnessed, I was left with a sense of hope and optimism. Hopefully, the peak of the epidemic of HIV/AIDS has passed. A renewed commitment by both the African and international medical communities could lead to a brighter future. Personally, the experience reawakened in me a new sense of urgency and commitment to the global community. This has encouraged me to start a couple of projects, still in the planning stage, of an exchange program for students from Canada and Uganda and Tanzania. In many ways, a small circle is complete, and it exceeded all of my expectations and has, perhaps, given me a new direction.

Acute Co-infection with Viral Hepatitis A and E

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It is uncommon to see patients with severely symptomatic hepatitis A virus (HAV; Figure 1) or hepatitis E virus (HEV; Figure 2) infection in North America, and co-infection is exceptionally rare.[1,2] Yet, HAV (a single-stranded ribonucleic acid [ssRNA] picornavirus) and HEV (an ssRNA calicivirus) are widely prevalent in regions such as Mexico, Central and South America, the Indian subcontinent, Africa, and the Middle East.[2] Developed nations have a low prevalence of HAV, which accounts for a low level of natural immunity. With increasing worldwide travel, the incidence of acute HAV-related hepatitis in Canada is rising. HEV is epidemiologically and clinically similar to HAV but is found almost exclusively in developing nations, where it is often the major cause of acute viral hepatitis.[2,3] Interestingly, these viruses tend to mimic cholestatic disease both clinically and biochemically on initial presentation, which may lead the clinician toward an erroneous diagnosis. Cases of co-infection often have atypical features and are more likely to lead to serious illness requiring hospitalization. Recognition of such presentations may prevent unnecessary invasive testing, such as liver biopsy, cholangiography, or endoscopic retrograde cholangiopancreatography (ERCP),[4] and ensure that close patient contacts receive post-exposure immunoprophylaxis.

Case Report

A 19-year-old woman presented to our community emergency department with a 4-day history of fatigue, anorexia, and fever. She sought medical attention after developing visible jaundice, vomiting, and right upper quadrant (RUQ) pain radiating into her back. Reviews of systems and past medical history were non-contributory. She took a few doses of acetaminophen for fever over the preceding 2 days. Her routine immunizations were up to date, and she denied recent travel or sick contacts, although her husband had recently returned from overseas travel and had been well.

On examination, her temperature was 37.5°C, heart rate 58 beats/min, respiratory rate 18/minute, and blood pressure 129/71. She was alert and non-toxic but jaundiced. Cardiovascular and respiratory examinations were normal. An abdominal examination revealed RUQ tenderness with a negative Murphy's sign.

Initial investigations revealed a slightly low random glucose level of 3.1 mmol/L; complete blood count (cbc), creatinine, electrolytes, amylase, and lipase levels were normal. Liver enzymes levels were elevated: aspartate transaminase (AST) 3,387 U/L (normal <45 U/L), alanine transaminase (ALT) 2,899 U/L (normal <45 U/L), alkaline phosphatase (ALP) 187 U/L (normal <70 U/L), and γ-glutamyltransferase (GGT) 260 U/L (normal <45 U/L). Lactate dehydrogenase was 3,025 U/L (normal <333 IU/L). Conjugated bilirubin was high at 49 μmol/L. International Normalized Ratio (INR) and partial thromboplastin time (PTT) were slightly abnormal at 1.3 and 17.2 seconds, respectively. Acetaminophen level was

