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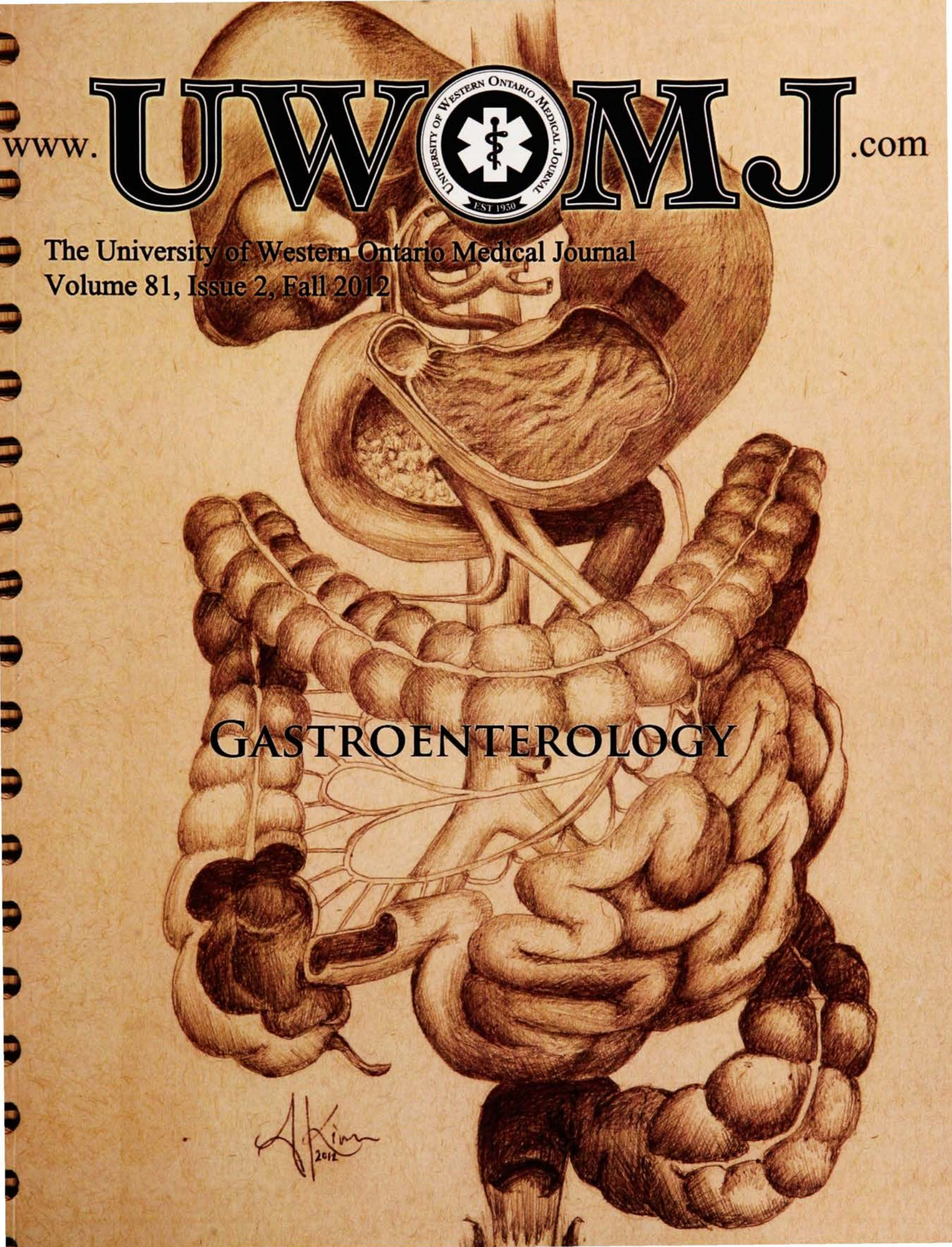

GASTROENTEROLOGY

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GASTROENTEROLOGY ARTICLES

The University of Western Ontario Medical Journal
EDITORIAL TEAM

COVER ART: ASHLEY KIM

FRONT: The gastrointestinal system illustrates the elegant coordination and co-dependence of several vital structures that work together to aid in digestion (Media: Pen and Ink, October 2012).

The wonders of the gastrointestinal tract

Melissa J. MacPherson, PhD (Meds 2014)

The human gastrointestinal (GI) tract is an impressive 9 m long,[1] extending from gums to bum. Its surface area is an astounding 4500 m^2 all packed neatly into the thoracic and abdominal cavities of the human body![1] It comprises an incredibly complex set of organs including the esophagus, stomach, liver, gall bladder, pancreas, intestines, and colon. It is the site of digestion, nutrient absorption, waste excretion and the primary site of metabolism. Without the GI tract, our bodies couldn't function. It's no wonder that the field of gastroenterology is enormous. Unfortunately, our current UWOMJ issue provides only a small snapshot of its breadth. One of its recurring themes is the use of technology in the treatment and diagnosis of disease, which several of our departments have chosen to highlight. As you read these pages, you will learn about radiofrequency ablation in the treatment of liver tumours and colonoscopy in the screening and diagnosis of colorectal cancers.

Other authors have chosen to highlight specific diseases and their management. You will read about a curious presentation of adult intussusception and the use of acupuncture in the management of irritable bowel syndrome. Michael Verbora discusses the progression of a rare case of gastric heterotopia in the rectum. Arthur Ling has written an interesting article outlining the use of fecal microbiota transplantation and metagenomics in gastroenterology.

A number of other articles are also not to be missed. Niran Argintaru and Jonathan Fairbairn from our department of ethics and law have written a thought provoking piece regarding the ethical and legal complexities of liver organ donation. The department of health promotion discusses the importance of nutritional knowledge and counseling among medical professionals. The history of medicine department has written an intringuing article on the discovery of the causative agent of duodenal ulcers and the reluctance of the medical profession to embrace the hypothesis of an infectious cause.

In every issue of the UWOMJ we interview a local physician or scientist. In this edition we had the privilege of interviewing Dr. John Howard, a pediatric gastroenterologist who also teaches us during our GI curriculum. The profiles article detailing his career is not to be missed.

I hope that you enjoy this issue of the UWOMJ and learn a bit more about the GI system as we take an adventure together down the gastrointestinal tract!

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Gastric heterotopia in the rectum: progression of disease

Michael Verbora (Meds 2013)

Faculty Reviewer: Dr. John Howard, MD, FRCP (Department of Medicine and Pediatrics)

Gastric heterotopia is a condition whereby gastric mucosa is discovered outside of its origin. Gastric heterotopia within the rectum is rather rare. To date less than 50 cases have been reported.[1] To our knowledge, no cases have been reported in which there is a review of progression, or elimination, of disease over time. We describe a case of a patient from age 5 to 24 and report on symptoms and effectiveness of several treatments for heterotopic gastric mucosa in the rectum.

A 5 year-old boy presented to the Emergency Department with rectal bleeding. He mentions a three-day history of constipation. He was treated with a fleet enema and prescribed mineral oil and told to return if further bleeding returned. A barium enema was negative at this time. He eventually is referred to gastroenterology for further investigation after complaining of rectal bleeding four years after his initial presentation.

On history, the 9-year-old boy mentions continued painless, bright red bleeding per rectum (BRBPR) several times per month. Despite the bleeding, he is currently plotting along the 60th percentile for height and weight. Past medical history was significant for asthma and family history revealed rectal polyps in his father. A previous trial of metronidazole did not improve his symptoms. Both a review of systems and physical exam were unremarkable. A flexible sigmoidoscopy was performed in clinic that day. A large multi-lobular sessile polyp was discovered just inside the rectum and multiple biopsies were taken. Pathology from the rectal lesion showed colonic mucosa with specialized gastric type mucosa. Glands were straight and lined by parietal and chief cells (gastric mucosa markers) with no evidence of erosion or ulceration. *Helicobacter pylori*, a bacteria that causes peptic ulcer disease, was not present.

One month later, the boy was scheduled for colonoscopic fulguration of the rectal heterotopia. An ovoid lesion approximately 5cm in length and 3cm in width with gastric rugae was removed using electocautery. Once again, pathology confirmed gastric type mucosa without *H. pylori*. He was prescribed 20mg omeprazole, which resolved bleeding.

At age 17, he complains of similar episodes of BRBPR. He mentions that episodes of constipation coincide with his episodes of rectal bleeding. A second 3x4cm lesion with gastric rugae was removed via argon plasma coagulation.

He presents again at age 24 with several episodes of rectal bleeding. He mentions that an over the counter weight loss supplement that he began taking has improved the bleeding and increased his bowel movements to 3-4 times per day. On sigmoidoscopy nothing is visualized. He was scheduled for repeat colonoscopy.

DISCUSSION

In pediatric studies, the ratio prevalence of gastric heterotopia in the rectum is twice that for males with a mean age of 5 years old. Heterotopic gastric mucosa has been discovered in all areas of the gastrointestinal tract.[2] It is most commonly found within the esophagus. The exact mechanism for the development of heterotopic gastric mucosa has yet to be determined. A number of theories exist including, the abnormal regenerative process following destruction of normal mucosa or the competing theory that an error of differentiation of pluripotent endoderm cells during embryonic development leads to heterotopic gastric mucosa.[3]

Gastric heterotopia typically presents with painless bleeding; however, cases have been reported with more serious complications such as major gastrointestinal bleeding, bowel perforation, megacolon, intussusception, perianal fistula and rectovesical fistula.[3] *H. pylori* has also been discovered as an active infection in gastric heterotopia in a case of a 5 year-old boy.[4] Infection can lead to ulceration and severe bleeding.

The definitive diagnosis occurs via analysis of the biopsied tissue. Typically the pathology is that of fundic-type mucosa but, case reports have reported lesions containing gastric body, pyloric, antral, chief, salivary and parietal cells within the tissue sample.[5]

Treatment at this point in time for gastric heterotopia lacks consistency and evidence. Some argue that the gastric mucosa has the potential to become malignant, as has been discovered for heterotopic gastric mucosa in the esophagus, and thus should be excised.[6] To date there are no reports of a malignant gastric heterotopia within the rectum. Successful treatments to suppress the bleeding include proton pump inhibitors or H2 receptor blocker. Co-infection with *Helicobacter pylori* may warrant triple therapy with antibiotics and proton pump inhibitors. Endoscopic ablation has the advantage of removing the tissue permanently.

CONCLUSION

Gastric heterotopia is a rare cause of gastrointestinal bleeding from the lower tract in children. Endoscopic evaluation with biopsy is fundamental to diagnosis. The type of tissue present in heterotopic gastric mucosa can vary, as well as the presence of *H. Pylori* infection, but to date no malignant lesions have been discovered in the rectum. Treatment varies from proton pump inhibitors and monitoring or removal of the lesion via endoscopy.

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Fight against obesity – is bariatric surgery the answer?

Chanseok (Chris) Rhee (Meds 2013), Yuding Wang (Meds 2013)

Faculty Reviewer: Dr. Vladislav Khokhotva, MD, BSc, FRCSC (Department of Surgery, Windsor Regional Hospital)

Obesity is a medical state in which an individual has excessive body fat that causes an increased risk of metabolic derangement. It is conventionally defined as a body mass index (BMI) of 30 kg/m^2 or more.[1] Although it may not be considered as a disease by itself, it has been long associated with many diseases that are often detrimental to health, such as coronary artery disease, stroke, diabetes, osteoarthritis, obstructive sleep apnea and more. Consequently, obesity leads to more functional limitations, decreased health-related quality of life, and increased utilization of the healthcare system.[2] Currently more than half of Canadians are reported as overweight (BMI of 25 kg/m^2 or higher) or obese,[3] with nearly a quarter of the population being obese.[4] A more concerning feature is that this proportion has doubled between 1980s and today, and it is still increasing.[4] A systemic review of articles published between 1990 and 2009 showed that obesity accounts for approximately 0.7% to 2.8% of a country's total healthcare expenditure[5]. In addition, the average medical costs spent on an obese individual were approximately 30% greater than the costs on an individual with normal weight.[5] In Canada where healthcare costs are universally covered, the total healthcare costs for being overweight and obese were estimated to be $6.0 billion, which is 4.1% of the total health expenditure in 2006.[6] Although direct comparisons between countries are often difficult due to different methodologies implemented in measuring associated medical costs, higher weight-associated healthcare expenditures in Canada can be linked to a higher rate of overweight and obese individuals. In Ontario, an obese individual lays an additional burden of about $180 to the healthcare system over one year compared to a normal-weight individual adjusted for other health-related factors such as age, gender, socioeconomic status, and physical activity status.[7] In addition, obesity is also associated with other factors that cannot be easily quantified in monetary value but nevertheless impact one's life, such as quality of life and level of education.[7]

Considering the socioeconomic downfalls of obesity, the benefits of weight loss are apparent both for individuals and society. As obesity is closely associated with lifestyle factors such as poor dietary choices and sedentary lifestyle, the current management of obesity focuses mainly on lifestyle intervention.[8] Weight loss interventions also often provide social and psychological supports for improved effectiveness.[9] The Counterweight Programme, a weight loss programme in primary care in the UK which provides dietary and physical exercise schemes and also follow-ups, is estimated to cost approximately $370 per individual per year.[10] This cost does not include many extra costs imposed on individuals, such as additional food costs and the costs of fitness club memberships.[10] A study by Roux and colleagues included medical, non-medical, and time per patient costs for weight loss programmes, and estimated an individual cost of US$3,040 per year.[11] Although lifestyle interventions may still be cost-effective, they require long-term commitment in both time and energy, with often less-than-expected results.[9] Several factors associated with attrition include decreased body image, decreased mental health, lower social support, lower self-efficacy, patient's higher weight loss expectation, and cost.[12] As a result, lifestyle modification is often combined with pharmacotherapy, such as orlistat, sibutramine and rimonabant. Although effective in weight reduction, the cost of intervention with anti-obesity medications per quality-adjusted life-year (QALY) was estimated to be US$20,000.[13] In addition, adverse effects of medication and high rates of weight regain limit the use of pharmacotherapy.[13]

Currently, the most effective treatment of obesity is bariatric surgery which results in 30% sustained weight loss, compared to 5-10% weight loss with behavioural and pharmacological intervention.[14] Three commonly-performed procedures are laparoscopic adjustable gastric banding (LAGB), laparoscopic sleeve gastrectomy (LSG), and Roux-en-Y gastric bypass (RYGB).[15] LAGB is a restrictive procedure where a hollow, flexible silicone band is placed distal to the gastroesophageal junction, reducing the stomach capacity.[16] This causes early satiety and decreased food intake, consequently resulting in weight reduction.[16] LSG involves resection of a large portion of stomach, thus also reducing the stomach capacity.[15] This is often a first of a two-stage procedure, where rerouting of the small intestine is performed to reduce calorie absorption, especially the absorption of fat.[16] RYGB is the most common procedure performed in North America, comprising 51% of the total bariatric procedures.[15] It is a combination of both restrictive and malabsorptive procedures and involves creating a small pouch of stomach and rerouting the small intestine. The mid-portion of the jejunum is dissected and the distal portion is anastomosed with the small gastric pouch. The proximal small bowel, connected to the excluded portion of the stomach, forms a biliopancreatic limb and is anastomosed with the distal jejunum.[16] A malabsorptive state from bariatric surgery results in favourable metabolic effects superior to those achieved by lifestyle and pharmacological intervention.[17] Its more substantial and long-lasting weight loss effects place bariatric surgery as an attractive method of weight reduction.[17]

In Ontario bariatric surgery is currently indicated for patients with BMI of 40 kg/m^2 who are refractory to medical management, including lifestyle modifications, or individuals with BMI greater or equal to 35kg/m^2 with a major obesity-related comorbidity such as hypertension, diabetes, or obstructive sleep apnea.[18] Currently, the only operative bariatric technique being insured in Ontario is the RYGB, although multiple private clinics offer the LABG technique. Although randomized control trials (RCT) comparing the efficacy of bariatric surgery with standard medical management are few, they do point to a significant benefit of surgical management to decrease morbidity and mortality.[19, 20] The landmark Swedish Obese Subjects (SOS) study (a large prospective multicenter matched cohort study) showed a significant mortality benefit for

patients who received bariatric surgery compared to non-surgical conventional treatment.[21] Subsequent retrospective and prospective studies have also shown similar results.[22] RCTs between RYGB and LABG have shown the RYGB procedure to have increased weight loss, improved resolution of comorbidities, lower reoperation rates and better patient satisfaction. However, LABG offers faster recovery time and a slightly lower rate of perioperative mortality and operative morbidity.[23]

The economic benefit from a payor's perspective show that the long term (10 years to lifetime) cost-effectiveness of surgery compared to non-surgery has been estimated to be US$1000-40,000 per QALY when using an incremental cost-utility ratio.[24] A recent systemic review and analysis for the Canadian Agency for Drugs and Technologies in Health (CADTH) estimated the cost of bariatric surgery from a health care payor's perspective to be CND$8,000-10,000 per QALY over the lifetime horizon in Canada when using an incremental cost-utility ratio.[25] This estimate represents clear cost benefit for surgery compared to medical treatment alone. Furthermore, analysis within subgroups such as obese type 2 diabetics incurs even greater health and economic benefits. Recent meta-analysis evaluating bariatric surgery in patients with diabetes shows an incremental cost-utility ratio of US$7,000-10,000 per QALY and appears to provide a clear health net benefits and cost savings over non-surgical management.[26] Moreover, from a payor's perspective, bariatric surgery represents an upfront investment with subsequent savings spread throughout the patient's lifetime in terms of both direct and indirect costs. Cost analysis between common surgical techniques are lacking and at this time no clear cost benefit can be assigned to RYGB versus LABG, although it is known that LABG when compared to RYGB offers shorter hospital stay and faster recovery time (measured as time to return to work).[23]

Currently, Ontario performs approximately 2,000 bariatric procedures per year funded through the OHIP.[27] There are estimated 300,000 Ontario residents that are believed to be in need of the procedure.[27] Even with recent funding to increase the number of bariatric procedures provided by OHIP, there is still a significant wait time for the procedure. As clinicians, prevention through life-style modifications before obesity sets in may yet offer the best results. Nevertheless, bariatric surgery has clear benefits over conservative and pharmacological treatments, and increased funding for bariatric surgery in addition to continued lifestyle modifications may warrant maximum long-term cost savings to OHIP.

