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The MJM is a biannual medical journal that publishes cutting-edge research conducted by academics around the world. We have been commended by various medical journals. The Royal College of Physicians and Surgeons of Canada commented "…[we are] equally impressed by the quality of the contents and by the rigorous editorial policies". We have also been mentioned by the New England Journal of Medicine as "the only regularly published and widely distributed student-run medical journal in the world". [Volume 336:885-886 March 20, 1997 Number 12].

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This year, we are in the process of undergoing a major reform. We are in the process of adopting theme-based approach. Upcoming issues will be organized into sections with a focus of areas such as Neuroscience, Cancer, Public Health, Bioethics, and Biotechnology. In particular, new issues will feature Public Health and Neuroscience.

The Journal is comprised of various sections that address a variety of subjects from advances in cancer research to relevant ethical issues. The Journal of the American Medical Association has recognized the MJM for "The original articles [that] have maintained a high level of scientific merit and quality. The review articles have focused on topical discussions on a wide range of disease processes with some introduction of new pharmacological agents."

The goal of the MJM is to provide its readers with a global perspective of clinical medicine, accentuate pressing social concerns and highlight new scientific breakthroughs. The MJM addresses diverse contemporary issues; from cancer research to ethical issues, our articles are relevant to medical students and health professionals across the globe.

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The executive committee further extends their gratitude to all those who worked hard to make this issue of the McGill Journal of Medicine a reality.

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LETTER TO THE EDITOR

Thank you letter for previous issue on aerospace medicine

Mark Lipset

As a McGill University alumni and a participant in the Canadian Space Agency's Aerospace Medicine Elective and the International Space University Space Studies Program, I would like to thank you for your engaging issue on aerospace medicine (Issue 13.2).

The aerospace medicine issue of the MJM brought to light how fortunate we are as Canadians to live in a country in which the fruition of our dreams are supported though entities such as the Canadian Space Agency. The Canadian Space Agency has been a driving force in Canadian aerospace development and education for decades. Dr. David Saint-Jacques' and Dr. Robert Thirsk's articles touched on the similarities between astronaut and physician training; similarities that are the foundation of the Royal College of Physicians and Surgeons of Canada's (RCPSC) physician development CanMEDS roles (which underscore the roles of being a medical expert, communicator, collaborator, manager, health advocate, scholar, and professional). These roles provide the fundamental backbone to becoming an excellent professional and providing the highest quality service.

Through their numerous research initiatives, the Canadian Space Agency has provided opportunities for physicians to enhance these CanMEDS roles to an even greater level, as illustrated by Jason Clement. This synergistic relationship between space and medical education is an enviable construct that we as Canadian medical students and residents should take full advantage of. In light of this, I would propose that the RCPSC, individual medical schools, and the Canadian Government at large recognize this synergistic relationship and capitalize on it in order to provide a greater opportunity to enhance the well-rounded education of Canadian physicians so that they may provide the best level of patient care.

The financial investment of tax payer's dollars to the Canadian Space Agency to support research and education in aerospace medicine not only provides unique learning experiences for passionate and accomplished young professionals and students, but also provides a "double-return" on investment by enhancing both Canada's space program and facets of healthcare delivery. Thus, this continued financial investment in aerospace medicine and subsequent creation of learning and growth opportunities is imperative to the further growth of future aerospace leaders and health professionals.

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CASE REPORT

Type IV paraesophageal hiatal hernia and organoaxial gastric volvulus

Alison Zachry, Alan Liu, Sabiya Raja, Nadeem Maboud, Jyotu Sandhu, DeAndrea Sims, Umer Feroze Malik*, Ahmed Mahmoud.

ABSTRACT: Organoaxial gastric volvulus occurs when the stomach rotates on its longitudinal axis connecting the gastroesophageal junction to the pylorus. With that, the antrum of the stomach usually rotates in the opposite direction in relation to its fundus (1). This phenomenon has often been known to be associated with diaphragmatic defects (2) Importantly, abnormal rotation of the stomach of more than 180° is a life threatening emergency that may create a closed loop obstruction which may result in incarceration leading to strangulation, and hence, a surgical emergency. We present the case of a middle-aged female who presented with organoaxial gastric volvulus and had an associated Type IV paraesophageal hiatal hernia that was treated electively. Normally an emergent gastric volvulus is diagnosed via Borchardt's classic triad (epigastric pain, unproductive vomiting and difficulty inserting a nasogastric tube); however in this patient the nasogastric tube (NGT) was passed into the antrum which allowed additional time for resuscitation with fluids and other symptomatic relief.