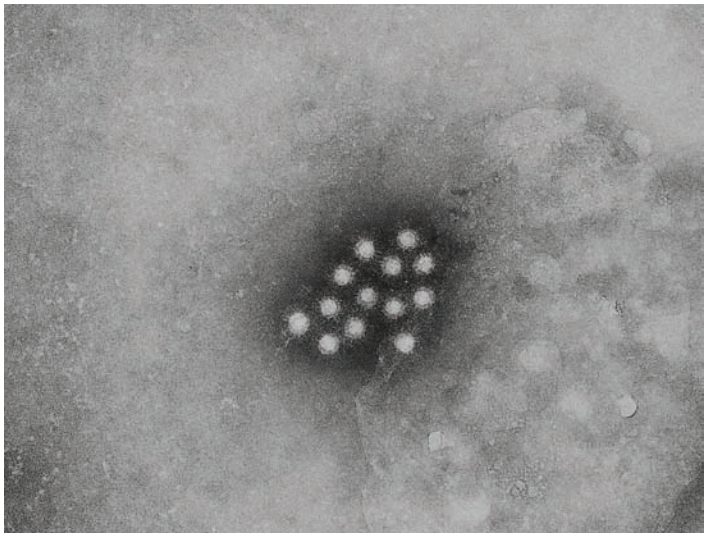

Figure 1. Electron micrograph of hepatitis A virus. (Courtesy of the University of South Carolina Department of Microbiology and Immunology)

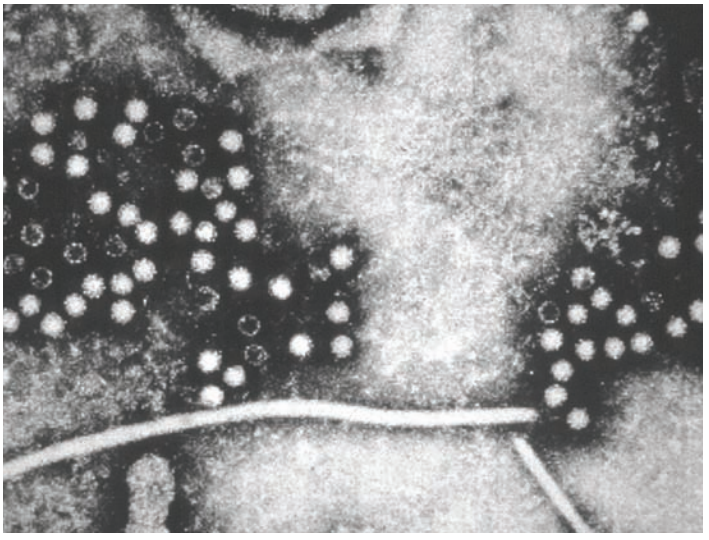

Figure 2. Electron micrograph of hepatitis E virus. (Courtesy of the University of South Carolina Department of Microbiology and Immunology)

low; results from the urinalysis and initial monospot and β human chorionic gonadotropin (β-hCG) tests were negative.

The abdominal ultrasound showed the gallbladder to be contracted, with bright echoic areas. A repeat fasting study did not show cholelithiasis. The patient was admitted for further testing, ongoing supportive therapy, and monitoring of her provisional diagnosis of acute hepatitis of unknown etiology. Results of a viral and autoimmune serology (including screening for HEV, done because her husband had been in an endemic area) and a haptoglobin level were normal. Results of a portal vein Doppler study were normal.

The patient improved clinically over the following 3 days. Upon discharge, her liver enzymes had decreased and total bilirubin had peaked, characteristic of viral hepatitis. Her blood cultures were negative. She was discharged with a diagnosis of acute hepatitis likely due to viral etiology, and she was referred to a gastroenterologist.

At follow-up, the autoimmune panel and direct antibody tests were negative. Interestingly, viral serology indicated a past infection with Epstein-Barr virus and recent co-infection with hepatitis A and E (positive immunoglobulin M [IgM] anti-HAV and anti-HEV). The patient had completely recovered by that time. She and her husband were educated on the natural history of HAV and HEV disease, and follow-up monitoring in 3–6 months time was arranged. Her husband was considered for HAV immunoprophylaxis with either post-exposure immune globulin or hepatitis A vaccine. Due to the specifics of this case and the fact that his HAV and HEV serology were negative, he received the hepatitis A vaccine.