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Fecal microbiota transplantation and metagenomic medicine

Arthur Ling (Meds 2015)

Faculty Reviewer: Dr. David Colby, MSc, MD, FRCPC (Departments of Microbiology and Immunology, Medicine and School of Dentistry)

INTRODUCTION

Have you ever had a gut feeling that you were not alone? Before you get up to lock the doors, consider that our gastrointestinal tract, in particular the distal colon, is home to trillions of bacteria and other microorganisms collectively referred to as the microbiome. Fortunately, most of the microbiota are not harmful, but instead provide physiological functions such as digestion and immune system development. Importantly, the intestinal microbiome acts as a front line defense against potential pathogens entering our gut. An important clinical example that highlights this is an infection by a bacterium called *Clostridium difficile*, which usually causes a diarrheal/colitis syndrome, but in some cases may progress into a life-threatening pseudomembranous colitis or a colonic distension called toxic megacolon. Although healthy individuals are resistant to the ingested spores, cases of *C. difficile* infection (CDI) are on the rise because of antibiotic treatments that disrupt the protective microbiota.[1] To compound this problem, there are reports of increased incidence and mortality rates, metronidazole resistance, and the emergence of hypervirulent strains (*e.g.* BI/NAP1/PCR 027).[1,2] This 'epidemic' has forced us to critically evaluate how we manage CDI cases, especially taking into consideration the inherent dilemma that antibiotic therapy itself is causing this infection.

What can be done? The standard treatment includes discontinuation of the inciting antibiotics and adding other antibiotics (metronidazole, vancomycin). Other additional therapies now include oral bacteriotherapy/probiotics, toxin binders, vaccination, and even performing surgical bowel resection.[2–4] However, despite additional medical therapy, there are some patients (15 - 35%) that continue to have chronic recurring disease or a severe presentation.[5] For these patients, there has been a last ditch protocol that focuses on replacing the disrupted microbiome through a procedure called fecal microbiota transplantation (FMT). Although this procedure has been around for over 50 years, it is not a mainstream practice even though it has been found to provide safe, relatively inexpensive, and rapid relief with potential long term protection. This is likely due to disinterest from patients (the 'yuck' factor), physicians ('natural' approaches without good evidence tend to be presumptively dismissed), and researchers. In this article, I will provide a fresh perspective of FMT and discuss how it is becoming an increasingly attractive option in light of our improved understanding of the colonic microbiome.

MI CACA ES SU CACA

FMT works on the principle of taking the bacteria in a healthy donor's stools and introducing them into the patient's colon in order to restore a 'healthy' intestinal microbiota population. Historically, FMT has been studied and performed in veterinary medicine to treat various disorders in farm animals (transfaunation).[2] The first instance of FMT in humans was in 1958, when a team of physicians in Colorado successfully treated four patients with pseudomembranous colitis.[6] At the time, three of these patients had severe life threatening post-operative colitis that was unresponsive to conventional treatments. In a final attempt, the physicians pioneered the FMT procedure and the patients miraculously recovered and were discharged after several days. It would be much later in 1978 when *C. difficile* was identified to be a cause of antibiotic-associated diarrhea/colitis, which was then followed by the first report of a successful FMT in a CDI case in 1981.[6,7] While FMT was originally performed by a crude colonic retention enema of homogenized stool samples obtained from closely related or intimate donors, the procedure has been refined through the 1990s. Nowadays, most studies use standardized donor screening and stool collection, cryoprotectant processing and freezer storage, and instillation with a nasogastric/nasoduodenal tube or guided infusion with a colonoscope or upper tract endoscope.[2,8,9] However, the basic engraftment principle applied in 1958 is so simple that there are even published 'do-it-yourself' guidelines that rely on easily acquired items (*e.g.* kitchen blender, enema bag) and a healthy friend.[10]

Today, the main indication for FMT is severe refractory CDI or chronic disease with a history of recurrence and a failure of multiple antibiotic regimens. While the evidence is limited to case series and reports of chronic CDI, recent systematic reviews have found an astounding 89-92% clinical resolution of the diarrheal syndrome in over 300 cases reported in the literature.[2,3,11] These numbers are encouraging, but only recently has there been interest in conducting a randomized controlled trial (FECAL trial, 2008 - ongoing).[12]

One possible objection to FMT is the concern for safety as there is the possibility for transmitting infections during the procedure. This is a valid concern for any attempt to administer foreign microbiota as evidenced in trials of *Saccharomyces boulardii* probiotic treatment in CDI patients, which had rare reports of sepsis and fungemia.[13] Surprisingly, in a systematic review of 376 cases of FMT in cases of CDI and other indications, there has not been a report of a major adverse event including transmitted infection.[3] Still, the possibility has been taken into consideration by developing protocols such as extensive donor screening in order to prevent transmission of enteric pathogens and provide reconstitution of 'healthy' microbiota.[8,14]

FMT TREATMENT FOR OTHER DISEASES

Ulcerative colitis (UC) and Crohn's disease are both types of idiopathic inflammatory bowel disease (IBD) that are possible candidates for FMT treatment because of the possible pathophysiologic role of the colonic bacteria. The first report of FMT in UC treatment was 1989 by Bennet and Brinkmann, in which Bennet, who suffered from persistent UC, successfully treated himself.[15] Another report near the same time used FMT to treat a variety of non-CDI associated colitis syndromes with some

degree of success.[16] In 2003, there was a landmark study on treating UC, which documented a case series of six patients with chronic UC who underwent FMT.[17] All of the patients in the study went into remission and at 1-13 years of follow-up, none of the patients had any evidence of active disease, indicating that the FMT treatments were associated with a lengthy remission period or possible cure. While the evidence is far from definitive, it does support the idea that FMT can be used to treat other diseases that involve the colonic microbiota. These diseases might include chronic constipation, obesity, metabolic syndrome/insulin insensitivity, irritable bowel syndrome, allergic disease, and potentially indirect neuropsychiatric alterations.[16-21]

PERSONALIZED METAGENOMIC MEDICINE

A lack of rigorous testing and abundance of biased anecdotal reports has made it difficult for FMT to become widely accepted. However, this may begin to change because of insights drawn from recent microbiome research. To start off, consider the question: what makes each person unique? Of course, many would say that it is a combination of genetic, epigenetic, and environmental factors, but traditionally few would consider the microbiome as a significant influence. Yet, while genetic sequence variations between individuals comprise a miniscule fraction of our genome, the differences in microbiota populations have been estimated to be as high as 50%.[21] Moreover, the microbiome is easily amenable to change and is also believed to demonstrate dynamic alterations with normal ageing, geography, and environmental changes.[22-24]

Within this spectrum of variation within the population, there is the possibility that the microbiome may contribute to disease susceptibility. Although many studies have experimentally implicated a role of the colonic microbiome in various diseases, there is a need for population based studies to establish an association between different microbiota populations and specific diseases. To accomplish this, we can take advantage of next generation sequencing (NGS) technologies. Already this year, there are several sequencing platforms (*e.g.* Nanopore, MiSeq, Ion PGM-proton) touted to be able to provide extremely rapid and cost-effective genetic sequencing capability. Using NGS, we can realistically envision mapping out the human metagenome, which comprises all of the microorganism genomes within the microbiome. Currently, there are various initiatives supported by the International Human Microbiome Consortium (IHMC) including the NIH Human Microbiome Project (HMP) and the European Metagenomics of the Human Intestinal Tract project (MetaHIT), which will perform metagenomic sequencing of hundreds of individuals.[25] One of the ground-breaking results has been the classification (like blood typing) of individual intestinal microbiomes into 3 major 'enterotypes'.[22] In addition, at the recent IHMC congress, there were presentations showing metagenome-wide association with both metabolic syndrome and type 2 diabetes.[21] Although much of the work is in the early stages, the future of personalized medicine may someday involve individual metagenomes used as a pertinent factor in diagnosis, disease management, and determinants of health. In this scenario, FMT could be used to treat people with disease-associated microbiomes.

While FMT began as a last ditch therapy for pseudomembranous colitis and CDI, our increasing understanding of the microbiome may mean that FMT has a role in treating other diseases. History has shown a lack of interest in FMT, but the anticipation from metagenomic research and the urgency of the CDI epidemic may be the much needed push for new advances. On an optimistic note, Kahn and colleagues report that patients with UC are in favour of moving forward with FMT, suggesting that patients may not be as adverse to the idea as what we might think.[26] With any luck, we may see substantial developments in the years to come.

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The built environment: how city design impacts child health

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ABSTRACT

Environmental factors, such as soil, air and water quality, are well known to influence population health. With the increasing urbanization of Canada and other countries around the world, more attention is now being paid to how the 'built environment' – all the elements of the environment designed by humans – also plays a crucial role in human health. This article briefly examines how a few key components of the built environment contribute to child health. Thoughtful placement of schools and efforts to create safe, walkable neighbourhoods can increase the number of students who walk to school instead of relying on cars. Providing children and their families with recreational infrastructure promotes physical activity. Creating farmers' markets in urban cores increases access to a less expensive source of nutritious food for a city's inhabitants. Knowledge about these interactions between urban design and child health can allow physicians to provide more practical advice to their patients about developing a healthy lifestyle within a city. It is also a promising field for physician advocacy: by offering their expertise to inform city planning decisions and persuading city planners to consider the health impacts of their decisions, physicians can help make it easier for their young patients to live a healthy, active lifestyle.

THE BUILT ENVIRONMENT AND URBANIZATION

When considering individual patients, we are taught to consider the impact of patients' environments on their health: where and with whom they live, what kind of work they do, etc. It stands to reason that factors of a larger environment – such as a neighbourhood or city – may influence the health of groups of people living there. Of specific interest is the built environment (BE) – all of the elements of the environment designed by humans –including the land-use zoning of a neighbourhood, road layouts, access to shops and facilities, and the presence or absence of sidewalks. A growing body of research illustrates that BE design in urban and suburban areas can have a significant impact on the health of people living in these areas. This article endeavours to give a practical overview of the influence of BE on health, with a specific focus on how BE can influence child health, activity levels and development.

Where people live in Canada has changed dramatically since World War II and the subsequent boom of industry, with an increased proportion of the population moving toward urban areas. Currently, 68% of the Canadian population lives in metropolitan areas and this figure continues to increase annually.[1] The development of sufficient housing and infrastructure for the rapidly growing number of city dwellers often results in urban sprawl. The low-density housing and partitioned land use common to suburban areas may now be contributing to chronic health problems.[2] At least four main threats of sprawl to population health have been identified: physical inactivity, poor air quality, more motor vehicle collisions due to reliance on cars, and mental health issues.[3] Mitigating such health effects requires an understanding of the interplay of city design and human health followed by appropriate urban planning.

THE CURRENT STATE OF CHILD HEALTH IN CANADA

The most recent estimates suggest that 26% of Canadian children are overweight and 8% are obese. The percentages of children that are overweight or obese have doubled and tripled, respectively, over the past 25 years and research indicates that these unhealthy body weights often persist into adulthood.[4] To curb this trend, public education has focused on the importance of children eating five or more daily servings of fruits and vegetables and engaging in regular physical activity. However, the role of a child's neighbourhood environment in influencing their physical activity and overall health is often not considered. Finding ways to create an environment that encourages physical activity is a novel, population-based approach to help curb the trend toward childhood overweight/obesity as well as the presence of 'adult' diseases in children (e.g., type 2 diabetes mellitus).

COMMUNITY PLANNING FOR HEALTHY LIFESTYLES

The School Commute

Walking to school was previously a staple daily activity for most children. However, this has been eroded by a trend toward building larger centralized schools to which children must be bused, increased parental fears over child safety and the construction of less 'walkable' neighbourhoods. Not surprisingly, the most important factor influencing whether or not children commute to school in a physically active way is proximity. Specifically, if children live $\leq$ 800 m from their school they are 5-10 times more likely to commute actively to school than if they live farther away.[5]

More subtle factors have also been identified that make a neighbourhood 'walkable,' namely what we associate with 'older' neighbourhoods – a grid system layout with lots of connections between roads, high population density and a variety of land uses including housing, shops, services, and recreational facilities. Conversely, most suburban housing developments are designed in such a way that walking is unappealing: streets are often convoluted in their layout, connections to stores and restaurants are limited, and there is a low population-density. These car-oriented neighbourhoods discourage physically active transport.[5] On the contrary, children and adolescents who live in 'walkable' neighbourhoods not only walk to school more often but are also more likely to be physically active outside of school hours.[5]

Both the real and perceived danger of a neighbourhood are critical factors in parents' decisions about allowing their children to walk to school and other local destinations. Similarly, older adolescents – especially girls – are more likely to be active in their neighbourhoods if they perceive them to be safe.[5] This may explain why males are more likely

to actively commute to school than girls – they tend to perceive their neighbourhoods as safer. Creating safe neighbourhoods in which residents perceive them as such is key to encouraging physical activity.[6]

Recreational Facilities

The availability of recreational facilities (parks, playing fields, pools, etc.) also plays a role in how active children are in a given environment. A survey study done in London, Ontario found that after controlling for season and demographic factors, youth who have two or more recreational facilities in their neighbourhood engage in an average of 17 minutes more daily physical activity than their comparable peers who have fewer local facilities.[7] Trails for walking and cycling can also help to promote physical activity. One Texas study found a 1.5 times greater odds of walking for a minimum of half an hour at least once a week among people who perceived themselves as living close to a trail.[8] This is a modest finding, but does show a potential role of trails as one small step in establishing a culture of physical activity for families. To maximize trail usage, city planners designing trail routes should note that trail segments with mixed views of urban and natural landscapes as opposed to only natural views experienced 39% higher trail traffic.[8] This further touts the health benefits of mixed land use mentioned in the studies on walkable neighbourhoods.[5]

Access to Nutritious Food

Much like recreational opportunities, access to a source of nutritious food can have a positive impact on a child's health. Unfortunately, disparities in food access related to socio-economic factors have been well documented in several studies in both the US and UK.[9] Recent studies have examined whether neighbourhood characteristics such as proximity to a grocery store serve to lessen such disparity. One Toronto study found that only 1% of variation in food security and even less of the variation in severe food insecurity could be attributed to one's neighbourhood of residence. This effect actually disappeared completely after accounting for covariates such as income, number of dependent children and status as a recent immigrant, leading the researchers to conclude "we found no evidence that geographic food accessibility mitigates the effect of financial constraints on household food security."[9]

Conversely, a different study examined the effects that the creation of a farmer's market in a food desert – a district with little or no access to healthy foods – in London, Ontario had on the price and availability of healthy food. The researchers found that the market improved access to fresh foods such as broccoli and green grapes and allowed for hundreds of dollars in potential annual savings for families.[10] Such savings could help to reduce the financial barriers to a healthy diet like those noted in the Toronto study, allowing parents to afford healthier foods for their children.

WHY SHOULD PHYSICIANS CARE?

Similarly to how overweight/obese children become overweight/obese adults, physically active teens are much more likely to be active as adults.[11] By taking steps to ensure that our children and adolescent patients are active and healthy in their younger years we are setting the foundation for healthy living in the years to come.

Preventing or delaying chronic disease in our children is one of the most efficient ways to help both our community's health and our overburdened health care system. Interventions to change the BE may serve as a powerful tool in achieving this goal. Notably, changing the BE is less reliant on evoking specific behavioural changes within individual patients – a difficult task to which any doctor can attest. As Dr. Leonard Syme, an epidemiologist at UC Berkeley's School of Public Health points out, "Changing individual behaviours in isolation may be more difficult than modifying the environment that facilitates and promotes them".[2]

WHERE DO WE GO FROM HERE?

For doctors to successfully harness urban planning as a new tool in patient care, there are two vital goals:

1. collaboration with other professionals such as politicians, city planners, public health professionals and teachers
2. advocacy for population health as a major factor in city planning decisions

For example, physicians could join with school board officials and other community partners in creating walk-to-school campaigns. This might involve having pamphlets and other literature available in their offices for parents, as well as speaking to their young patients about how walking to school can help keep them healthy. City planning advocacy could follow the lead of the campaign that banned smoking in public places, in which physicians played a crucial role. Hopefully as physicians become more informed about the impact urban design can have on their patients, similar advocacy gains can be made in the field of city planning.