CASE REPORT

A 56 year old Caucasian female presented with inability to eat or drink due to persistent nausea and small amount of non bilious, non bloody emesis. The patient reported no bowel movements and an inability to pass flatus for one week. Patient had no other symptoms of intestinal obstruction and denied any urinary symptoms at that time.

Her past medical history included a chronic hiatus hernia of unknown etiology. The patient did not recall any further details regarding this hernia at the time. No previous images were found. Past surgical history included a laparoscopic cholecystectomy. She denied smoking, drinking alcohol, using recreational drugs, or having a relevant history. Aside from obstructive gastrointestinal symptoms, a systemic review was negative. Abdominal examination revealed hyperactive bowel sounds. The patient's abdomen was mildly distended in the epigastric region. Her abdomen was soft with tenderness upon palpation in both the left upper quadrant and epigastric regions. There were no signs of an acute abdomen or peritonitis.

A complete laboratory workup revealed mild hypokalemia with no other significant findings. ABG and lactate levels were not obtained at that time. Chest and abdominal radiographs showed an obvious stomach shadow in the thoracic area (Figures 2a and 2b). Computed tomography (CT) scans of the abdomen and pelvis showed a large hiatal hernia in the vertical sections (Figures 1a, 1b and 1c) however, it was even more apparent in the horizontal sections (Figures 3a and 3d). Air-fluid levels were seen in the thoracic cavity extending left of the midline above the diaphragm at the level of T6 approximately. Fluid and a small amount of air was also visible in the abdominal cavity in the left

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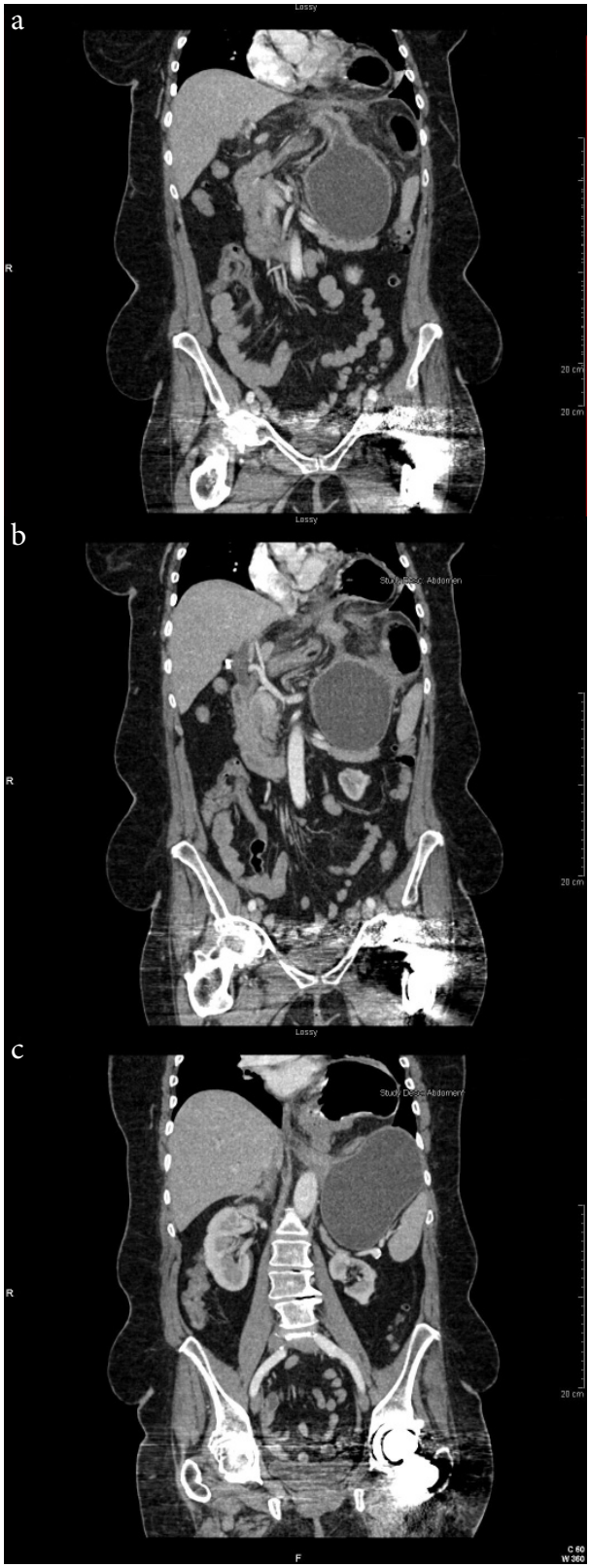