Discussion

HAV and HEV replicate in the liver, are transported through bile, and are shed in stool, where they are transmitted through the fecal-oral route. These viruses rarely spread through blood or blood products, and transmission via infected food handlers is extremely rare. Children are the dominant reservoir and source of transmission; almost 70% of those 6 years of age and under remain asymptomatic. The viruses shed for 1–3 weeks prior to the onset of symptoms and for approximately 1 week after the patient develops jaundice. As transmission occurs mainly in the asymptomatic period and the average incubation period is 28 days (range 15–40 days), the source of infection usually remains unknown.[1,2,5]

HAV and HEV infections are self-limited and do not lead to chronic infection. Early on they can often mimic a cholestatic process.[3,4] Co-infection generally leads to more severe illness.[3] Illness typically lasts 4–6 weeks but occasionally may persist for months; 15% of patients may experience a renewed infection for up to 1 year after infection. Pregnant women infected with HEV have a 20% increased mortality rate.[5,6] During recent infection, anti-HAV and anti-HEV IgM antibodies appear in the serum, whereas antibodies of the IgG class predominate later on and confer lifelong immunity. Although the vast majority of those infected recover by 6 months, serious complications such as biliary obstruction, coagulopathy, encephalopathy, acute renal failure, prolonged debilitation from the length of disease, or fulminant hepatitis may occur.[5,7]

Prevention of HAV/HEV infection is key. In addition to minimizing exposure, the use of immune globulin preparation provides passive immunoprophylaxis (HAV only), and vaccination provides active immunoprophylaxis (HAV only). When travelling to areas of endemic HAV or HEV, patients need to also be counselled regarding food and water precautions.[1,5,8]

Minimizing exposure during the early phase of clinical HAV or HEV infection – especially when the contact is jaundiced – is critical. Family members should avoid close contact and thoroughly cleanse their hands after contact for 1–2 weeks post-jaundice (at which point, viral shedding has stopped). The patient should not share eating utensils or serve food to others.[1,5,9]

Passive and Post-Exposure Immunoprophylaxis

Passive immune globulin (IG) is derived from pooled blood containing high titres of anti-HAV and is around 80–85% effective in preventing severe clinical disease but does not provide lifelong immunity. IG was previously recommended only for post-exposure prophylaxis and was given up to 1–2 weeks after exposure. If given later during the incubation period, it will not prevent disease but may reduce the severity and duration of illness.[1,5,9,10] IG is not effective in people whose only exposure occurred more than 1 week after the patient's onset of jaundice – even for restaurant patrons and household and sexual contacts of an HAV-infected person.

It is not necessary to perform serology testing for HAV antibodies prior to administering IG, and this should not delay treatment. The dosage of IG is 0.02 mL/kg in the gluteus muscle. If the patient was vaccinated against HAV more than 1 month before exposure, there is no need to give IG. For household and daycare contacts, recent studies have shown that

Table 1. Persons Currently Considered to Have an Indication for HAV Vaccine or Immune Globulin

HAV Vaccine
Children at least 2 years of age living in an area with a high rate of infection (≥20 cases per 100,000 population)
Travellers at least 2 years of age to countries with high or intermediate rates of disease
Men who have sex with men
Users of illicit drugs
Persons who have chronic liver disease or who have received or will receive a liver transplant
Persons who use clotting-factor concentrates
Laboratory personnel who work with HAV or with non-human primates that are infected with HAV
For post-exposure prophylaxis in healthy individuals between 2 and 40 years of age with no history of HAV infection or chronic liver disease
Immune Globulin
Persons who will be travelling to countries with high or intermediate rates of disease within the next 2 weeks
Children younger than 2 years of age who will be travelling to countries with high rates of disease
For post-exposure prophylaxis, within 14 days after exposure, especially in children younger than 2 years of age, in adults older than 40 years of age, and in persons considered immunocompromised or who have chronic liver disease

HAV = hepatitis A virus.

despite HAV vaccination being slightly less effective than IG in post-exposure cases, if given 2 weeks after exposure, the vaccine still confers longer immunity even with a single dose.[1,9,10] Furthermore, the vaccine is easier to administer, is less expensive, is less painful, confers no risk of acquiring blood-borne infections, and does not interfere with childhood immunizations. Today, it is the preferred post-exposure prophylactic method in healthy individuals between 2 and 40 years of age with no history of HAV infection or chronic liver disease.[9] Thus, the use of IG should be continued for post-exposure prophylaxis (within the requisite time period) in children younger than 2 years of age, in adults older than 40 years of age, and in persons considered immunocompromised or who have chronic liver disease (Table 1).[10]