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Maladaptive coping behaviours of medical students

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ABSTRACT

Background/Context: Medical school, and particularly clerkship, is stressful. Little research exists regarding the use of substances and potentially addictive behaviours to cope with medical school stressors. Such coping strategies present an ethical issue as they may hinder academic or clinical performance.

Objective: To compare the use of five maladaptive coping behaviours – caffeine, alcohol, gambling, tobacco, and drugs – between pre-clerkship and clerkship students.

Methods: A cross-sectional study was performed using an anonymous online survey distributed to all medical students at the Schulich School of Medicine & Dentistry. Data was analysed using Student *t*-tests to compare the mean number of coping behaviours used. Subgroup analyses using Mid-P Exact chi-squared tests were conducted to examine the prevalence of each.

Results: The total number of maladaptive behaviours was not statistically different between the pre-clerkship and clerkship years. Subgroup analyses indicated no significant differences in the use of any one behaviour, while there were trends towards significance in the prevalence of non-prescription drug use.

Conclusion: The study lacked statistical power to show an increase in the total use of maladaptive coping behaviours between pre-clerkship and clerkship students. There were also no significant changes in the use of any specific behaviour. Future studies would benefit from a larger sample size and longitudinal study design.

INTRODUCTION

In health literature, the term 'stress' signifies a negative experience produced from the interaction between the person and his or her environment, resulting in psychological, physical and behavioural consequences.[1-4] According to the American Psychological Association (APA), stress has become a growing concern because of its physical and psychological consequences.[5] People employ various coping strategies in an attempt to manage stress. Coping can be defined as behavioural efforts employed to manage, reduce, or control stress.[6] In a 2009 survey performed by APA, 81% of those surveyed believed they were managing their stress well; however, many of them were using maladaptive strategies such as tobacco, gambling, or drinking alcohol as coping mechanisms.[6]

Several studies worldwide have demonstrated that being in medical school is one of the most stressful experiences due to the volume of information, long hours of study, and limited time for self and/or family.[7] Moreover, the clerkship period is particularly stressful since the students transition from didactic-based learning to direct patient care.[8] Overall, these stressors can cause a detrimental effect on academic performance, physical health, and psychological well-being, ultimately influencing performance, not only as students, but also later as caregivers.[9, 10] Despite the potential importance of coping strategies, few investigators have studied how physicians cope with stress. Of these, most report positive coping behaviours, such as seeking counselling, meditation, and exercising.[7, 11] However, no recent literature has reported maladaptive coping behaviours as a way to manage stress as a medical student. It was hypothesized that there would be an increase in use of potentially addictive behaviours as coping mechanisms in medical school from pre-clerkship to the clerkship years. Specifically, the presence and prevalence of the following maladaptive behaviours were examined: caffeine, alcohol, gambling, tobacco, and non-prescription drug use. The aim of this study is to provide a deeper understanding of the maladaptive coping mechanisms that medical students use.

METHODS

Medical students from the classes of 2014, 2013, 2012, and 2011 at the Schulich School of Medicine & Dentistry were asked, via electronic-mail, to complete an online survey of their use of caffeine, alcohol, gambling, tobacco, and drugs. Participation in this study was voluntary and anonymous. This study was approved by the Schulich research ethics board (REB consent #17613E).

For each of the five maladaptive behaviours, the participant was asked to i) report the frequency of use in the last six months, ii) gauge his or her dependence on each coping mechanism. As well, questions regarding whether the student felt those coping mechanisms had ever influenced their performance in social, academic, or professional situations were included. The data were collected in January 2011, which gave first year clerks an opportunity to experience the stressors of clerkship for five months before responding.

A cross-sectional analysis of the 242 respondents was conducted with students divided into pre-clerkship (2014 and 2013) and clerkship (2012 and 2011) years. Since all survey data were de-identified, only group analyses were conducted. The differences between the total number of maladaptive coping mechanisms employed by pre-clerkship and clerkship students were compared and analysed using two-tailed Student *t*-tests. In addition, subgroup analyses were performed using two-tailed Mid-P Exact chi-squared tests to identify differences between pre-clerkship and clerkship groups with respect to the prevalence of each.

RESULTS AND DISCUSSION

Numerous studies have discussed the stresses and pressure that students face during their medical training.[12, 13] Several have also suggested that clerkship is particularly stressful for students.[8] Most studies of the methods used by medical students to cope with these stresses have focused on engagement and disengagement or active and avoidance mechanisms.[7,

Table 1. Subgroup analyses of the five maladaptive behaviours in Pre-Clerkship and Clerkship Students.

	Pre-Clerkship (%)[SD] N=149	Clerkship (%)[SD] N=93	P-value	Total (%) N=242
Gender				
Male	71 (47.7)	37 (39.8)	0.231	108 (44.6)
Female	78 (52.3)	56 (60.2)	0.231	134 (55.4)
Caffeine				
Used in last 6 months	141 (94.6)	90 (96.8)	0.645	231 (95.4)
Mean weekly[1]	7.67 [6.68]	9.96 [7.82]		
Dependence	53 (37.6)	33 (36.7)		86 (37.3)
Coping	91 (64.5)	44 (48.9)		135 (55.8)
Alcohol				
Used in last 6 months	141 (94.6)	86 (92.5)	0.509	227 (93.8)
Mean weekly[1]	4.20 [3.97]	3.80 [4.77]		
Dependence	2 (1.4)	0 (0)		2 (0.9)
Coping	21 (14.9)	23 (26.7)		44 (19.4)
Influence on performance	43 (30.5)	20 (23.2)		63 (27.8)
Gambling				
Used in last 6 months	26 (17.4)	14 (15.1)	0.636	40 (16.5)
Mean monthly[1] dose	1.60 [3.82]	1.32 [1.56]		
Dependence	0 (0.0)	0 (0.0)		0 (0.0)
Coping	0 (0.0)	0 (0.0)		0 (0.0)
Influence on performance	0 (0.0)	0 (0.0)		0 (0.0)
Tobacco				
Used in last 6 months	13 (8.7)	14 (15.1)	0.139	27 (11.2)
Mean monthly[1] dose	0.31 [0.86]	1.01 [2.14]		
Dependence	1 (7.7)	2 (14.3)		3 (11.1)
Coping	2 (15.4)	4 (28.6)		6 (22.2)
Drugs				
Used in last 6 months	29 (19.5)	28 (30.1)	0.062	57 (23.6)
Mean monthly[1] dose	0.89 [1.79]	1.41 [2.05]		
Dependence	1 (3.6)	1 (3.6)		2 (3.6)
Coping	5 (17.2)	4 (14.3)		9 (15.8)
Influence on performance	7 (24.1)	7 (25.0)		14 (24.6)

[1]Mean use of each behaviour reported weekly or monthly excluding responses where survey participants denied use within the last 6 months. Values reported as: mean [standard deviation].

[14] This study is one of the first to directly examine the use of substances and potentially addictive behaviours as methods of coping with stress. Specifically, we examined the use of caffeine, gambling, tobacco, and drug use in medical students across the four years of Schulich School of Medicine and Dentistry (Table 1).

The total prevalence of maladaptive coping behaviours (caffeine, gambling, tobacco, and drug use) in the clerkship years and the pre-clerkship years was not significantly different (P=0.227) with reported average number of inappropriate strategies used of 2.49 and 2.35, respectively. While this did not support the hypothesis, it may be secondary to the small sample size. The prevalence of these behaviours is displayed by group in Figure 1. Over 80% of the students reported the use

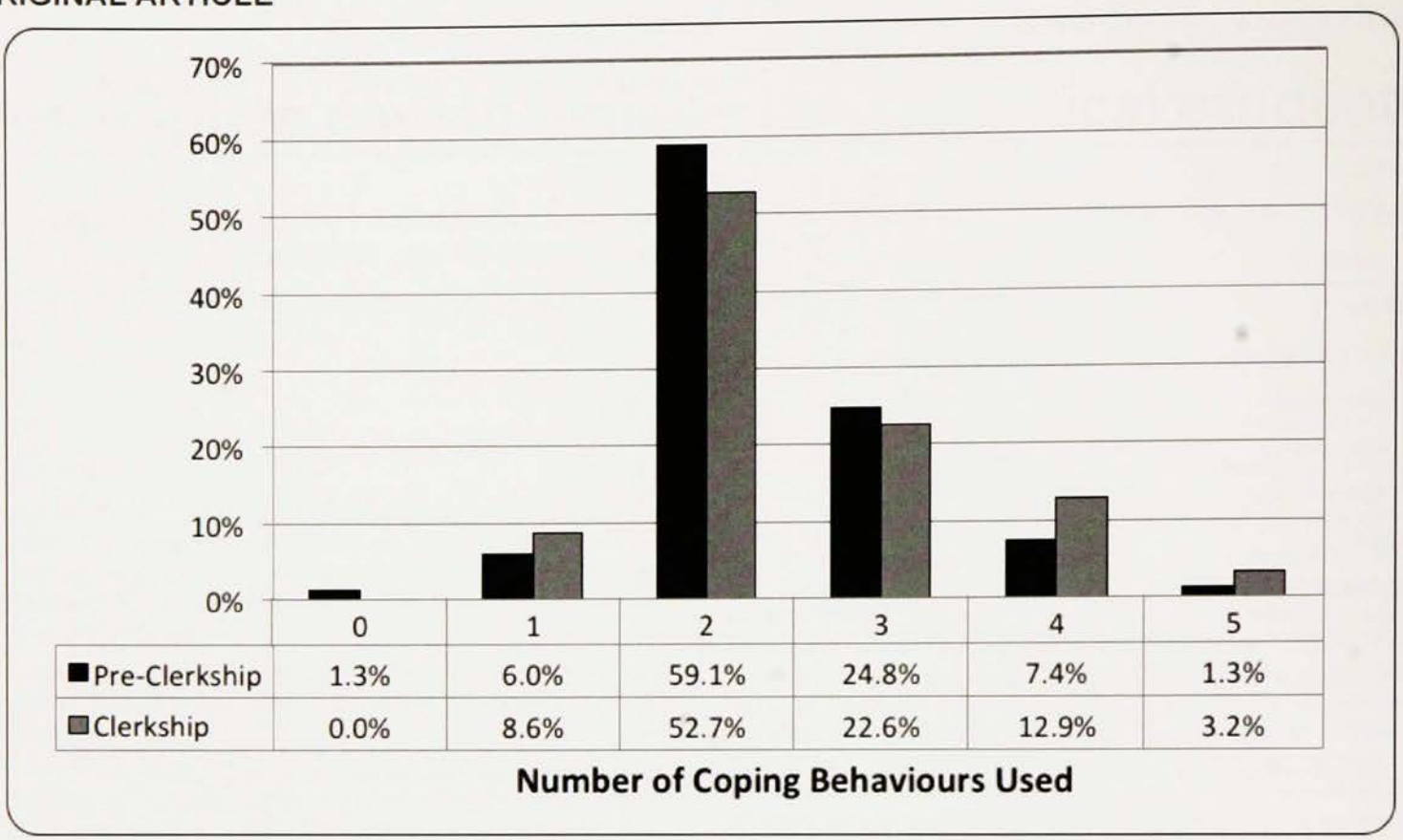

Figure 1. Bar graph showing number of maladaptive coping behaviours in pre-clerkship and clerkship students. The total number of the five coping mechanisms –caffeine, alcohol, gambling, tobacco and drugs (x-axis) – with frequency of use in percent (y-axis) is depicted as bar graphs for the pre-clerkship and clerkship groups.

of two or three maladaptive behaviours. The most commonly reported behaviour was caffeine use (95.4%), followed by alcohol use (93.8%). Interestingly, 23.6% of medical students reported the use of drugs in the past six months. Additionally, 27.8% of students who reported alcohol use and 24.6% of students who reported drug use also indicated that it has had a negative influence on their performance or attendance at school or in the clinic and/or hospital setting.

Subgroup analyses were performed for each coping mechanism looking at prevalence. The frequency of use, dependence, use of the behaviour to cope with stress, and influence on performance are presented in Table 1 for interest, but not statistical analysis. In subgroup analysis, no statistical difference was found between the clerkship and pre-clerkship groups. However, there is a trend towards significance in the prevalence of non-prescription drug use ($P=0.062$). This suggests there may be a greater amount of drug use in the clerkship years as a coping strategy. Since the survey defined drugs to be 'mood-altering substances' as well as 'pharmaceuticals used not as directed', it would be of interest to investigate the specific drugs that are being consumed in order to better categorize the level and type of dependence. Specifically, future study may differentiate illicit drugs like marijuana, cocaine, and heroin from the unintended use of Gravol for sleep induction, which have very different social perceptions.

Although this is a novel study looking at the students of one Canadian medical school and their maladaptive behaviours, it does have two main drawbacks: the sample size and the type of study. The sample size of this study was limited to the 242 medical students who completed the voluntary survey. Consequently, this study has many trends towards significance, yet only a few statistically significant observations. For future studies, more than one Canadian medical school should be enrolled to achieve a greater number of participants. In addition, this study was a cross-sectional study of a group of pre-clerkship and clerkship students, rather than a longitudinal study of the same class during the transition to clerkship. Unlike a longitudinal study, any differences observed could be a blend of cohort effects and true changes in the outcomes over time. These preliminary results should be further explored using a longitudinal study to follow the same cohort of medical students through their pre-clerkship and clerkship years.

While there was no significant difference found between the pre-clerkship and clerkship groups, all of the survey respondents were medical students, and as such were exposed to the stress of medical education in general. A similar study of students in other professional degree programs or post-secondary education may be prudent; this would allow for examination of the effect of exposure to medical school stresses on coping, without the distinction of exposure to clerkship. Further study might be complicated by the difficulties of assigning an appropriately matched cohort. For example, medical students are typically older than students enrolled in other undergraduate programs.

In conclusion, this study did not find significant differences in the average number of maladaptive coping behaviours used by pre-clerkship and clerkship medical students. Further analysis likewise did not demonstrate significant differences in the prevalence of caffeine, alcohol, gambling, tobacco, and non-prescription drug use as a coping strategy. There were, however, trends towards significance in the greater use of non-prescription drugs by clerkship students. This study cannot conclude that the elevated stress of clerkship years in medical school is correlated with maladaptive behaviours. Consequently, these results

illustrate the need for further study, focussing particularly on the use of non-prescription drugs. Future study may benefit from longitudinal design and greater sample size, as well as the inclusion of non-medical students. With more information, it may be valuable to consider implementing programs to help students cope with stress in a more productive and positive manner.

DISCLOSURE

The authors declare that no conflicting interests exist and that no direct or indirect funding was received to conduct this study.

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Radiofrequency ablation (RFA) in the treatment of liver tumours

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BACKGROUND AND HISTORY

The incidence of primary liver cancer in Canada has been steadily increasing, having more than doubled since 1980.[1] This increase is partially attributed to the increasing rates of hepatitis C infection, alcohol abuse, and immigration from developing countries where the incidence of hepatocellular carcinoma (HCC) is much greater.[1,2] The liver is also the most common site of metastases, especially from colorectal cancers.[3] The best treatment option for HCC and liver-only metastases is surgical resection, however, only 10-15% of patients are suitable candidates for this procedure.[4] As such a small proportion of patients are eligible for surgical resection or able to receive a liver for transplantation, a number of different modalities have been explored as treatment options, including, but not limited to, radiofrequency ablation (RFA), radiotherapy, percutaneous ethanol injection, and transarterial chemoembolization. RFA is safe, and associated with fewer side-effects and shorter hospital stays compared to surgical resection.[5]

The use of heat in medicine dates back to antiquity when various ancient societies from the Greeks to the Chinese knew of the use of cautery to stop bleeding. In 1891, Jacques-Arsene d'Arsonoval found that alternating current at 20kHz or higher can heat tissue in the human body without muscle excitation.[6] Nearly four decades later, Harvey Cushing and William T Bovie developed the Bovie knife, a small knife where an alternating current was passed so that it can burn through or cauterize the tissue on contact.[7] In the early 1990's radiofrequency electrocautery was further explored, and modified into what is now RFA as a way of treating small liver tumours.[6]

EVALUATION AND CONTRAINDICATIONS

Prior to operation, the nature of the liver tumours are carefully evaluated by abdominal CT or MR imaging. Tumours larger than 5cm or numbering greater than five are contraindications for treatment by RFA due to the difficulty in ablating a tumour of such a size.[4] Their location relative to pertinent structures such as other visceral organs, bile ducts and vessels are noted as it complicates the procedure. It is difficult to completely ablate tumours near vessels due to the cooling effect of the blood flow. Ablation also poses a risk for causing necrotic damage to nearby organs such as the bowel or diaphragm, as well as causing biliary obstruction and damage. Although the majority of RFA in the liver are performed on primary HCC tumours or colorectal metastases, it is also performed on metastases from other areas such as the pancreas and breast. Despite the advantages presented by RFA, surgical resection is still considered the gold standard, and should be considered if the patient is found to be eligible on evaluation. However, this is rapidly changing as more advanced RFA techniques emerge. Extra-hepatic involvement is also a relative contraindication for RFA. Hematology tests for coagulopathies are performed as the procedure may require multiple insertions of large gauge needles as well as poses a risk of complications resulting in surgery.[8]