Figure 1 **a)** Computed tomography (CT) scan of the abdomen showing a large hiatal hernia in the vertical section.. **b)** Different view of Computed tomography (CT) scan of the abdomen and pelvis showing a large hiatal hernia in the vertical section. **c)** Computed tomography (CT) scans of the abdomen and pelvis with a large hiatal hernia in the vertical section.

upper quadrant below the diaphragm. Furthermore, the antrum was identified in the thoracic cavity and the fundus was identified in the abdominal cavity. Organoaxial gastric volvulus was diagnosed radiographically as the stomach appeared twisted longitudinally.

Subsequently, the patient was admitted for close observation and further monitoring. An NGT was placed in the emergency department to decompress the stomach. When suctioned, the NGT removed 800 mL of clear gastric nonbilious fluid. An esophagogastroduodenoscopy (EGD) revealed scattered white exudation and circumferential inflammation of the esophageal mucosa, in which the severity was noted to be increased towards the distal end of the esophagus. Pressure at the lower esophageal sphincter was nearly absent. The distal gastric anatomy was distorted by the presence of a paraesophageal hernia. With slight resistance, the EGD passed into the antrum, which was noted to be entirely located within the thoracic cavity. Images of the antrum revealed diffusely granular and friable mucosa, and multiple small superficial mucosal erosions. During the EGD, the diseased mucosal margins were biopsied. Due to the marked anatomical distortions, the pylorus could not be identified. Pathology results showed chronic ulcerative gastritis with focal acute inflammatory changes. Biopsies were negative for Helicobacter pylori, dysplasia or malignancy.

After initiating conservative management and evaluating all treatment regimes, we concluded that the most necessary treatment was surgery. The patient was then taken to the operating room for reduction of the hiatal hernia and primary repair with gastropexy and pyloromyotomy of the incarcerated hiatal hernia. The reduction included much of the greater omentum in addition to part of the colon, which had also herniated into the thoracic cavity. The stomach was noted to be very large and floppy. The repair was successfully completed without complications. Following the procedure, complete relief of all gastrointestinal symptoms were achieved. Repeat CT scans confirmed resolution of the gastric volvulus and hiatal hernia (Figures 4a and 4c).

DISCUSSION

The very well known enigma, gastric volvulus, was first described by Berti in 1866 while performing a postmortem exploration (3). In 1896, Berg performed the first successful operation on a patient with gastric volvulus (4). In 1904, Borchardt described the classic triad of this condition: severe