Active Immunoprophylaxis

The HAV vaccine is the most effective form of pre-exposure prophylaxis for those over the age of 2 years. Two vaccines, Havrix or Vaqta, are given at least 6 months apart (dosage intervals differ between the two manufacturers). The first dose alone provides 94–100% seroprotection within 1 month and lasts more than 20 years. A "booster" dosage is not recommended. If a patient is visiting an endemic area prior to receiving the second dose, then a dose of IG is given with the first dose. IG alone confers immunity for only 1–2 months and has been largely replaced by the HAV vaccine.[10]

Conclusion

The natural rate of HAV and HEV infection in Canada is extremely low. However, with widespread international travel and diasporas, we will continue to see an increase in the prevalence of diseases not endemic to Canada. Primary caregivers should be aware of common worldwide infectious causes of hepatitis (such as HAV or HEV) since they are the first to be exposed to patients presenting with symptomatic illness. In addition to our role as diagnostician, we also play a critical role in preventive care by counselling patients prior to travel and after they return through available post-exposure options. In this case, although the patient's husband was eventually vaccinated after his wife's diagnosis, he should have been vaccinated prior to travelling.

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Can We Do It? Yes, We Can! But Ought We?*

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The modern era of health science centres dominating state-of-the-art, "high-tech" treatments in an ever-increasing range of subspecialties has evolved over the past 30 years. In marked contrast to the recent past, the majority of medical students today opt against a career in family practice, in keeping with this new vision of multiple specialist treatment. This multi-treatment approach is simplistically equated to better patient care. The extraordinary success of tertiary care at curing individuals of life-threatening illness is seen across all age groups, from tiny premature infants to very elderly patients. New high-tech treatments abound; bypass machines and mechanical hearts for kids and adults, lifelong dialysis over decades, organ transplants, and joint replacement have all become part of the medical treatment arsenal. The success of such treatments causes them to become gradually integrated into what is offered as "standard care." The public and health care professionals' acceptance of this technology-driven treatment as uniformly beneficial leads to very high expectations, especially in a single-payer (government) health system such as exists in Canada.[1]

The short-term effectiveness of many high-tech interventions is well established with respect to improved early survival, but longer-term outcomes are less clearly beneficial.[2] And yet, it is the broader socioeconomic demographics of persons, rather than specific treatments, that truly reflect their lifelong health.

Life-saving treatment in intensive care units (ICUs) is improving at such a rate that even medical textbooks are out of date by the time they are published. But is this success of emergency life-saving treatment as clear-cut as it seems? Depending on what is valued in terms of *success* (let's avoid the hunt for definitions) and who answers the question, the answer is *yes, no,* or *maybe*.

Yes, because many individuals survive previously fatal illnesses due to extraordinary skill, technology, and care and go on to live long and happy lives. **No**, because we see enormous amounts of time, expertise, care, and resources expended on people who die, without any interval of improvement, within hours or days of the treatment. Sometimes the result of ICU treatment is weeks or months of bare survival, with little or no hope of eventual recovery. Is it possible to distinguish between critically ill patients who will benefit from treatment to the extent that they will be discharged home in relative health rather than to merely survive "at all costs" and die a complicated slow death soon afterwards?[3,4]

Maybe, because a variety of clinical and test-based scoring systems allow survival or death of groups of patients to be predicted with some degree of certainty. Across a range of illnesses and demographics, a high risk of death can be predicted.[3] However, the "exceptional case" undermines this data-based approach to prognostication. Are we willing to doom the occasional, exceptional potential survivor based on the overall statistics for the group? Are we willing to refuse to begin life-saving attempts or to discontinue treatment based on a futility argument?[5] Usually we are very reluctant to embark on this nihilist road, despite the widespread promotion of evidence-based medicine (EBM) as the basis of treatment. This so-called EBM is now firmly established in medical undergraduate and residency education.[6] The view of the expert clinician as one possessing a mysterious art born of learning and experience, who can prescribe treatment solely on that basis, has become obsolete. Despite this fact, we continue to see "miracle cases," where treatments are used against all the odds (and against the evidence too) and the patients survive. These patients reinforce the **Yes We Can and So We Must** school of medical treatment. Physicians tend to present these cases as triumphs over the EBM dogma. There is reluctance to discuss similar patients who die, other than to say death was predictable anyway.