RADIOFREQUENCY ABLATION

There are three primary approaches to performing an RFA: percutaneous, laparoscopic, and open. Percutaneous RFA is above all the preferred approach as it is the least invasive, requires only conscious sedation, inexpensive, has minimal side effects, and the patient can be discharged within 24 hours. Earlier percutaneous procedures were limited to those with a few small tumours in the periphery and away from the diaphragm. However, with advanced techniques such as hydrodissection these challenging lesions can also be treated. Advanced ultrasound and 3D ultrasound, coupled with CT scanning has helped to visualise the entire liver to help in abalation.[9]

There are only a few centres where interventional radiology is not available that perform laparoscopic RFA, and this is usually used in conjuction with liver resection, or other debulking surgeries. This approach is generally used on patients with centrally located tumours, tumours located near large blood vessels, and those with minimal abdominal procedures performed in the past. As it is a more invasive approach, it is less cost-effective, associated with more complications, and requires a longer hospital stay. It is also much more technically challenging to perform, as the angle of approach of the radiofrequency needle is restricted.[10]

The open approach is generally reserved for those patients with multiple large tumours ranging from 4-5cm or involves a large vessel. An open approach allows for the temporary occlusion of the hepatic artery and portal vein, known as a Pringle maneuver, which minimizes blood flow. As the cooling effect from the blood flow is minimized, the larger tumours are more likely to be completely ablated. If the patient also presents with a separate tumour that cannot undergo RFA but is suitable to be resected, it can be surgically removed during the same operation. The disadvantages of this approach are similar to those of other open surgeries as it is more expensive, requires general anesthesia, a longer hospital stay and is associated with increased morbidity and mortality.[4]

Prior to the operation, the site of entry is locally anesthetized and the patient is given an IV sedative. General anesthesia is indicated for percutaneous RFA when poor tolerance is expected with local anesthetic alone as in cases of drug abuse or cancer patients, or if the operation is expected to last more than 3 hours.[8]

The RFA needle is guided towards the tumour by ultrasonography. The aim of the procedure is to ablate the entirety of the tumour as well as a 1-2cm tumour-free margin.[11] However, ultrasounography is unable to accurately show the extent of the ablation, and tumour margins tend to be obscured by the ablative action, so care must be taken to ensure complete ablation.[12] Tumours are usually treated from the deepest to the

most superficial as the ablated area may obscure ultrasonographic visualization of deeper tissue. Single ablations are usually suitable for small tumours smaller than 3cm, but for larger tumours, multiple overlapping ablations should be considered. The RFA needle remains active during removal from the tumour to prevent seeding of malignant tissue along healthy liver tissue. Post-operatively patient is given an antiemetic and analgesics to control the nausea and pain often associated with RFA.[8]

POST-OP AND COMPLICATIONS

An abdominal CT is performed one month after the operation to assess the extent of the tumour ablation. A waiting period is necessary as ablation causes a temporary hyperemic ring to appear on CT that may obscure any remaining tumour areas. After this a repeat CT is performed routinely to look for possible intra or extrahepatic tumour recurrence. If an intrahepatic tumour recurrence is found, the patient can undergo percutaneous RFA again. Percutaneous RFA can be repeated as many times as necessary in contrast to the other RFA approaches which are often one-time procedures. If the recurrence is large or complicated, then other treatment modalities may be considered such as chemoembolization.[8]

A portion of patients may experience flu-like symptoms 3-5 days post-operation that is also described in patients of similar procedures such as chemoembolization and cryoablation. The fever may be accompanied by fatigue and night sweats lasting anywhere from 1-3 weeks. Supportive care is recommended, but if the fever lasts longer than 5 days, the patient is assessed for possible sepsis. RFA is generally considered safe, but some serious complications have been reported such as pleural effusions, intraperitoneal bleeding, and burns to the diaphragm and colon.[8]

FUTURE DIRECTIONS

A major hurdle in RFA is the difficulty in fully ablating large tumours. Currently, a single ablation can reach a tissue volume 2-3cm in diameter, but multiple ablations in the same area or reducing hepatic vascular inflow can increase the effective ablated volume. Newer and more effective needles and radiofrequency generators have been developed since the advent of RFA to increase ablation volume and further improvements continue to be researched. One such innovation being investigated is the use of pulsed current RFA as opposed to constant current RFA where the former was found to produce a larger volume of tissue necrosis.[13] Other energy sources such as Microwave technology are also being used for ablation.

The benefits of the minimally-invasive nature of percutaneous RFA are obvious in the treatment of small tumours in early stage HCC. However, in a situation where a patient would be suitable for both RFA and surgical resection, the latter would be the standard of care, but very few patients are candidates for surgical resection due to pre-existing complex liver disease. If a large randomized control trial can show that best curative treatment between RFA, surgical resection, and liver transplantation in early HCC is RFA, then it may become the new standard of care due to its cost-effectiveness and minimal complications.

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Colonoscopy in screening and diagnosis of colorectal cancer

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INTRODUCTION

Colonoscopy is an endoscopic tool used for the visualization and biopsy of the large intestine with important applications in the investigation of colorectal cancers. Colonoscopy has been used to diagnose colorectal cancer since the late nineteen sixties, and is currently the gold standard. However, colonoscopy is not without shortcomings and attempts have been made to improve this technique. This paper will briefly review the history of colonoscopy, its current applications, and the limitations of colonoscopy for the diagnosis and screening of colon cancer. It will lastly examine innovations in colonoscopy and the advantages they might offer.

HISTORY OF COLONOSCOPY

Dr. William Wolff, and Dr. Hiromi Shinya, pioneered the development of the colonoscope.[1] Their invention, in 1969, was an advance over the barium enema and the flexible sigmoidoscope because it allowed for the visualization and removal of polyps from the entire large intestine.[1, 2] Wolff and Shinya advocated for their invention and published much of the early evidence needed to overcome skepticism about the device's safety and efficacy.[2] Once the basic technology of the colonoscope had been accepted, the device lent itself to adaptations that have bettered its performance, and broadened its applications. The use of colonoscopy to screen and diagnose colorectal cancer continues to rise.[1, 4, 5] Ultimately, the significance of the test has been to permit an understanding of colorectal cancer through the collection of biopsies, and to lower mortality through screening and diagnosis.[6, 7]

COLORECTAL CANCER AND COLONOSCOPY: CURRENT INDICATIONS

Colorectal cancer is the second most common cause of death from cancer among both Canadian men and women; an estimated 22 000 cases were diagnosed in 2011.[8] Most colon cancers begin as small protruding growths called polyps. The chance that a polyp will develop into cancer varies from 2% in lesions under 1.5 cm in diameter to approximately 10% in lesions over 2.5 cm in diameter. [9] Premalignant polyps are estimated to progress over a period of approximately 10 years.[10] Early forms of colorectal cancer are amenable to treatment. If the disease is detected in a local stage, the 5 year survival rate is 90 percent.[6] However, if the cancer has spread regionally the survival rate is 68%, and if disease has metastasized the survival rate is only 10%.[6] Unfortunately, most cases of colon cancer are asymptomatic until advanced stages of the disease.[11] Given the long progression time of this form of cancer and the high success rate of early treatment, it is not surprising that screening programs for colorectal cancer have been able to show substantial survival benefits.[6] Colonoscopy has played an important role in these programs.

The current guidelines on the screening of colorectal cancer acknowledge that a wide range of acceptable options exist. For individuals of average risk over 50 years of age, the recommendation is colonoscopy every ten years, flexible sigmoidoscopy (FISG) every five years, or annual fecal occult blood testing (FOBT).[6] Colonoscopy is the recommended screening test for most individuals with increased risk for colorectal cancers.[6] Additionally, colonoscopy is the recommended follow-up procedure for positive FOBT and FSIG.

As a screening test, colonoscopy has two distinct advantages compared to other means of screening for colorectal cancer. One advantage is that it can be used to remove polyps from the entire length of the colon, which reduces the incidence of colorectal cancer.[6, 9] Furthermore, colonoscopy provides biopsy samples which screen for patients that are at a higher risk of developing cancers in the future; these patients will benefit from more frequent screening.[6, 12]

LIMITATIONS OF COLONOSCOPY

While colon cancer is a serious disease, the lifetime prevalence is approximately 6% in North America; 94% of patients who are screened with colonoscopy do not benefit from undergoing the procedure. [11] Therefore, despite the obvious potential for colonoscopy to prevent colorectal cancer, it is necessary to examine the discomfort and risk that patients are exposed to, the limitations in sensitivity, and the costs of colonoscopy.

Patients undergoing colonoscopy require moderate sedation and dietary bowel preparation.[11] The preparation involves consuming a fluid diet and Pico-Salax, a mix of osmotically active and laxative substances. Not all patients manage to complete the entire preparation as required and this can decrease test sensitivity as polyps may be missed in stool. [13] In addition, the test is uncomfortable and patients require mild sedation at the minimum. Despite sedation, the test is perceived negatively.[14] As a consequence, compliance has substantially hindered the effectiveness of colonoscopy based screening programs.[15] Furthermore, a general anesthetic is often required for patients who feel too much pain or discomfort on mild sedation alone. This substantially increases the cost.[11]

As well as discomfort to the patient, undergoing colonoscopy also carries the risk of complication. The most severe complications, bowel perforation and bleeding, are estimated to occur approximately 1.64 and 0.85 times, respectively, per thousand tests.[16] The rate of complication has also been reported to rise substantially following polypectomy, to approximately 8 per one thousand tests.[17]

When evaluating the test performance of standard colonoscopy, polyps are estimated to be missed at a rate of 27% overall and 6% for adenomas larger than 1 cm.[18] Colonic cancer is also reported to be missed at a rate of 5% with standard colonoscopy.[18] However, there is substantial variation in test characteristics based on the operator.[19]

From a health care system perspective, colonoscopy has significant facility and equipment costs and requires technical expertise to be performed effectively. In Canada, it is estimated to cost $352 per diagnostic procedure, or $467 per therapeutic procedure, when overhead costs and the physician's fee are included in the estimate. [20]

The limitations of colonoscopy must be considered in the context of the primary alternatives. FSIG is an endoscopic technique done with minimal bowel preparation and without sedation. However, FSIG only allows the only distal third of the large bowel to be visualized, making it less sensitive than colonoscopy.[6] The FOBT is a less invasive, test for the finding of occult blood in the stool, which is suggestive of colorectal cancers and large polyps. However, the FOBT is significantly less sensitive and specific than colonoscopy. Also, the test characteristics of FOBT vary significantly depending on the brand, collection technique, and number of samples taken per test.[6]

Although imperfect, colonoscopy does offer improved sensitivity compared to other tests. And while the invasiveness, cost, and risk of complication are frustrating drawbacks, they have not obscured its importance in the screening and diagnosis of colorectal cancers. Rather, they have spurred innovation aimed at modifying standard colonoscopy to address its limitations.

ADVANCED TECHNIQUES

Virtual Colonoscopy

A less invasive alternative to traditional colonoscopy is virtual colonoscopy, also known as CT colonography. A helical CT image is used to create a computer generated 3-dimentional model of the colon. The model can then be visualized digitally for the presence of polyps.[19] CT-colonography is non-invasive, does not require sedation, and avoids major risks such as bleeding and perforations.[21] However, in the event of a polyp being detected a standard colonoscopy is still required for its removal. As with standard colonoscopy, bowel preparation is required and the result depends upon the operator's skill in the interpretation of the results.[21] A possible risk of screening with CT- colonography is that the radiation exposure might promote new cancers – a published estimate is a 0.14% risk.[19] Though few centres are equipped to carry out the procedure, recent guidelines have endorsed it as sufficient screening once every five years for average risk individuals.[19, 6] Currently, CT-colonography is mostly used in the situation of a technically difficult colonoscopy (excessive colonic looping) or diverticulosis, and may be advantageous to increase compliance in patients who cannot tolerate standard colonoscopy.[21, 19]

Capsule Endoscopy

Similar to CT-colonography, capsule endoscopy aims to avoid the invasiveness of traditional colonoscopy. In capsule endoscopy, a small pill equipped with a camera is swallowed and passed through the bowel to collect images.[22] Capsule endoscopy does not allow for biopsy or operator steering, and still requires a dietary bowel preparation, but does not require sedation.[23] Though at present it is used in Europe, investigations of the current technology indicate a lack of sensitivity to warrant replacing other screening test.[24]

CONCLUSION

Since its development, colonoscopy has been widely used to screen for and diagnose colorectal cancers. However, because it is an invasive and costly test that requires extensive preparation by the patient and technical expertise to be performed it is not ideal for this purpose. In response to these limitations, several innovations have focused on less invasive and more accurate means of screening and diagnosis to compliment standard colonoscopy in the management of colorectal cancers.

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The final gift: ethical and legal considerations of liver donation and patient selection

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The first liver transplants were performed in 1963 on three patients, with the longest surviving for 22 days.[1] The ability to sustain patients beyond the 25% one year survival seen throughout the 1970s was made possible by the introduction of a key immunosuppressant agent, cyclosporine A in the early 1980s.[2] Living donor liver transplantation (LDLT), which involves a liver resection of the right liver lobe in adults, and the left lobe in children was first performed in 1988 in a pediatric recipient and 1996 in an adult recipient.[3] At press, 1,742 living and deceased donor liver transplants have been performed in London, Ontario.[4]

Liver transplantation is a life-saving procedure with the ability to significantly decrease mortality and morbidity for high-need patients. Procurement of organs for any type of transplantation is a major limiting factor and presents a significant challenge to their fair and equitable distribution. Currently, there are 218 people waiting for a liver transplant in Ontario.[5] Patient selection, therefore, aims to maximize the benefits of transplant while minimizing the risks associated with the procedure.

There are multiple ethical considerations applicable to patient selection and organ donation practices. Legislation governing organ and tissue transplantation also play a central role in patient selection. Here we explore some of these ethical and regulatory considerations of liver transplants and the widening gap between demand and supply in Canada.

RECIPIENT SELECTION

Organ donation represents a "final gift" one can bestow on another individual. This sentiment imposes substantial responsibility on the medical system to select suitable recipients in an ethical and just manner. In addition to numerous immunological and physiological considerations, relevant social factors need to be considered when allocating a finite resource for which there is such high demand. Should patients who require transplants as a result of their own actions, such as alcohol related disease or IV drug use (Hepatitis B, Hepatitis C), be considered on equal grounds with those requiring a liver transplant due to circumstances out of their control?

Eunice Booker, the mother of an organ donor was quoted in The Guardian as saying "I find it offensive that one in four livers donated goes to alcoholics... [The liver should go to] the one who's not an alcoholic, they are more entitled."[6] Further, the rate of alcoholic recidivism post-transplantation is estimated at 11 to 22%.[7] In addition, IV drug use (IVDU) use is a significant cause of Hepatitis C, which is the most common indication for liver transplantation among adults. Retransplantation for recurrent HCV infections is estimated at 3.6%-5.0%.[8]

Whether a patient is responsible for their past alcoholism or IVD use poses the question of whether individuals that abuse substances are exercising free will. If they are deemed not to be free agents, penalizing them would be unfair. Many arguments could be raised on both sides of the issue, including the strong genetic preponderance to alcoholism, and the higher prevalence of comorbid psychiatric illnesses among substance abusers. In addition, the time elapsed between when the causative behavior has ceased and when transplantation is necessary may be a significant duration, even decades. The legal system has tended to believe those abusing substances should be held accountable. However, given the aims of the legal system are to uphold justice and apply criminal punishments, while the medical system aims to allocate medical resources and heal, the role of free will in decision-making may not be the same. Further, this can lead down a slippery slope: Do alcoholics deserve a liver? Do smokers deserve a lung? Does a street-racer deserve an ICU stay following a crash? [9]

As medical innovations result in an increased number of chronically ill and older patients being eligible for liver transplant, it is important to consider the presence of comorbidities and the patient's age. Thus, should an elderly individual with multiple comorbidities be considered on equal grounds with a young adult without any comorbidities, who has the potential of a considerably longer lifespan and better outcomes? Utilitarian ethics would favor donation to the younger and healthier patient. However, widespread application of this criterion would systematically exclude older and sicker patients from transplantation. Given the moral obligation of providers to all patients, this would lead to an unjust outcome.

The solution of Canadian transplant organizations to these issues is a pragmatic one, which generally avoids passing moral judgments, and circumvents adding qualifiers to the value of human life. The Model for End-stage Liver Disease (MELD) is a scoring system used to estimate disease severity. This model is widely implemented in the US, and increasingly in Canada.[10] When an organ becomes available, recipients are considered starting with the patient in greatest need and sequentially going down the list, checking for compatibility between the donor and potential recipient (including body size and blood type).[11]

In Ontario, the relevant human tissues legislation is the Trillium Gift of Life Network (TGLN) Act. The Ontario waiting list is managed by TGLN. The transplant organizations have protocols to communicate with one another, and will cross-match medically urgent patients. When an interprovincial donation occurs, transportation, even across Canada, can be arranged in a matter of hours. However, in part due to the fragmented transplant network, organs are only occasionally donated outside a province. The system in Canada is in contrast to the U.S., which has a national registry, known as the United Network for Organ Sharing (UNOS).[9]

ORGAN DONATION AND SUPPLY

There are two sources for liver donations: living donors and cadaveric

donors. Out of the 6,000 transplants performed in the United States annually, only 320 are living donor transplants.[13] Donation after Cardiac Death (DCD), or "non-beating heart donors", are cadaveric donors who donate following withdrawal of life support. While DCDs were performed many years ago in Canada, they were re-introduced after a national forum in 2005.[14] The London Health Sciences Centre (LHSC), a Canadian leader in the field, is the provincial leader, having transplanted over 30 of the 100 DCDs performed in Ontario.[15]

Regarding determination of death, there is no federal legislation which defines death in Canada. Some provinces, including Ontario, have legislation that requires the determination of death be made by two physicians. The United States' *Uniformed Determination of Death Act* specifies that death may be established by irreversible loss of neurological function ("brain death"), or irreversible cessation of cardiorespiratory function.[16] The latter criteria is used in cases of DCDs.