How can we deal with this conflict between the welfare of the immediate patient and the requirement to use only treatments supported by best evidence? This conflict is more apparent than real in most cases. There is no ethical obligation to undertake a course of treatment in the absence of evidence to support benefit. Often a patient or surrogate will request, demand, or insist that "everything must be done" to save the patient's life. In clinical practice, *doing everything* can have different meanings depending on the conditions of care: the patient's condition, the patient's wishes and beliefs, the diagnosis, and the risks and benefits of life-saving treatment. *Everything* may involve extraordinary treatment including surgery, extracorporeal membrane oxygenation (ECMO), transplantation, etc., or it may mean high-quality compassionate end-of-life care.[5] In patients with clearly expressed or previously expressed wishes (verbal or written), the decision making about treatment must be guided by these wishes. But this is not unqualified. A wish to have "everything possible done" to save life does not include consideration of treatment with no biological basis or clinically demonstrable benefit. Terminal respiratory failure from metastatic cancer should not be treated by lung transplantation irrespective of what a patient or family requests.

Treatment judgments become difficult in situations where new evidence is beginning to accumulate but is not yet conclusive. In the ICU setting, this is frequently the case. A small number of patients may demonstrate

*The views expressed here are those of the author and do not necessarily reflect the views of the journal's editorial board, the publisher, the Stollery Children's Hospital, or the University of Alberta.

improved outcomes with a novel treatment, but widespread clinical experience or appropriate research (randomized or other trials) has not yet occurred. The academic medical response to this dilemma at the bedside is to either enrol the patient into an appropriate study or proceed with "innovative treatment." But what if there is no research study available? The clinicians may embark on innovative treatment if there is even a small probability of benefit, and if the patient or surrogate agrees. Unfortunately, physicians' ability to predict an outcome accurately in an individual patient with complex life-threatening illness is poor. This underscores the necessity to be extremely cautious whenever we depart significantly from the standard approach to treatment because of the potential to do great harm to the patient. Every "miracle cure" is always memorable as an "'against the odds survivor," even if it is not always beneficial to the patient in the long term.

The difficult question of whether we ought to do many of the things we do in the name of saving a life cannot be answered in general terms. The practice of spending time with patients and families in an ongoing conversation about clinical condition, goals of care, benefits and risks of treatment, and underlying values about what survival means is essential. This practice is difficult in the hurly-burly atmosphere of an ICU but can be undertaken well if the physician culture values such a process. Outside assistance from others (such as the family doctor) who may have known the patient well can assist in resolving conflict. Physician language and non-verbal cues when discussing complex issues in the ICU can mean the difference between harms to a patient and family or mutual agreement about what ought to be done.[7] Only by remembering the importance of **caring for and about each patient** as well as trying to cure patients will we approach an ethically acceptable answer.

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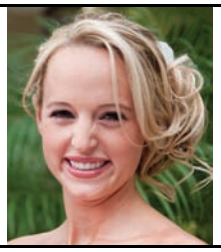
Defining and Optimizing Collaboration between Emergency Medicine and Internal Medicine Physicians

Douglas Wright MD, Claire Kenny-Scherber MD, Ameen Patel MD, Kulamakan Kulasegaram BSc, Jonathan Sherbino MD



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The increasing complexity of health care makes collaboration essential to achieve good patient care. Current evidence shows that collaboration has many benefits, including being a positive predictor of perceptions of effectiveness and individual well-being, improving behaviours and attitudes toward teamwork and the institution, and improving health care quality – such as reducing length of hospital stay, clinical error, and mortality.[1–5] Recognizing these benefits, the Royal College of Physicians and Surgeons of Canada (RCPSC) and other major international medical certification bodies have identified collaboration as a key skill in competent clinical care.[6] RCPSC has defined physician collaboration as effectively working within a health care team to achieve optimal patient care. In order to fulfill this competency, physicians must be able to participate effectively and appropriately in an inter-professional health care team to prevent, negotiate, and resolve inter-professional conflict. Although identified by numerous national certification bodies, the process to achieve effective collaboration is unclear.[7,8] The interaction between emergency medicine (EM) and internal medicine (IM) requires extensive collaboration, and while a continuity of care occurs countless times daily between these two specialties, there is no evidence to inform this process. A comprehensive search of the literature revealed no studies addressing effective collaboration between EM and IM. The purpose of this study was to perform a needs assessment to optimize collaboration between EM and IM physicians.

Methods

This study was a prospective, qualitative needs assessment. Approval was granted by the McMaster University Faculty of Health Sciences Research Ethics Board.

All EM residents and attending faculty physicians from the four teaching hospitals associated with McMaster University were invited to participate. All IM residents and attending faculty physicians involved with the Clinical Teaching Units of the teaching hospitals associated with McMaster University were invited to participate. Between June and October 2009, participants were asked to complete an anonymous survey eliciting common attitudes and barriers to collaboration between the services, using a modified Dillman methodology (survey available upon request).

Demographic data were analyzed using descriptive statistics. Likert data were analyzed using an analysis of variance (ANOVA) with a significance set at $p < .005$ and a Bonferroni correction t test applied to any significant results. All qualitative, narrative responses were analyzed using formal grounded theory methods. Grounded theory is an inductive analysis of a qualitative database without a priori generation of hypotheses. Each data point is compared with every other, informing the final results. Surveys from each group were independently reviewed by the two investigators to generate a code of general categories and specific qualifiers. The independent codes were then merged by consensus into a common code. All surveys were independently re-coded by the two investigators using the common code. Inter-rater agreement was high ($\kappa = 0.83$). Disagreements in coding were resolved by consensus to produce a uniform inventory of survey response categories and qualifiers. The results were analyzed using the modified χ^2 statistic, the Fisher exact test. All analyses were performed using SPSS Version 16.

Results

The overall response rate was 56.4%. All groups described collaboration as involving *teamwork, working toward a common goal,* and *mutual respect.*

On average, all groups believed the collaborative relationship was slightly more than satisfactory, with the faculty being more satisfied than the residents of both specialties ($p = .033$). The EM staff believed the relationship was significantly better than the EM residents perceived the relationship ($p = .004$). All groups agreed that a good working relationship is important to very important ($p = .025$).

The staff physicians of both services reported making the least amount of negative comments, slightly more than once monthly. IM residents reported making negative comments most frequently, approximately once weekly. This was significantly more than the IM staff physicians ($p \leq .001$). All groups were perceived by their peers as making more negative comments than were self-reported. When negative comments were made, all groups either said nothing or contributed to negative comments. Respondents did not report defending the opposite clinical service when criticized by peers. Positive comments were made on a weekly basis in all groups, although less often as perceived by their peers.

The IM service identified *poor initial workup, poor initial treatment, lack of involvement of other services,* and *untimely referrals* as major problems. The EM service identified *poor consultation response* as the major negative factor, with *refusal of consultations, lack of medical resident supervision by IM staff,* and an *overloaded IM service* (slow to respond) being the main problems. Both services believed that disrespect is a factor, but IM service felt it was for the time needed to complete a consultation, while the EM service felt their expertise was not respected.

The most inappropriate referrals reported by the IM service were *social admissions, incompletely worked-up or treated patients*, and *lack of use of other services and subspecialties.* Low risk or atypical chest pain was the most frequent inappropriately referred diagnosis (46–61%) according to IM. There was no statistically significant difference between faculty and resident responses ($p = .291$).

According to the EM service, r*eferrals for social concerns, patients refused by a subspecialty service*, and *surgical diagnoses not receiving surgical intervention* were the most difficult referrals to get accepted by IM. Of the specific diagnoses,

undifferentiated problems (20–47%) and low risk/atypical chest pain (20–33%) were the most difficult to refer.

All groups identified *working together* (e.g., mutual discussion concerning patient management, help with more emergent or complicated aspects of patient care), *interpersonal interaction*, and *professional respect* as the major positive elements of the IM-EM relationship. Both services valued open communication, with emphasis placed on good handover for the IM service and receiving dictated notes and staff-to-staff communication for the EM staff. Both EM and IM identify a need for *improved collegiality*, mainly through an interdisciplinary task force and structured feedback mechanisms to address the collaborative relationship. All groups also identified the need for *improved communication* to optimize the relationship, specifically more detailed handover, and a feedback system for individual referrals. Lastly, suggestions for *educational improvements* included rotations in both specialties and joint academic activities such as rounds and conferences.