Critics of DCD have noted that since the patients are sustained on life support, their death is not inevitable. Further, DCD associates withdrawal of end-of-life care with organ procurement, in a manner nearly ideal for transplantation. In order to prevent conflicts of interest, and to maintain public support of DCD, it is imperative to ensure the medical professions who decide to withdraw end of life care are not associated with organ transplantation. This supports the "dead donor rule" that organ donation should neither cause nor hasten death.

Even with DCDs as a source for organ donation, the organ supply is unable to meet demand. One strategy proposed to increase the supply is switching to an "opt-out" system. Currently, Canada's "opt-in" system assumes one *does not* wish to donate unless they otherwise specify. In an opt-out system, such as Spain's, one is assumed to want to donate their organs unless otherwise specified. In addition, given society's reverence for the importance of the human body, even though an individual's rights cease with death, an opt-out policy may be seen as a transgression of the state. Further, public health campaigns to increase awareness and improve cadaveric donation rates, including the recent Ontario Gift of Life Campaign (http://www.giftoflife.on.ca/en/) have been widely implemented.

In most provinces, except Manitoba and Quebec, a patient's recorded consent constitutes legally-binding consent to organ donation. Nonetheless, patients are encouraged to make their substitute decision maker aware of their choices, to ensure wishes are followed. In Ontario, the TLGN Act notes consent is legally binding and provides legal immunity to physicians who act in good faith with regards to organ procurement. However, even if the deceased patient's consent is clearly indicated, physicians tend to consult family members before proceeding with organ procurement.

Living donor liver transplantion (LDLT) has been effectively used in Canada for the past forty years. However, since a living donor has an estimated 0.2% mortality risk in adult-to-adult transplants, the procedure is not without ethical considerations.[17] Potential living donors are often healthy individuals, for which the occurrence of even a low probability of mortality is costly and should be avoided. This may explain the low rate of LDLT in Canada. Even though they are willing and informed donors, performing such a risky procedure violates the non-maleficence principle. Further, these donors often incur significant costs from lost income and travel expenses. While it is ethically unacceptable to purchase an organ, it may be fitting to compensate donors for their personal costs. Currently Canada does not have a national strategy to reimburse living organ donors.[18]

Donor compensation raises the issue of organ trafficking, in which patients circumvent waitlists by paying for and receiving an organ and medical care. When the procedure occurs in a foreign nation, it is common referred to as transplant tourism. Often the donor receives insufficient medical care, placing them at risk. The Canadian government condemns organ trafficking, and the various provincial Human Tissue Graft Acts directly outlaw paying for human tissues. The Criminal Code outlaws any situation where a person is compelled to provide organs or tissues. However, how this will be applied in relation to organ trafficking remains to be seen. Further, Canadian physicians may feel uncomfortable treating patients who have been involved with organ trafficking. Nonetheless, as with other cases in which physicians are conscientious objectors, this cannot prevent a patient's access to care.[9]

CONCLUSIONS

In many ways organ transplantation represents the pinnacle of our biomedical understanding of human physiology. Despite medical advances, progress is hindered by the lack of supply, which has struggled to keep up even with the introduction of living donation and DCDs as well as massive public awareness campaigns. It is therefore the responsibility of every health care provider to ensure patients are well-educated and informed of the desperate need of organ donation. And as far as the question of why to donate, we asked Michael Bloch, the donor coordinator at LHSC and his view is that:

"You have an opportunity of providing numerous people with improvement of their health and in fact save their life. It is human nature to help fellow human beings, so if it is the last good thing you do in your life, or even the only good thing you do in your life, I can't see why you will not". [19]

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Biologic agents in the management of inflammatory bowel disease: is it worth it?

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INTRODUCTION

Inflammatory Bowel Disease (IBD) represents a group of disorders that affects the gastrointestinal (GI) tract. In this disease, an abnormal immune response in the body causes inflammation and ulceration of the GI tract. The two main forms of IBD include Crohn's disease (CD) and ulcerative colitis (UC), which differ in their presentation and treatment.[1] Crohn's disease can affect any part of the GI tract, and the entire thickness of the intestinal wall is generally involved. Ulcerative colitis, on the other hand, is limited to the rectum and colon and the exterior layers of the intestinal wall are generally not affected. IBD is a lifelong disease that has a substantial impact on the quality of life of patients and has a tremendous impact on a patient's wellbeing. There are currently no cures available for IBD and treatment is aimed towards keeping the patient symptom-free.[1]

IBD is most commonly found in the developed world, although cases have begun appearing more frequently in developing countries.[2] Globally, Canada and Sweden have the highest incidence of both CD and UC.[2] It is estimated that more than 5000 cases of CD and 4000 cases of UC are diagnosed in Canada each year, with a total of more than 200,000 Canadians living with one of these diseases at any given time.

The heavy burden that IBD imposes on patients in turn leads to substantial financial costs for the Canadian healthcare system. Due to the nature of IBD, these costs include both direct costs associated with treating the disease and indirect costs such as lost productivity and time missed from work. In a 2008 report by the Crohn's and Colitis Foundation of Canada, it was found that the indirect cost associated with IBD is approximately $1 billion dollars annually, with CD comprising roughly $600 million of that value due to its higher prevalence.[3] Direct medical costs for IBD in Canada are estimated at over 750 million, with CD accounting for two-thirds of that value.[3] Although these costs will continue to increase as the prevalence of IBD grows, the distribution of the direct medical costs have recently undergone significant changes due to the introduction of new treatment options. The remainder of this article will address these specific changes.

TREATMENT – PRE BIOLOGIC ERA

Prior to the introduction of biologics, the major categories of medication prescribed for the treatment of IBD included aminosalicylates, corticosteroids and immunomodulators.[4] In the event of failed medical therapy, surgery was also considered. Resections were ideally conservative and only undertaken for symptomatic patients.[5]

In both CD and UC, roughly one-third of total costs are concentrated in the most severe patients (2% of all patients), who are often resistant to traditional drug therapy.[6] Medication costs are relatively inexpensive when compared to the surgical interventions and related hospitalizations required by these patients. In fact, surgical interventions account for the greatest portion of the cost of IBD.[6] Parenteral nutrition is another costly intervention, which was reported to be responsible for majority of overall pharmacy costs, despite infrequent use.[6] Pharmaceuticals used to represent less than 10% of overall health care cost related to the treatment of IBD, but this value has increased in the post-biologic era.[3]

TREATMENT - POST BIOLOGIC ERA

The first biologic agent was approved in 1998 and has since become a popular IBD treatment choice. In most instances biologic agents are initiated for patients who demonstrate an inadequate response to conventional therapies. There are currently four agents approved by the US Food and Drug Administration for treating CD and one agent available for use in UC. Infliximab is a murine chimeric monoclonal antibody directed against tumor necrosis factor (TNF) -alpha, and can be used in both acute attacks and maintenance therapies.[7] It is also the only agent available thus far in treating UC.[8] Adalimumab and Certolizumab pegol are humanized anti-TNF agents and are approved for use in treating patients who have lost response to Infliximab.[7] Lastly, Natalizumab is a humanized anti-alpha-4 integrin antibody and is used in patients who cannot tolerate anti-TNF agents.[7]

In Canada, the cost for biologic agents was estimated to be over $110 million in 2008, comprising over two-thirds of overall drug cost.[3] This value has since increased with more agents appearing in the market. World-wide, it is estimated that anti-TNF sales will peak at over 2 billion in the coming years, and the overall market for IBD will reach 4 billion US dollars in 2017.[9] In addition to this growing selection of available agents, there has also been a change in the prescription habits of physicians that has contributed to this increase in cost. The average time from diagnosis to biologic treatment initiation has decreased from 7-8 years to 3-5 years, and it is likely that this trend of early treatment will continue.[5] In light of this trend, many studies have been done to study the cost effectiveness of said agents.

COST EFFECTIVENESS OF BIOLOGIC AGENTS

Overall, most studies done to investigate the cost effectiveness of biologic treatment of IBD have demonstrated a decrease in necessary hospitalizations and surgical interventions. One study done at the University of Chicago demonstrated a decrease in all surgeries by close to 40%, emergency room visits by over 60% and decrease in hospitalization by over 50%. 6 Another study in Spain reported that the cost of hospitalization was reduced from 60 percent down to 6% of total annual health expenditures for the treatment of IBD.[10] Despite these positive outcomes, these studies also indicated that the overall cost of IBD management actually increased as a result of biologics usage. That being said, a more costly intervention can still be cost effective as long as there is a sufficient increase in health outcome. For example, the National Institute

for Health and Clinical Excellence (NICE) suggests that an incremental cost-utility ratio of 20,000 to 30,000 pounds (roughly $32000 to $48000 CAN dollars) per quality adjusted life year (QALY) gained can be considered cost effective.[11]

Early studies reported induction therapies of infliximab for acute attacks to be greatly cost effective according to the above NICE guideline, however, these were all short-term one year studies.[12] This short time frame likely led to an overestimate of the cost-effectiveness ratio due to the chronic nature of IBD. Indeed, subsequent studies where the study time horizon was expanded to 5 years revealed that the use of biologic agents in acute attacks approached cost effectiveness. Lindsay *et al.* reported that Infliximab was cost effective for both luminal and fistulising forms of CD, however, body weight was an important factor affecting cost effectiveness.[13] An evidence review group in the United Kingdom reviewed the use of infliximab in exacerbations of UC and found an incremental cost-utility ratio of roughly $32,000 US dollars, with the results being sensitive to the patients' colectomy rates.[14] A systematic review on the use of infliximab in CD was done by the National Institute for Health Research and it reported that infliximab was cost-effective for episodic treatment of active CD.[11]

Contrary to the evidence found in induction therapies, studies have reported poor results for the use of biologics in lifelong maintenance therapies. French authors reported that the incremental cost per QALY for infliximab in lifetime maintenance therapy of CD was more than 10 times that of the ratio for induction therapy.[15] Similarly, Bodger *et al.* found continuous therapy of infliximab to only be economically feasible for up to 4 years.[16] Evidence for models with a shorter time horizon has also been mixed. "The *Crohn's Trial of the Fully Human Antibody* Adalimumab for Remission Maintenance trial" data reported that for a 5 year horizon, maintenance of adalimumab will result in an incremental ratio of less than $48,000 per QALY in CD.[17] The Active Colitis Treatment trials" also reported similar findings for the use of infliximab in UC patients.[18] On the other hand, Kaplan *et al.* from the United States have found an incremental ratio of $332,000 per QALY for infliximab use in CD[19], and a systematic review done by the Canadian Agency for Drugs and Technologies in Health reported an incremental ratio of over $200,000 for both infliximab and adalimumab in CD and $350,000 for using infliximab in UC.[20]

Part of the reason for the heterogeneity of results can be attributed to differences in the cost of administering the agents between countries. Although the cost for 100mg of infliximab is fairly stable at a price range of ($700-900 US dollars), patients in the United States, but not the UK must pay a substantial fee for the services of an infusion center.[6] Greater cost containments in both drug and administration costs will likely be needed to ensure cost effective care. Another significant caveat of these studies is the fact that indirect costs were not accounted for in their cost effectiveness models. This is likely to cause a gross overestimation of the cost effectiveness ratios for biologic agents.[6] Lastly, it should be noted that meta analyses were not performed as a result of significant heterogeneity between studies, so a definitive answer on the matter is unavailable.[11,20]

CONCLUSION

Biologic agents have been shown to provide clinical benefit in patients with moderate to severe attacks of CD and UC. In turn, the increasing use of these agents in treatment of IBD has raised concerns about whether or not these drugs are a cost-effective use of health care resources. Current evidence suggests that biologic agents are likely to be cost effective when used to treat moderate to severe acute attacks of CD and UC. Evidence for its use in maintenance therapy is inconclusive and more research in this area is recommended.

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Is it what you know or how you use it? A review of nutrition knowledge and counseling among medical professionals

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It is no secret that a number of chronic diseases, including cardiovascular disease, cancer, diabetes mellitus, and obesity, are causing increasingly more disability and premature death around the world, and that poor nutrition is a modifiable risk factor for these diseases.[1] Given the prominent role of nutrition in the global burden of disease, it is essential that today's medical students receive an adequate amount of nutrition education. It is also important that practicing physicians are providing their patients with evidence-based nutritional counseling.

Based on a series of surveys conducted between 1999 and 2009, 62%-73% of medical schools in the United States were not meeting the minimum target of 25 hours of nutrition education across the four years of undergraduate medical education, as recommended by the National Academy of Sciences.[2] Canadian medical schools do not seem to be faring much better, at least according to students. A questionnaire given to 9 of the 17 Canadian medical schools revealed that 87.2% of medical students who responded felt that their program needed to devote more time to nutrition instruction.[3] There may be a number of barriers to achieving the optimal amount of nutrition education, including limited time in the curriculum, lack of nutrition specialists on faculty, and greater weight being given to the treatment of disease rather than its prevention.[2,3,4]

The questionnaire given to Canadian medical students indicated that some components of nutrition curricula may be stronger than others. The majority of respondents were comfortable with basic nutrition concepts and the role of nutrition in health promotion.[3] However, most lacked confidence in their knowledge of nutritional requirements at different points in the lifecycle and their ability to discuss the role of nutrition in the treatment of disease.[3] It is important that medical students are exposed to nutrition education that provides them with practical skills, such as nutritional assessment and counseling, in addition to the basic science component.[2]

Regardless of the quality of nutrition education received, it is likely that medical students will vary in their attitude towards nutritional counseling. Several studies have found that female medical students are more likely to ask their patients about diet or engage in nutritional counseling than their male counterparts.[5,6,7] It has also been found that medical students intending to specialize in primary care were significantly more likely to consider nutritional counseling important than students intending to pursue a career in a subspecialty.[7] Interestingly, the same study determined that medical students who consumed more fruits and vegetables themselves were more likely to deem nutritional counseling relevant to their clinical practice.[7] Educational methods for increasing students' provision of nutritional advice might therefore include demonstrating the relevance of nutrition in subspecialty practice and encouraging students to improve their own diet and knowledge of healthy cooking.

Some programs have found ways to overcome the many barriers that stand in the way of achieving adequate nutrition education in medical schools. The University of Arizona College of Medicine managed to increase the time devoted to nutrition instruction in their program from 35 hours to 75 hours by implementing an integrated nutrition curriculum that incorporated nutritional topics into a variety of courses, including biochemistry, social and behavioural sciences, and preparation for clinical medicine.[4] This approach also improved the students' clinical application of nutritional knowledge and skills. Nutrition scores on the Objective Structured Clinical Examination (OSCE) were significantly higher ($P < 0.05$) for students who had been exposed to the new curriculum, compared to those who had graduated before it was implemented.[4]

While an integrated curriculum represents one approach to contend with a limited number of lecture hours, another way to overcome this barrier might be to have students complete some of their nutrition education online. Researchers at the University of North Carolina at Chapel Hill have developed an online nutrition curriculum called the Nutrition in Medicine (NIM) project, which was being used by 90 of the 156 American medical schools when their paper was published in 2010.[2] The online modules are designed so that users will develop practical skills such as assessing a patient's nutritional status or prescribing nutritional interventions as treatment.[2] This kind of online program would likely help to address existing deficits in nutritional education, like the clinical application of nutritional knowledge, while compensating for time constraints and standardizing nutrition instruction across different medical schools.

When one considers the current state of knowledge among primary care physicians, an interesting pattern emerges. Over 80% of Canadian family physicians rated their medical school nutrition training as inadequate. Many doctors stated that they wanted more direct training on nutrition during their undergraduate and postgraduate education.[8,9] However, surveys asking physicians about their current state of knowledge demonstrate that over 60% believe they know 'very much' about prescribing diets for weight-loss[10] and over 75% believe their nutritional knowledge is "up-to-date".[11] In one focus group, most doctors agreed that their level of nutritional knowledge was adequate to deal with most common health problems.[12] Indeed, when given objective tests of nutrition knowledge, most family physicians answer the majority of questions correctly, albeit with certain gaps.[11] When asked about the sources of their nutritional information, most physicians cite self-directed learning and reading,[8,12] while some cite Continuing Medical Education (CME) courses.[13]

Most studies agree that primary care physicians seem to have an adequate level of knowledge about nutrition. Nonetheless, only 40% of obese patients are counseled to lose weight by their physician[10] and there is a significant difference between the number of patients that would ben-

efit from dietary advice and the number of patients that actually receive counseling.[8] When asked about barriers to providing dietary advice, the answers were mixed. A Canadian study cited lack of time and lack of compensation as the largest barriers,[8] and lack of time was echoed in a UK study as well.[14] A Scandinavian study reported lack of nutritional knowledge as the primary barrier[9] and an Israeli study mentioned patient apathy and non-compliance as a barrier to providing nutritional advice.[15]

Patient and physician beliefs can also be barriers to effective nutritional counseling. While the large majority of primary care physicians believe that counseling is part of their role,[15,16] many doctors believe that nutritional counseling usually does not help their patients[13,14] and report feeling frustrated and pessimistic about the effectiveness of dietary advice.[10] Interestingly, physicians that reported more nutritional knowledge were more likely to discuss nutrition with their patients, and more likely to believe that it was effective.[8,10] Patients report lack of nutritional knowledge as the primary barrier to making dietary change; physicians, however, overwhelmingly believe patient apathy is the biggest barrier.[14] Both patients and physicians often believe nutritional counseling is not necessary without an active medical diagnosis, with patients much less likely to view obesity as a medical diagnosis.[15,16]

Moore *et al.*[14] provide a compelling explanation for the gap between having adequate nutritional knowledge and providing effective nutritional counseling. They believe that the problem lies in knowledge translation – the ability to apply knowledge in a way that leads to behavioural change. Physicians are primarily trained in the management of disease, and not in health promotion or preventative medicine. Physicians that consciously include motivational statements in their dietary advice, or who were trained on motivational counseling techniques, were more successful in achieving dietary change from their patients.[8,14]

Pignone *et al.*[17] defines counseling as "a cooperative mode of interaction to assist patients in adopting behaviours associated with improved health outcomes". There are many styles of counseling used by physicians. An informational style includes providing patients with nutritional facts and written materials. A reference style includes referring patients to a dietician for specific nutritional advice. A motivational style includes a holistic assessment of the patient's readiness for change, and is widely considered the most effective method.[12,14] Many physicians are already attempting to provide strong nutritional counseling to their patients, and 80% believe that they are "occasionally" successful in helping patients make dietary change.[14]

A recent systematic review describes nutritional counseling techniques and interventions that are most successful at improving patient health.[17] This review included 21 RCTs with objective endpoints – biochemical markers (i.e. serum triglycerides) or anthropomorphic measurements (i.e. waist circumference). The most effective interventions had a number of shared characteristics. They included an initial dietary assessment, family involvement with social supports, group counseling, and goal-setting. They also discussed not only food intake, but also food preparation techniques. While these are admirable goals, it is not always feasible in a primary care setting. Eaton *et al.*[18] found that physicians spend an average of 1 minute discussing nutrition in a routine primary care appointment. However, Pignone *et al.*[17] also discussed 'medium-intensity' interventions that were moderately effective and would be feasible in primary care. These included a combination of targeted self-help materials, given directly by the health care provider, followed by brief, face-to-face provider advice. Moore *et al.*[14] supports this finding, stating that the goal of primary care physicians should be to reinforce and legitimize the available public health advice on nutrition.

How can we design educational programs that will help medical students and current physicians develop into strong nutritional counselors? The introduction of innovative nutrition modules should focus on two main areas: the application of nutritional knowledge in the prevention of disease and management of common chronic conditions, as well as techniques for counseling and motivating patients to change their dietary habits. New interventions, designed for both medical school and primary care practice, seem promising in their ability to meet these goals. Nutrition is a vital tool in primary prevention and health promotion, and hopefully will be increasingly recognized as such in the medical community.

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Acupuncture in the treatment of irritable bowel syndrome

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INTRODUCTION

Irritable bowel syndrome (IBS) is a gastrointestinal disorder characterized by chronic abdominal pain and irregular bowel function in the absence of an organic cause. It is estimated to affect ten to fifteen percent of the North American population, with higher prevalence among younger and female patients.[1] While only a minority of patients seek medical treatment, IBS constitutes more than a quarter of gastroenterology referral each year.[1]

As IBS is a chronic condition with no known cure, treatment plans have focused on relief of abdominal symptoms and addressing any other patient concerns.[1] This has grown to include alternative therapies, including acupuncture. In 2003, the World Health Organization listed irritable colon syndrome as a syndrome for which "acupuncture is worth trying because treatment by conventional and other therapies is difficult", though they stress that there are only individual controlled trials reporting some therapeutic effects.[2] At present time, the evidence for effectiveness of acupuncture for treatment of IBS remains inconclusive. Acupuncture theory, recent research findings and implications of acupuncture use in IBS treatment will be discussed below.

Acupuncture is an ancient form of Chinese medicine which involves inserting solid, 'atraumatic' and stainless steel needles into the skin at specific points on the body. These points, known as acupoints, have been theorized to have a lower resistance to passage of electricity than the surrounding skin, and are connected by the flow of Qi, or energy, throughout the body.[3] Any imbalance, obstruction or misdirection of this movement of Qi is thought to lead to disease, or potentially increase susceptibility to illness.[3] Supporters of the practice believe that acupuncture is used to correct the Qi imbalance, restoring a balance in autonomic nervous system function, treating symptoms and preventing illness.[3] Specifically for IBS, acupuncture is thought to restore balance to the autonomic nervous system, which is in dysrhythmia due to disparity in Qi of the spleen, kidney and/or liver.[3] Research has suggested that treatments of traditional and electroacupuncture can influence the physiology of the gastrointestinal tract, including altering the motility, pain threshold, hormone levels and acid secretion of the gastrointestinal system.[4-7] Although there has been no conclusive evidence regarding its effects in IBS, many acupuncturists now cite IBS as a potential indication for their treatments.

LITERATURE REVIEW

Current evidence show conflicting results over the benefit of acupuncture. Lim *et al* (2006) reviewed six randomized control trials of poor quality and heterogeneous intervention, and found the benefit of acupuncture use in IBS to be inconclusive.[8] They noted that in studies comparing acupuncture with sham acupuncture, treatments did not offer improvements in overall well-being, or in individual symptoms such as diarrhea, constipation, or abdominal pain. However, in a study using Chinese herbal medicine as the control, the effect of acupuncture was found to be statistically significant.[8] In a German study by Schneider *et al* (2007), effect of acupuncture was assessed based on autonomic nervous system response, pain, and quality of life.[9] Sham acupuncture served as the control. Autonomic nervous system response to acupuncture was measured by salivary cortisol levels and changes in heart rate during a tilt table test. It was found that for both groups of patients, there was an improvement in health related quality of life as indicated by patient responses to questionnaires. However, for the group treated with acupuncture, pain control was statistically improved after 10 treatments. It was also found that patients treated with acupuncture had lower salivary cortisol levels, and reduced heart rate increases during the tilt table test, indicating increased parasympathetic tone.

On the other hand, several studies with double blind, sham controlled trials have yet to convincingly prove the benefit of acupuncture for treating IBS.[10, 11] In a recent study by Lembo *et al* (2009), while it was found that interactions with the health care professional performing either the sham or real acupuncture offered improvement in IBS symptoms when compared to no intervention, there were no differences in improvement between the two acupuncture interventions.[11]

The majority of studies investigating the benefits of acupuncture in IBS were under powered, with the largest randomized control trial including only 230 patients.[11] Study methodologies and acupuncture techniques were heterogeneous, specifically in the number and duration of treatments.[8, 12] These variations made it difficult for reviewers to pool together smaller studies to elucidate the treatment effect.[8]

DISCUSSION

Acupuncture is becoming increasingly recognized in Canada as an adjunct therapy and health care practitioners are beginning to incorporate acupuncture into their skills of practice. In most Canadian provinces, health care practitioners require extra training beyond their basic professional training to perform acupuncture. The standard for training is set by the regulatory bodies for each profession, but in many provinces there are still no standards.[3] Currently in Ontario, the practice of acupuncture is regulated by the Traditional Chinese Medicine Act, 2006.[13] The Ontario government is also in the process of establishing a college whose mandate will be to oversee the implementation of policies and regulations relating to the acupuncturist profession.

Any discussion about the use of acupuncture in clinical practice should always take into account the patient perspective. Current drug therapy for IBS provides little benefit to patients, thus it is not surprising that almost 50% of IBS patients turn to complementary and alternative medicine therapies.[14] Furthermore, despite the lack of evidence to provide a convincing argument for an actual therapeutic benefit of acupunc-

ture compared to sham acupuncture, there is at least some perceived benefit due to a placebo effect. In fact, all trials indicated a significant increase in quality of life independent of the kind of acupuncture (real or sham).[15] It is important to note that the study quality was poor in many of these trials. Further investigation is necessary to delineate the efficacy of acupuncture in the treatment of IBS. Finally, there is no evidence to indicate any potential harm for the use of acupuncture in the treatment of IBS. Given these circumstances, physicians should consult their patients about the options they are considering and not be openly dismissive of acupuncture as an adjunct therapy.

On a final note, while many studies focus on the effect of traditional acupuncture compared to placebo (i.e., sham acupuncture), considerably fewer studies compare acupuncture with standard drug therapy. Certainly, while the use of tricyclic antidepressants in the treatment of IBS is supported by strong clinical evidence,[14,16] there is little evidence to support the use of antispasmodics or selective serotonin reuptake inhibitor antidepressants.[14,17,18] We believe that current drug therapies deserve the same level of scrutiny as acupuncture. Lundeberg *et al* (2011) suggest that the therapeutic effects of acupuncture can be compared to those of standard treatment, taking into consideration individual responses and circumstances, before deciding on the use or disuse of acupuncture in the treatment of IBS.[19]

IBS remains a difficult syndrome to treat, with the main focus of management on relief of symptoms. Although the research remains inconclusive, acupuncture may play a role in alleviating some gastrointestinal symptoms and increasing the quality of life for some IBS patients. It is up to us as future physicians to work with our patients to determine the best management plan combining allopathic and naturopathic medicine.

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The use of gene expression profiling in the personalization of colorectal cancer treatment

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Colorectal cancer (CRC) is the third most common cancer in Canada.[1] This year in Ontario, it is estimated that 8700 people will be diagnosed with CRC and 3450 people will die of the disease.[2] Due to the high mortality rate of CRC, screening programmes have been designed to screen the population for CRC prior to the onset of symptoms. The high burden of disease CRC causes has also made the field of CRC screening, diagnosis and treatment a prime area for the development of novel medical technology. Historically, these technologies have been limited to the fields of biochemical testing of stool and fiber optic visualization of the colon using the colonoscope. A new and exciting field for technology development is the application of molecular genetics in the profiling of colorectal tumours. Genetic profiling will allow clinicians to develop a personalized treatment plan for the administration of chemotherapeutic agents and biologics in the treatment of CRC. Personalized medicine has the potential to improve outcomes by selecting the chemotherapeutic agent that has the best likelihood of effectiveness for a given patient's specific tumour. In order for this practice to become the standard of care, links between genetic profiles and chemotherapeutic effectiveness must be known and technologies for analysing the relevant gene profiles must be developed. The application of this technology to stage II CRC in particular is an active field of research.

Currently, the five year survival rate for stage I CRC is approximately 93%. This survival rate falls to approximately 80% for patients with stage II disease.[3] The effectiveness of adjuvant chemotherapy for stage II CRC disease is currently an area of debate in the field of oncology.[4] Moertel et al. conducted a retrospective study looking at patients with stage II CRC to identify clinical characteristics that are predictive of recurrence of disease in order to identify patients who might benefit from adjuvant chemotherapeutic treatment. These characteristics include T4 lesions, bowel obstruction and tumour perforation.[5] Patients with high risk stage II disease, identified using these characteristics, are often treated with adjuvant chemotherapy, despite the lack of validation with a randomized clinical trial.[4] An analysis of the American SEER-Medicare database--one of the largest medical databases in the United States--has demonstrated that patients with stage II CRC who received adjuvant fluorouracil based chemotherapy did not have improved outcomes with either high risk or low risk disease.[6] Conversely, the QUASAR study has shown that the standard chemotherapy regimen of fluorouracil plus leucovorin produces a 3% survival benefit in stage II CRC; however, the toxicity of the treatment causes death in 0.5% of patients.[7] To make matters more complicated, the addition of oxaliplatin to a chemotherapeutic regimen of fluorouracil and leucovorin improves the outcome in stage III CRC but does not improve the 6 year survival outcomes of stage II CRC.[4,7] This surprising finding highlights the need for improving the clinical criteria for selecting stage II CRC patients who will benefit from adjuvant chemotherapeutic treatment. The findings in this paper also suggest that CRC is not necessarily a stepwise progression from stage II to stage III disease and demonstrates the need for further research into the molecular biology of stage II disease.

Despite the criteria for high risk stage II CRC outlined above and the limitations of these criteria, the morbidity associated with treatment for stage II CRC could be greatly reduced if physicians were able to further delineate which patients could benefit from adjuvant treatment. The molecular genetic profiling of a patient's colorectal tumour could potentially yield this information by analysing for the expression of genes which are known to respond better to adjuvant chemotherapy. While this approach is very exciting and holds great promise, physicians and researchers need to make sense of the extensive data that can be generated using a genomics approach. Knowing the expression levels of all the genes in the CRC tumour is not a practical approach to deciding treatment options for the disease. Several research groups have addressed this challenge by selecting groups of genes to profile in an effort to determine which genes in stage II CRC's are clinically significant for recurrence.

An interesting product that is beginning to become available in the clinic is the Oncotype Dx Colon Cancer 12 gene assay. This assay measures the expression levels of seven cancer related genes (Stromal Group: BGN, FAP, INHBA; Cell Cycle Group: MYC, MK167, MYBL2; Early Response Group: GADD458) and normalizes these genes to a group of reference genes that have very little variability in expression (ATP5E, GPX1, PGK1, VDAC2, UBB).[8] The seven cancer related genes were selected based on the results of a series of development studies which included four independent cohorts for a total of over 1800 patients. Starting with a panel of 761 genes known to be associated with CRC, the seven genes most associated with recurrence risk and differential benefit with adjuvant chemotherapy in stage II CRC were selected to be used on the Oncotype Dx 12 gene assay.[7] Tissue samples for use in this particular assay are fixed in formalin, a significant technical advancement over other assays since it means that pathology samples and gene expression profiling can be obtained from one tumour sample. It also allows gene expression profiling to be conducted on previous biopsies or tumour resections. Briefly, RNA is extracted from the formalin fixed tumour and quantified to determine the amount of RNA present in the sample. The RNA is then reverse transcribed to complementary DNA using a gene specific primer for each assay gene. The expression levels of the 12 genes are then measured using quantitative polymerase chain reactions (PCR) (see Figure 1 for a schematic of the assay). After the molecular biologic analysis is completed, a recurrence score between 0 and 100 is then assigned based on an algorithm outlined by Clark-Langone et al..[8] A low score ($\leq$30) corresponds to a 3 year recurrence risk of 8%, an intermediate score (31-40) has a 3 year recurrence risk of 11% and a high score ($\geq$41) has a 3 year recurrence risk of 25%.[7]

This algorithm takes the combined expression values from each of the gene groups (Stromal, Cell Cycle and Early Response), allowing for co-expression, and combines these values with varying weights to create an overall recurrence score, an individualized risk estimate for colon cancer recurrence. While initial results based on a retrospective analysis using the QUASAR trial do show an association between the recurrence risk score and prognosis, the predictive value of the recurrence score for treatment benefit has not yet been shown. Further trials are underway to determine the full clinical effectiveness of the Oncotype Dx Colon Cancer Assay.[9]

Other similar products on the market include the Coloprint 18 gene assay;[10] however, this assay is of limited utility since it only makes use of fresh frozen tumour samples. The Oncotype Dx Colon Cancer Assay uses formalin fixed tissues allowing for the flexibility to also perform pathological analysis of the same tumour sample. While these emerging technologies are not likely to replace the role of pathological evaluation of tumours in the diagnosis and staging of colorectal cancers within our lifetime, they may have the ability to complement current practices by providing more detailed information on which treatment options are best for a particular patient. Despite their promise, several questions need to be addressed regarding their utility. Since a patient has many CRC tumours and not all tumours have an identical genotype, will the assays be valid at selecting those patients who will benefit from adjuvant chemotherapy? Moreover, since the genotype of a CRC tumour changes during the course of treatment due to the development of drug resistance, will the assay be a worthwhile clinical tool in the treatment of the ever evolving stage II CRC tumour? Also, how much of a survival advantage will adjuvant therapy provide and will the assay be cost-effective when analyzed using QALY? Despite these questions, the use of molecular