IM residents suggested the timing of referrals could be improved with the prevention of multiple simultaneous referrals, not handing over a patient at the end of an EM shift unless appropriate and worked up, and holding non-urgent referrals until the morning. The IM faculty believed the referrals could be improved by the completion an initial workup prior to consultation. The EM service believed that increased IM faculty presence and supervision could improve collaboration.

Discussion

Collaboration between EM and IM is essential to facilitate optimal patient care. Although all groups agree that effective collaboration is very important, our study suggests that the quality of the current relationship between services is only satisfactory. The components of collaboration identified are consistent with the definitions stated by major authorities of medical education.[6] The main attributes of a "good" EM referral and a "good" IM consultation have been identified, as have problematic referrals, potential solutions, and current attitudes. The identification of these factors can allow each service to accommodate the other; however, these factors need to be viewed within the context of their working environment.

Contributing tensions between EM and IM include an increasingly complex patient population, limited in-patient services of other specialties calling for expanded roles of EM and IM, and the Ontario provincial government's mandate to lower emergency department wait times. With the aging population and the demand for long-term care facilities exceeding the supply, social referrals for temporary hospitalization of patients awaiting placement has become a problematic issue. Furthermore, constrained resources have led to medical and surgical subspecialties limiting in-patient care and focusing on short hospitalization and the quick turnover of in-patients. Consequently, as reported in this study and another that surveyed EM physicians, institutional referral protocols are often unclear and IM receive excess referrals, often as a default service, with chest pain being a common diagnosis.[9] Similarly in the outpatient referral process, the size of the referring physician's patient list and the availability of resources are associated with the number of referrals to the IM service.[10] The combination of increasing patient responsibilities and an IM teaching service emphasis on thorough pre-admission investigations and treatment often impede the EM service focus on rapid assessment and disposition. This conflict may explain why EM physicians feel that IM consultants do not respect their expertise and resist accepting referrals.[9]

Overall, few interventions to alter the referral process have been studied rigorously.[11] Education about barriers and pressures unique to each specialty has been recommended as a possible mechanism to improve inter-professional relationships.[9,12] Currently, McMaster University teaching hospitals are working on interventions to optimize this relationship, such as creation of a general IM rapid assessment clinic.

Limitations

The survey response rate was 56.4%; this rate is typical for this type of survey. Also, the results may represent unique relationship characteristics of this institution and self-selected groups that returned the survey. Lastly, inherent in this research is a concern of social desirability bias. This may explain the more positive self-assessments than assessments described by peer reporting.

Conclusion

Competent physicians collaborate. The complexity of patient care and the movement toward team-based care emphasize this requirement. This needs assessment is the first to objectively report the elements that comprise a collaborative relationship between EM and IM. These pilot data may facilitate further research to more generally define clinical collaboration between specialties and potential interventions for improvement.

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*Full references available by contacting the authors.

Removal of a Guidewire Trapped in Left Main Coronary Artery

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A 60-year-old dyslipidemic, hypertensive lady with a family history of premature arteriosclerosis underwent double coronary artery bypass grafting of the left main and circumflex arteries. The operation was complicated by extensive anterior myocardial infarction, followed by cardiogenic shock. Coronary angiography revealed occlusion of the bypass grafts. When stenting of the left main artery was attempted, an angioplasty wire became trapped in the stent (Figure 1). The patient required support from an intra-aortic balloon pump and was considered for possible heart transplantation. Echocardiography showed an ejection fraction of 35%, pulmonary arterial pressure of 34 mm Hg, a left ventricular diastolic dimension of 39 mm, left atrial size of 39 mm, trivial mitral regurgitation, and moderate tricuspid regurgitation. Several attempts were made to retrieve the guidewire, using various snares to entrap the wire. These proved unsuccessful as the wire was firmly attached to the left main coronary artery, and additional attempts were finally abandoned for fear of further complications.