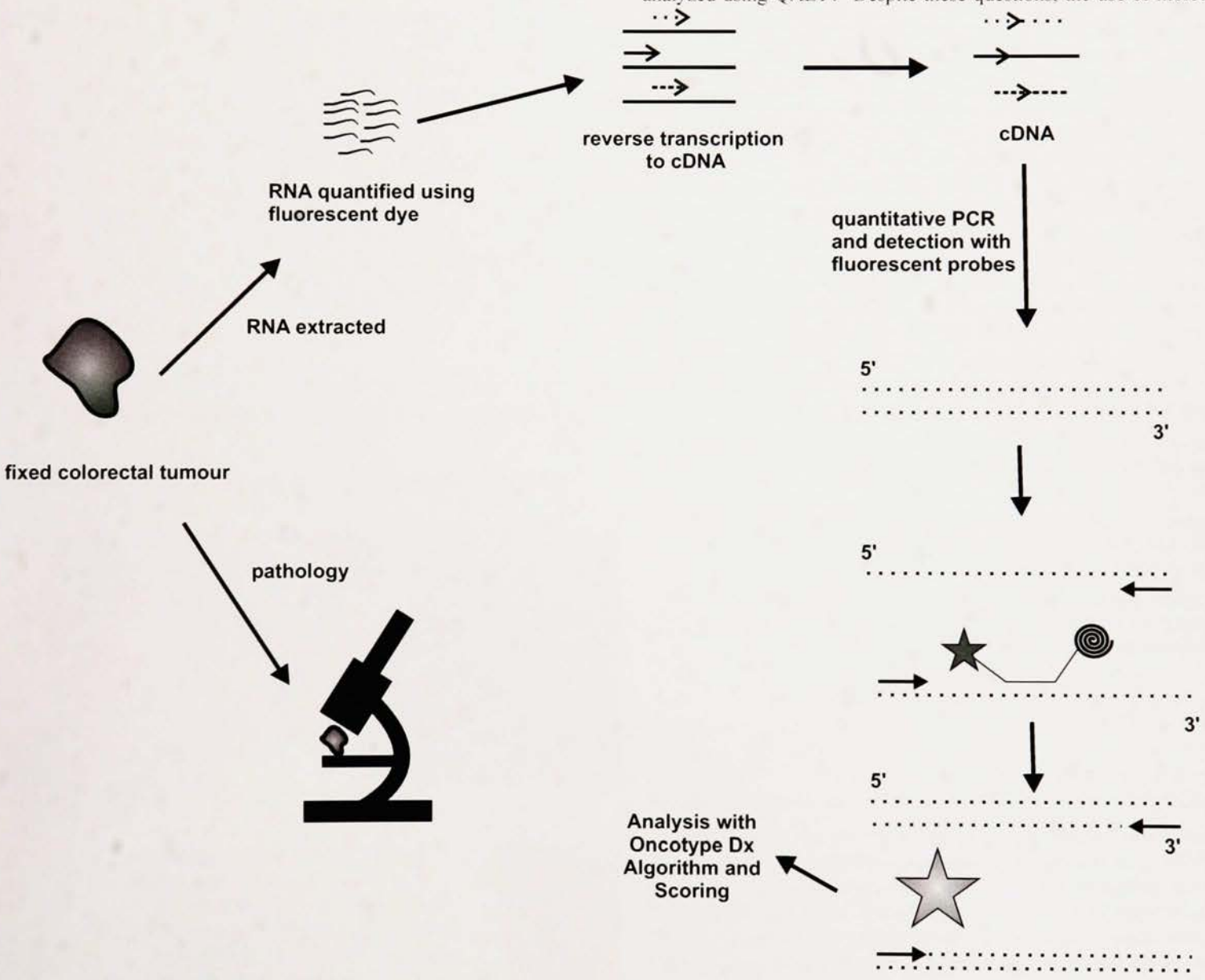

Figure 1: A schematic diagram illustrating the Oncotype Dx Colon Cancer Assay. A colorectal tumour is fixed in formalin, sent for pathological analysis and used concurrently in the Oncotype Dx assay. RNA is extracted from the tumour and is quantified using fluorescent dyes. A known amount of RNA is added to a reverse transcription reaction. The RNA is reverse transcribed to complementary DNA (cDNA) using primers specific for each of the 12 genes of interest. Quantitative polymerase chain reaction (qPCR) is performed using the cDNA and fluorescent probes. The probes are specific for each gene of interest and have a fluorescent molecule (star) bonded to one end and a quencher (spiral) that stops the fluorescence bonded to the opposite end. During the PCR reaction the Taq polymerase enzyme cleaves the probe thus, releasing the fluorescent molecule from the quencher. The amount of fluorescent signal in the reaction increases and is measured. The expression levels of the genes of interest are normalized against the reference genes using the Oncotype Dx algorithm.

genetics tools in personalized cancer treatment is sure to become a reality over the course of our medical careers.

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Gastroenterology profiles: Dr. John Howard

Lauren Sham (Meds 2014), Abdul Naeem (Meds 2014), Joyce Zhang (Meds 2015)
Faculty Reviewer: Dr. John Howard, MD, FRCPC (Departments of Medicine and Pediatrics)

During the "Transcending Borders" conference hosted by the University of Western Ontario earlier this year, Dr. John Howard offered some sage advice to eager students: to focus on the things we can change, and celebrate our small successes. This genuine counsel is perhaps the result of a multitude of experiences aimed at producing positive change. Currently the Chief of Paediatric Gastroenterology and Assistant Program Director for Paediatrics at Victoria Hospital in London, Ontario, Dr. Howard has also held the position of Assistant Dean of Undergraduate Medicine, where he spearheaded the development of a new undergraduate curriculum. He is also the Chair of the Canadian Association of Physicians for the Environment (CAPE). His passion for medical teaching is immediately felt the second he enters a lecture hall, and he has been recognized many times as the recipient of numerous teaching awards.

As a kid, Dr. Howard had his heart set on becoming a veterinarian, but as he says, he just happened to "stumble into medicine." Looking back, he sees that this is probably why he is in paediatrics: "Saying 'My cow's not performing well' is kind of like saying 'My kid's not performing well' – they're both very observational!" He completed his medical training at Queen's University and his residency in Internal Medicine at the University of Western Ontario with subspecialty training in Gastroenterology. When practicing adult gastroenterology at Victoria Hospital in London, he shared the paediatric patients because they didn't have anyone to look after them specifically. In 2004, he made the switch from adults to mainly kids. He has the privilege of having a unique practice – he calls himself a "family gastroenterologist": his major practice consists of kids, but he doesn't have to say goodbye to them when they're 18.

What does he like most about his job? Without hesitation, Dr. Howard says it's about the life stories, which is particularly true in pediatrics. "You get to look after them as kids, and then they grow up and get married, and now they have kids!" He thoroughly enjoys being part of people's lives. This is especially due to his interest in the "doctor-patient relationship." Challenging patients are often the ones that stick out in his mind. He mentions this one tough guy, with bad gastrointestinal disease, a guy that should have been dead 10 to 15 years ago from complications but still carries on. One night at 5 a.m., Dr. Howard gets a call from him, finds out that he had lost his son very suddenly, and helps takes him through it over the phone. Another patient of his with terrible inflammatory bowel disease has major psychiatric difficulties. He sees the patient every four to five years, but their entire medical relationship is on e-mail because the patient has difficulty dealing with face-to-face communication. "But it's so interesting," he remarks, "The patient will show up at my kid's performances and just say hi. So I know what the patient looks like. It's a wonderful therapeutic relationship – and I don't bill anything for it."

Dr. Howard takes his philosophy of the doctor-patient relationship directly into the running of his clinic. "I have three kinds of relationships with patients: positive energy, neutral energy, and negative energy. My clinics are set up in this way. Most of my encounters are neutral: I'm in a high energy state, they're low, I transfer some energy and the patient feels better and takes up my energy. Positive energy is when I'm high, they're low, I see them through the interaction and give them energy - but as the relationship develops, they give me energy with their trust and friendship, and we're both energized. The bad kind is when I'm high, they're low, and I give more energy and it just evaporates – the energy isn't transferred." He says that the key in medicine is to change states: negative to neutral, and neutral to positive. Just like relationships in life: some people suck energy from you, most friends are neutral energy, and some are what you would call love, the traditional positive energy relationship. The positive energy doctor-patient relationship is akin to love – a professional love.

His secret key to teaching? Seeing the logic in a wrong answer. "If you're asking a student what he thinks this patient has, and the patient has irritable bowel syndrome but the student says Crohn's disease – you could just say "No." Or you could say, "I could see how you might think that, but this is my perspective." He likes to acknowledge and see the logic in a wrong answer – otherwise students just won't answer. He sees it as a wonderful academic exercise to see just how that wrong answer came out. He also likes to be a personal professor, rather than a big professor. One of the ways he does this is bringing in his own patients to lecture – an exercise many students consider to be their favourite part of class. He also learned, though, there is a right and a wrong time to do it. He used to bring in a patient that had been previously abused by a physician – right in the first part of medical school. "It was great for FIFE-ing, but people would get so wrapped up in the case and not look at the method!" He has now learned to bring in more complicated cases in second or fourth year – at a level students can come to appreciate.

Dr. Howard's interest in ecosystem health started with his role in developing the new medical curriculum: he identified a huge void in the old curriculum that lacked the topics of health stewardship, advocacy and public health. After discovering a new ecosystem health program in Guelph, he realized that public health can be taught to medical students through ecosystem health. Some of the issues he is working on through CAPE include: banning the cosmetic use of pesticides, shifting to renewable energy, namely wind power, and elimination of coal generation. Dr. Howard believes that the environment has a fundamental impact on our health in a way that most of us are not aware of. Keeping in mind how our presence alters the environment may be the key in understanding the increasing prevalence of certain diseases. Though it can be challenging to balance his clinical duties and his obligations to CAPE, Dr. Howard tries to achieve the balanced integration of the two by giving

grand rounds on ecosystem health, encouraging students to become interested in the field, and being conscious of the impact of his clinical practice on the environment. He poses the question to his students: are we doing the right things in medicine, not only for our patients but also for the environment? "Most people come into medicine with a [sense of the environment], but they lose it. My job is to maintain it and hopefully stimulate it." For patients, it comes in their own empowerment. "People will ask for their kids, 'So Bob has Crohn's disease, how do I prevent the other two from getting it?' You could say, "Nothing," which is very disempowering. But you could tell them instead that there's this epidemic of Crohn's disease – it's gone up at least 1 log unit since my starting practice. And I don't know what that is – but I have to look at that and live as naturally as possible."

What does he see for his future? "I'm retiring April 1, 2015!" he says, with a chuckle. He sees himself as being in a nice part of his career: not coasting, but having opportunities he can pick for himself. "I can say no to things because I'm retiring in 3 years!" He says he will probably go around the world and not be so work-oriented, but then likely will come back and work in the community in non-invasive gastroenterology. "At this point in my life, I don't worry about anyone. A GI bleed doesn't bother me, a 1 year old bleeding doesn't bother me. They used to, but I've seen so many and I won't be doing those types of cases." He also would like to write a book on environmental issues, but doesn't want to pressure himself. "People say the bad thing about the environment is – where do you start? But they have grey coloured glasses on. I have rose coloured glasses on – and say instead, look at all the opportunities and different places we can start."

His advice to medical students: "Remember who you were when you came into medical school and the values that you had – hold onto them. Think about creating your own personal mission statement and keep to it." His mission statement? "To be a patient centred physician who is accountable to our community and to deliver that to students." Many students struggle with picking a specialty and exactly what they should do in life. Dr. Howard's philosophy counters that idea: "Don't get hung up on what you're going to be, but more who you're going to be."

Thinking like an emergency doctor

Elaine Tang (Meds 2015), Roman Shapiro (Meds 2014), Kimberly Fielding (Meds 2014)

Faculty Reviewer: Dr. Naveen Poonai MSc MD FAAP FRCPC (Department of Paediatrics/Internal Medicine)

THE PRESENTING PROBLEM

A previously healthy 14-year-old girl develops acute lower abdominal pain and vomiting. The pain comes in waves, and the girl is in obvious distress. Her parents have now brought her to the emergency room.

THE PATIENT'S STORY

The girl had been running and playing soccer with friends outside when she suddenly had felt a sharp, radiating pain in her abdominal region. At first, she ignored it and continued playing, but eventually the pain became so intense that she couldn't stand. Becoming concerned, her parents tried to get her to stand, but she was unable to walk. They carried her to the car and drove her straight to the emergency department. Since the onset of the pain, she began vomiting intermittently. She is now curled on a stretcher and guarding her stomach.

THE EMERGENCY ROOM

The parents are frantic. Repeatedly, they have demanded that their daughter be given some form of analgesia or narcotics to control the pain. The girl's pain seems to be getting worse. The emergency doctor works quickly to first assess ABCDE: Airway, Breathing, Circulation, Disability, and Exposure. Outside of the girl's pain, it appears that the girl is stable.

GENERAL APPROACH

The most important thing to determine in children with abdominal pain is whether this is a life-threatening condition that will require immediate intervention. If not life-threatening, more time can then be taken to identify the proper cause of the pain.[1] There are three areas of examination that are important:

History – Use the history to try and understand the cause of the abdominal pain. Ask about any trauma to the area, previous surgeries, fever, vomiting, the location of the pain and pattern of symptoms.[21]

- *Trauma:* Abdominal trauma can be life-threatening, especially if organs are damaged. Remember that for some abdominal injuries, symptoms may not appear immediately, such as left shoulder pain from a slowly developing splenic hematoma, or a duodenal hematoma from a lap seatbelt injury.[32]
- *Characteristic of Pain:* Obtain information about the onset, frequency, duration, characterization, and location of the pain. Specific diagnoses have particular characteristic patterns of presentation.[41]
- *Associated Symptoms:* Signs of fever and abdominal pain are often correlated with infectious etiologies such as gastroenteritis, viral syndromes, or pharyngitis. Vomiting in connection with abdominal pain, especially without diarrhea can be indicative of life-threatening bowel obstruction or appendicitis. Volvulus and intussusception should also be included on the differential and ruled out, although the latter is less likely in this age group. A history of a cough should also be elicited because children with pneumonia frequently complain of abdominal pain. Lower urinary symptoms should be elicited since abdominal pain may be a presenting symptom of urinary tract infection (UTI).[52] An often missed etiology is a gynecologic emergency such as ovarian torsion, ectopic pregnancy, etc., necessitating a complete gynecological history.[63]
- *Past Medical History:* Previous abdominal surgeries, UTIs and pre-existing conditions such as Sickle Cell Disease should be taken into consideration.[72]

Physical examination – Vital signs and detailed abdominal examination are essential.[81]

- *Appearance:* Look at the patient
  - Hypovolemia can be indicative of abdominal injury, volvulus, or intussusceptions
  - Jaundice can indicate hepatitis or hemolysis
- *Vital Signs:* Key features to keep in mind are fever, which would suggest an infection, tachypnea, which may indicate respiratory illness or metabolic acidosis, and hypotension, which can develop from intravascular volume loss or peritonitis.
- *Abdominal Examination:* Look for distention, listen for bowel sounds, localize quadrant pain, and percuss for tenderness, rebound, or involuntary guarding. Rectal exam may be indicated, and stools should be observed for softness and blood.
- *General Examination:* Extra-abdominal findings can help determine the cause of abdominal pain, such as respiratory symptoms suggestive of pneumonia, altered heart sounds indicating either pericarditis or myocarditis, flank tenderness suggestive of pyelonephritis or urolithiasis, or rashes/bruises indicative of Henoch-Schonlein purpura.[92] For sexually active females with lower abdominal pain, bimanual pelvic examinations should be done to look for pelvic inflammatory disease, adnexal masses or cysts, uterine pathologies, etc.[103] The costovertebral angle should also be percussed.

Ancillary studies – Laboratory and radiographic testing should only be done if there are focal concerns that suggest a particular diagnosis that can be confirmed with imaging/lab testing.

- *Laboratory Test:* WBC, hematocrit, serum chemistries, urine dipstick, urine pregnancy test, rapid Streptococcal antigen testing, etc.
- *Imaging:* Plain radiography, ultrasound, CT scan
  - FAST: Focused abdominal sonography for trauma – performed in the emergency room to quickly determine free fluid in the abdo-

men.[111]

- *ECG:* Can assess voltage, ST changes and T wave abnormalities that can suggest pericardial disease

ANALGESIC USE

Children with acute abdominal pain should receive an effective analgesic based on their level of discomfort.[121] While there have been concerns about the use of analgesics altering the accuracy of clinical findings, clinical trials have shown that morphine analgesic use in children with acute abdominal pain is able to provide pain relief without significantly changing clinical examinations or determination of surgical conditions. NSAIDs are also acceptable for pain control. Despite the presence of this data, current observational studies indicate that children often do not receive adequate pain control in these acute circumstances.[131]

THE SPECIALIST EXAM

In a debriefing by the parents, the emergency doctor conducted a quick test to rule out potential life-threatening causes of the girl's pain. When making a secondary survey, think AMPLE: allergies, medications, past illnesses, last meal, and events preceding the injury.

History – The parents did not report any significant trauma incurred during the soccer game. Other than the lower abdominal pain, the girl is not complaining of discomfort anywhere else. She is localizing the pain to her right lower abdominal quadrant and radiating to her back. She describes the pain to be sharp and stabbing. She also reports other recent "stomach pains" that resolved spontaneously, believing these pains may have been due to menstrual cramping. She has no previous medical conditions. She is currently experiencing some nausea, and has vomited twice in the last few hours.[144]

Physical examination – The patient does not appear to be hypovolemic or jaundiced. She has a unilateral, tender adnexal mass with some tenderness to palpation. There are no other remarkable findings. Stool samples have been normal.[154]

Ancillary studies – Blood is drawn and a CBC shows normal levels of WBC and hematocrit. β-HCG levels are ordered, and the results are not suggestive of an ectopic pregnancy. Since she has lower abdominal pain, it was decided that a pelvic ultrasound would be carried out. Results showed an enlarged ovary to one side, with multiple small immature follicles along the periphery.[164] Concerned about cysts, cancer, or other pathologies, a color Doppler U/S and CT scan were performed to show morphological and physiological changes in the ovary, and to assess blood flow. Very little intraovarian venous flow was present.[174]

SOLVING THE MYSTERY

After taking a detailed history and imaging, the diagnosis of ovarian torsion was made with the help of a gynecologic consult.[184] The presence of an enlarged ovary with a decrease in intraovarian venous flow alerted physicians this diagnosis. Laparoscopic surgery was quickly booked. In the meantime, morphine was used to control the girl's pain until she was able to go to the OR.