With aggressive medical therapy, she improved markedly over the following weeks. Within a month, her echocardiogram showed an ejection fraction of 50% and moderate mitral regurgitation. Two weeks later, she was discharged home. She was started on anticoagulation with warfarin, clopidogrel (Plavix), and acetylsalicylic acid. A year later a coronary angiogram showed a 90% occlusion of the left main stent, an occluded circumflex artery, and a normal right coronary artery. The left internal mammary artery graft was occluded, and the saphenous vein graft to the first diagonal showed a 99% distal stenosis. There was severe left ventricular dysfunction with an ejection fraction of 20% and severe mitral regurgitation. She was referred for consideration of coronary artery bypass grafting and removal of the foreign body. A few months later, she underwent single coronary artery bypass grafting, and the guidewire was removed by aortotomy.

Retained broken guidewires have been previously described in the literature. Fractured fragments may be removed either percutaneously or by surgical intervention. As in our case, aortotomy is the procedure most commonly used to retrieve foreign bodies.[1–3] As percutaneous coronary procedures become more commonplace, mechanical complications are likely to become more frequent. When immediate intervention is not possible or successful, and if the patient remains stable, we advise close monitoring and long-term anticoagulation until a safe removal of the foreign material can be performed.

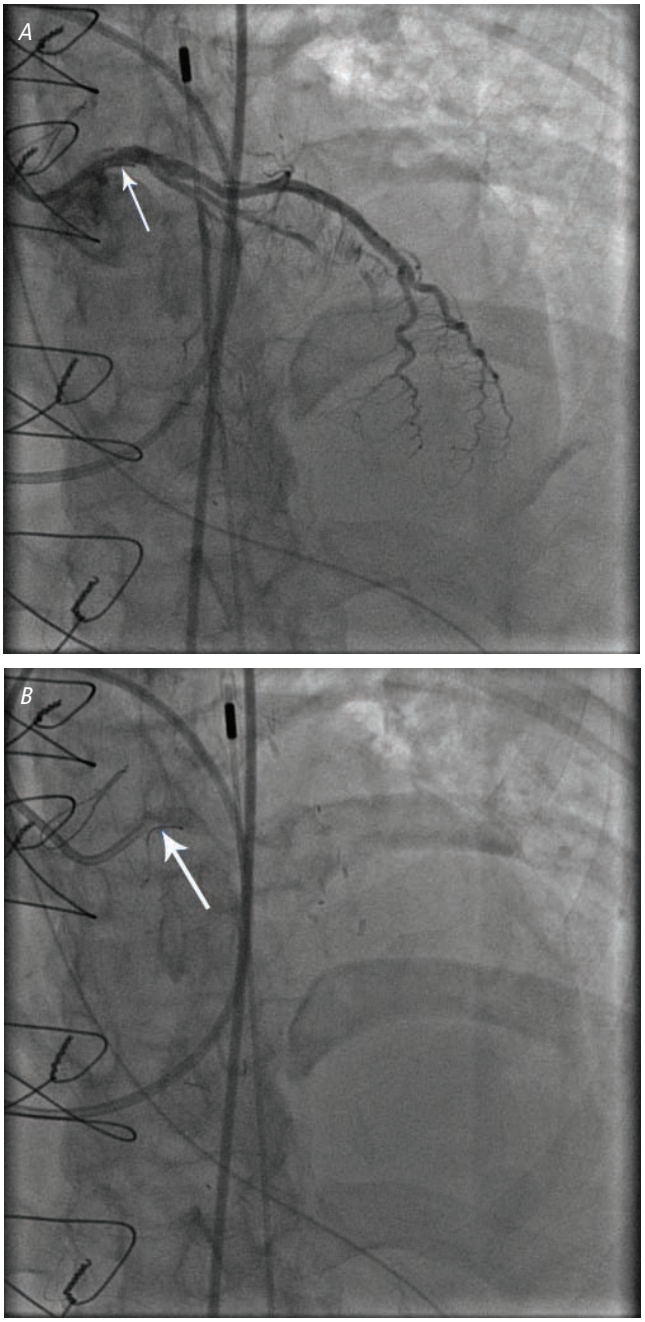

Figure 1. Angioplasty wire trapped in a stent *(arrows)*: *A*, with contrast; *B*, without contrast.

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