CONCLUDING REMARKS

Ovarian torsion can easily mimic other GI causes of acute abdominal pain such as constipation, bowel obstruction, appendicitis, intussusceptions, gastroenteritis, renal colic, ans mesenteric adenitis.[194] Despite its rarity in presentation, ovarian torsion should still be on the differential diagnosis when females present with severe, acute, lower abdominal pain. Due to its variable presentation and often non-specific findings, the diagnosis of ovarian torsion is often missed and ramifications for the delay can result in a necrotic ovary. Laparoscopy is used for confirmation of diagnosis and treatment, usually on an in-patient basis. Prompt diagnosis and timely management help save the adnexal structures from infarction and facilitate a speedy recovery.[204]

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A case of adult intussusception: a curious presentation

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It is well established that a diagnosis can be made solely on the basis of a patient's history in the majority of cases. Physical examination may reveal more clues to the patient's complaint, diagnostic tests are used to identify, assess, and confirm any physiological basis for disease. However, a thorough history and good clinical acumen contribute most to a medical diagnosis and treatment selection. This daunting idea is also reassuring, in that there is no substitute for a sound diagnostic approach that one can gain from experience. There is, however, always opportunity for a rare occurrence, a peculiar presentation, a proverbial 'zebra' to slip past our detection despite our most diligent efforts. Disguised by common or vague symptoms rather than stripes, these 'zebras' are a chance to step outside of the usual diagnostic process, summon a protracted differential diagnosis from our training, and regard an unsolved medical problem with new eyes. When the patterns of everyday medicine are broken by such a case, the importance of an astute doctor is starkly illuminated.

The following case was described by Yalamarthi and Smith.[1] A 42 year old male with a three day history of melena presented to his general practitioner, who referred the patient for consultation. He had been previously investigated for iron deficiency anemia, with no cause having been identified. At the time of consult, the patient's haemoglobin was low (86 g/L) and was suggestive of an iron deficiency etiology. The initial investigation that was performed was an upper GI endoscopy, which revealed minimal esophagitis. The absence of significant esophagitis is of interest because iron deficiency has been known to coincide with both hiatal hernias and esophagitis.[2] The patient elected for a conservative investigative approach and underwent a normal barium enema.

Since this patient's initial presenting complaint was an acute history of melena, it may be helpful to review the differential diagnostic thought process that would be triggered by this symptom. Melena refers to black, tarry stool caused by the presence of blood. The tarry appearance is created by the digestion of red blood cells and their contents (specifically the oxidation of iron in hemoglobin) by the activity of the GI tract as it passes through the intestine and colon.[3] For the blood to be digested in this way, its source must originate early in the gastrointestinal tract; this fact allows physicians to classify a GI bleed as being an 'upper GI bleed' by the presence of melena. About 90% of melena originates proximal to the ligament of Treitz (a structural support connecting the duodenum to the diaphragm), but some cases can originate in the small intestine or proximal colon.[4] Conversely, the presence of bright red blood in the stool is indicative of a 'lower GI bleed', from the distal colon or rectum. This distinction can be very helpful in pursuing a diagnosis.

Causes of upper GI bleed can vary greatly, and a detailed history is critical to ruling in or ruling out these potential situations. Potential bleeding causes in the upper GI tract include peptic ulcer disease, esophageal varices, portal hypertensive gastropathy, malignancies, angiodysplasia, and aorto-enteric fistula.[5] Peptic ulcer disease is a common cause of upper GI bleeding, and is seen in patients with a history of Helicobacter pylori infection. Marginal or anastomotic ulcers can be present in patients with gastroenteric anastomosis. Esophageal varices and portal hypertensive gastropathy can be seen in patients who have a history of alcohol abuse or liver disease. Malignancies can occur in the upper GI tract in patients with a history of smoking, alcohol abuse, or bacterial infections such as *Helicobacter pylori*. In patients with renal disease, aortic stenosis, or hereditary hemorrhagic telectasia, resultant angiodysplasia can lead to bleeding in the upper GI structures. Finally, an aorto-enteric fistula can develop in patients who have a history of aortic aneurysm or an aortic graft. An assessment of medications is also necessary to determine if there may be a pharmacological basis for the upper GI bleed, which can be seen in the following situations: non-steroidal anti-inflammatory drugs leading to peptic ulcer disease, irritation of the esophagus by medications leading to pill esophagitis, anti-coagulants which promote bleeding, and bismuth or iron which can give stool the appearance of melena without causing a bleed.[5]

The patient was seen again in clinic, and upon this second visit he complained of left upper quadrant pain.[1] He was still anemic at this time, with a haemoglobin of 98 g/L, despite being advised to take iron supplements after his first consultation. There were no signs of overt blood loss, and no apparent clues to suggest a hidden source. A barium meal follow through showed distortion of the terminal ileum, which was initially assessed as extrinsic compression of the intestine by the sigmoid colon. Further investigation using computed tomography (CT) showed an abnormally thickened region of the ileum. On the scan, this region had a target-like appearance as well as intra-luminal fat present, a finding consistent with our gastrointestinal 'zebra' condition.

Our patient's first investigations were barium studies. The contents of the GI tract are difficult to discern on an X-Ray, so barium salts, which are non-toxic radio-opaque, are inserted to help with visualization. The first test performed was a barium enema, which investigates the colon. After a patient empties their colon, a well-lubricated enema tube is inserted into the patient's rectum. The colon can be filled with barium alone – a "single contrast" barium enema - or barium followed by air – a "double-contrast" barium enema.[6] X-Ray fluoroscopy reveals details about the intestinal lumen and mucosa, with double-contrast barium enemas providing better information on the lining. Our patient's lesion was located above the range visible via a barium enema. The second investigation, a barium meal, is a similar process that investigates foregut structures instead of the colon.[7] This investigation revealed a compression of the terminal ileum. With CT imaging, hallmark signs of an intussusception were visualized, specifically a target-shaped appearance indicating overlapping bowel walls, and intra-luminal fat, which indicates entrapped mesenteric fat.[1]

An intussusception is the telescoping of one segment of bowel into an immediately adjacent segment of bowel.[8] It is found far more commonly in pediatric populations (95% of all intussusception cases are in children), and accounts for less than 5% of adult cases of gastrointestinal obstruction. In children, it is almost always benign and idiopathic, and resolves with the barium enema that is used to diagnose it – the hydrostatic pressure of barium fluid - with or without air - will cause the telescoped bowel to reduce into anatomical position.[9] Furthermore, children often present with the classic triad of intussusception symptoms: vomiting, rectal bleeding, and abdominal pain. In adults, intussusception often presents with vague abdominal symptoms, which a careful clinician may be able to discern. Abdominal pain associated with intussusception is generally periodic and intermittent, and is sometimes accompanied by blood in vomit and/or stool.[10] Furthermore, intussusceptions in adults are rarely idiopathic, with malignant growths accounting for 6-30% of adult intussusception cases, and majority occurring from benign pathology. Our patient had a traumatic ulcer in a Meckel's diverticulum that served as the lead point for the telescoping to occur.

Meckel's diverticulum is a congenital anomaly of the small bowel, occurring in 2% of the population, and more commonly seen in males than females.[11] If it is present in an individual, it is usually found within two feet of the ileocecal valve. This vestigial structure represents an incomplete closure of the omphalomesenteric or vitelline duct, which connects the midgut of the developing embryo to the yolk sac while in utero. A Meckel's diverticulum is typically asymptomatic, with only 2% of cases actually developing any complications over their lifetime. As was seen in our patient, bleeding from the diverticulum is painless, and can result from mucosal ulceration within ectopic gastric tissue. This ectopic tissue can continue to produce secretions that are characteristic of the tissue's embryological origin, such as acid and protease-containing digestive fluid. These secretions can gradually break down the mucosal lining of the diverticulum causing ulceration and bleeding.

The finding of melena in this case was curious because the Meckel's diverticulum was located in the distal ileum. As was previously mentioned, gastro-intestinal bleeding from the lower digestive tract (distal to the ligament of Treitz in the duodenum) would normally present as bright red blood in the stool. The approach presented by Cappell and Friedel for the evaluation of acute upper gastrointestinal bleeding states that some cases of melena can arise from pathology in the distal small bowel and even the proximal colon.[4] With this in mind, this case truly was atypical: an uncommon presentation of an unusual pathology.

There are generally two options in treatment – resection of the involved bowel sections, or reduction – i.e. returning the bowel to anatomical position. Generally, pediatric cases of intussusception will be resolved via reduction of the telescoping regions, with the option to resect the affected region if it is irreparably damaged.[12] In adult patients, due to the high prevalence of malignant tumors and the associated risk of dissemination if reduction is attempted, the preference is for resection. Colo-anal intussusceptions are the notable exception, as reducing could spare the anal sphincter, which is needed to retain bowel continence, as well as post-traumatic and idiopathic intussusceptions in which the risk of malignancy is insignificant.

Our patient underwent a laparoscopic procedure under general anesthetic to resect a section of his small bowel.[1] Depending on the amount of healthy bowel left after resection, the remaining bowel can be reconnected, or an ileostomy can be performed in which remaining bowel is directed through an opening in the abdomen to a drainage bag. Our patient had approximately 1 foot of bowel removed, thus his remaining bowel segments were reattached. He made an uneventful post-operative stay and made a full recovery to normal bowel function.

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Helicobacter pylori: hiding in the modern miasma

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When Ignaz Semmelweis proposed and demonstrated that hand-washing would decrease the incidence of puerperal fever in the mid-nineteenth century, he was ignored, criticized, and ridiculed. Miasma, or bad air, was believed since ancient times to cause disease, and consequently, hand-washing had no place in medical care.

Of course, this is no longer the case, but decades passed before Semmelweis' recommendations gained widespread acceptance. His discovery was controversial and met with resistance. Eventually, the germ theory of disease replaced the miasma theory, and Koch's postulates provided a concrete method to establish a causal relationship between a microorganism and a disease. Despite the struggles of earlier researchers and clinicians to advance medicine, resistance to new knowledge and discoveries still prevails. The story of the bacterium *Helicobacter pylori* provides a modern example of this resistance.

Today, when a person is diagnosed with peptic ulcer disease (PUD) and an *H. pylori*

infection, they are promptly treated with a brief course of two antibiotics.[1] Elimination of the bacterial infection is associated with more rapid healing of ulcers and reduces the risk of relapse.[1] The association between bacterial infection and peptic ulcers was discussed within scientific literature as early as the late 19th century but a definitive link between peptic ulcer disease and specific bacteria was not established until 1984.[2] Furthermore, in 1995, a study of treatment patterns of peptic ulcer disease in the United States showed that only 5% of patients were being treated with antibiotics in order to eradicate *H. pylori*.[3] Why did this happen? Firstly, the characteristics of *H. pylori* made it difficult to study. Secondly, there was already a well-established theory regarding the etiology of peptic ulcers when the bacteria were first successfully cultured. Finally, the medical community was more hesitant than the scientific community to accept infection as causative of peptic ulcers.

Unlike many other disease-causing bacteria, *H. pylori* did not easily fulfill Koch's postulates for peptic ulcer disease. The second postulate states that a disease-causing microorganism must be isolated and grown in pure culture.[4] With the advent of microscopy and germ theory, early bacteriologists and pathologists identified bacterial colonies associated with ulcer tissue samples on several occasions.[5] However, *H. pylori* was not successfully cultured until 1982, by Drs. Barry Marshall and Robin Warren.[2] The bacteria are especially difficult to culture even today because they grow 10 to 15 times more slowly than *Escherichia coli*, are microaerophilic, and require specific culture media. Interestingly, Marshall and Warren's early experiments were only successful when a plate that was accidentally left over the Easter weekend instead of being discarded after 48 hours without growth grew colonies.[2]

Furthermore, Koch's third postulate states that disease should be reproduced when the cultured microorganism is introduced into a healthy, susceptible host.[4] This postulate was memorably proven by Dr. Barry Marshall when he ingested a culture of *H. pylori* isolated from a patient with gastritis.[6] This was the only way to fulfill Koch's third postulate at the time because most *H. pylori* strains only infect humans.[6] This proved to be problematic for early animal studies on gastritis. Bacteria associated with inflamed gastric mucosa of rhesus monkeys and with human gastric tissue was studied by J.L. Doenges in 1938 and later by Freedberg and Barron in 1941.[5] Unfortunately, the bacteria from rhesus monkeys were histologically different from those in humans and bacteria were more difficult to identify in human tissue samples. Therefore, it could not be definitively concluded that bacteria caused gastric inflammation.[5] Later, when Dr. Marshall initially attempted to implement Koch's third postulate, he unsuccessfully attempted to transfer *H. pylori* cultures to piglets.[7] It was only more recently that more suitable animal models were developed.[8,9] Fulfilling Koch's postulates in the case of *H. pylori* was more difficult than for many other types of bacteria. These characteristics of *H. pylori* delayed the development of efficient methods for its study can partially explain why it was not easily established as one of the causes of peptic ulcer disease.

Although identifying *H. pylori* was difficult, once Marshall and Warren presented their findings to the world, other microbiologists verified and accepted them. However, gastroenterologists were more reluctant to accept this new information. Eventually, Drs. Marshall and Warren's work became formally recognized when they were awarded the Nobel Prize in Physiology or Medicine in 2005. In his Nobel Lecture, Dr. Marshall stated that the greatest obstacle to his work was that the cause of peptic ulcer disease was "already known".[10] When Warren and Marshall isolated and cultured *H. pylori*, H2 receptor antagonists were an established treatment for peptic ulcer disease.[11] The use of these drugs, which decreased acid secretion in the stomach, helped validate a theory of the etiology of peptic ulcer disease at the time: the stomach was secreting too much acid or the mucosal lining was less resistant to stomach acid, causing damage, ulcers, and pain. It was thought that intrinsic factors such as psychological stress or habits such as smoking made the stomach lining more vulnerable to damage.[11] In the case of ulcers caused by *H. pylori*, is suggested that it is mainly the bacterial infection which results in increased acid secretion due to the body's reaction to the infection.[12] Another predominant theory was that the stomach was too acidic for bacteria to grow.[11] Therefore, when bacteria were historically observed on samples of gastric tissue, they were thought to be artefacts.[5] Based on what had been traditionally taught in medical schools at the time of the discovery of *H. pylori*, Drs. Marshall and Warren's research would have been very extraordinary.

There are several others reasons why the medical community did not eagerly embrace Marshall and Warren's findings. To begin, testing for *H. pylori* was originally invasive and inaccurate and physicians did not

want to treat people with antibiotics unnecessarily for fear of antibiotic resistance.[13,14] Secondly, throughout the 1980s, the pharmaceutical industry continued to pursue the development of treatments that did not account for a bacterial etiology of PUD.[15] In 1988, proton pump inhibitors, such as omeprazole, were launched as an alternative to H2-antagonists.[15] The pharmaceutical company producing omeprazole organized an international symposium on PUD that year, featuring 33 notable gastroenterologists, yet only one of the 67 posters and abstracts presented dealt with *H. pylori*.[15] Finally, continuing medical education may not have been as effective at keeping physicians aware of changes in medical practices in the past as it is today.[16] It was traditionally based on self-directed learning and self-assessment, which could lead to deficiencies in medical knowledge and a lack of accountability.[16] In addition, some continuing medical education has historically been funded by the pharmaceutical industry, which could potentially introduce bias into the curriculum.[17] Accepting new theories that challenge previously-established beliefs can be very difficult. In this case, the lack of resources and information likely contributed to the delay in eradication of *H. pylori* becoming the standard of patient care for gastritis and PUD.

One of the most important factors in the acceptance of the eradication of *H. pylori* from the stomachs of symptomatic patients was the discovery that *H. pylori* is carcinogenic.[18] Research into the relationship of *H. pylori* and certain cancers began shortly after its discovery and by 1994 the International Agency for Research on Cancer reviewed the available literature and concluded that people infected with *H. pylori* are at increased risk for developing gastric adenocarcinoma and gastric B-cell mucosa-associated lymphoid tissue (MALT) lymphoma.[18] Gastric adenocarcinoma is a leading cause of cancer death worldwide and is typically associated with a poor prognosis.[19,20] Interestingly, MALT lymphoma can be treated by eradication of *H. pylori* and it has been suggested that *H. pylori* eradication could help prevent future gastric cancer.[21] Cancer is one of the most notorious diseases in our society, and the association of *H. pylori* infection with malignant disease was further evidence to support that an *H. pylori* infection requires medical attention.

The journey towards establishing an etiology for peptic ulcer disease was long and exceedingly difficult. *H. pylori* possesses many characteristics that make it difficult to culture and establish a cause-and-effect relationship with peptic ulcer disease. Furthermore, the idea was unappealing to many because it challenged previously established views and challenged physicians to revisit traditional medical knowledge. In order to truly provide the best possible care to patients, physicians must embrace the dynamic, surprising, and ever-changing aspects of the field of medicine. With improved continuing medical education and with improved access to medical journals online, this has never been more possible. Many fields of medical science, including *Helicobacter pylori*, are still active areas of research locally and globally and emerging knowledge will certainly continue to challenge physicians to improve medical practices in the future.

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