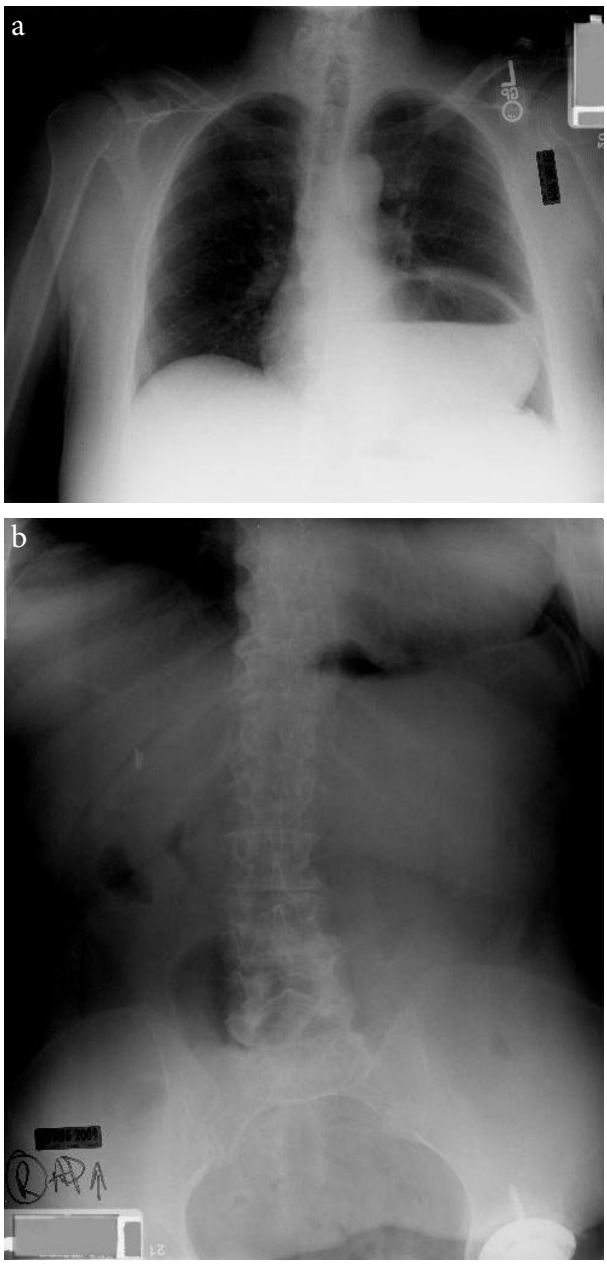

Figure 2. a) Chest x-ray showing stomach shadow in the thoracic area. **b)** Chest and abdominal radiograph revealing stomach shadow in the thoracic area.

epigastric pain, retching without vomiting, and the inability to pass an NGT (5). With technical advancements, surgeons have described this entity in various settings enabling physicians to more efficiently and effectively manage patients with this condition.

On occasion, a gastric volvulus may form as a complication of a hiatal hernia. This most commonly presents with the stomach displaced through the esophageal hiatus of the diaphragm into the thoracic region. Three different types of gastric volvuli exist: organoaxial, mesenteroaxial, or a combined volvulus. There are four different types of hiatal hernias that may result in a gastric volvulus: sliding, paraesophageal, combination of sliding and paraesophageal, or complex paraesophageal hiatal hernia.

Type I, also known as sliding hiatal hernia, is the most common type and usually associated with gastroesophageal reflux disease (GERD). The stomach, or part of it, usually slides in and out of the hernia. When a part of the stomach squeezes through the hiatus into the thoracic cavity, adjacent to the esophagus, it is called a Type II or paraesophageal hiatal hernia. A combination of sliding and paraesophageal hiatal hernias is categorized as Type III. If additional abdominal contents are found in the thoracic cavity then a diagnosis of Type IV or complex paraesophageal hiatal hernia is given. A Type IV hernia may include the whole stomach, the small and large bowels, spleen, pancreas, or liver (6).

A patient may present with one of the four types of hiatal hernias in addition to having a gastric volvulus. Organoaxial gastric volvulus occurs when the stomach rotates on its longitudinal axis connecting the gastroesophageal junction to the pylorus. With that, the antrum of the stomach usually rotates in the opposite direction in relation to its fundus (1,7). It is the most common type of gastric volvulus, making up 59% of all cases (8). In a mesenteroaxial volvulus, the stomach rotates around the gastrohepatic omentum in a left/right or right/left direction (9). The mesoaxial gastric volvulus makes up 29% of all cases of gastric volvuli (8). The combined form is a rare occurrence in which the stomach twists in a mesentericoaxial and organoaxial fashion. Regardless, in all types, the patient may become symptomatic from vascular compromise or gastric outlet obstruction and present with the classic Borchardt's triad. With vascular compromise the mortality rate is nearly 30%, making a gastric volvulus an emergent diagnosis (10). In this case, the patient suffered a type IV paraesophageal hiatal hernia with organoaxial gastric volvulus. With emergent diagnosis, gastric ischemia was prevented.

The paraesophageal hernias, as seen in our patient, tend to enlarge overtime, increasing the risk of gastric volvulus. Once this occurs, there is an even greater risk of incarceration, possible strangulation, or even perforation. Surgical management is indicated in roughly 5% of paraesophageal hernia cases (11).

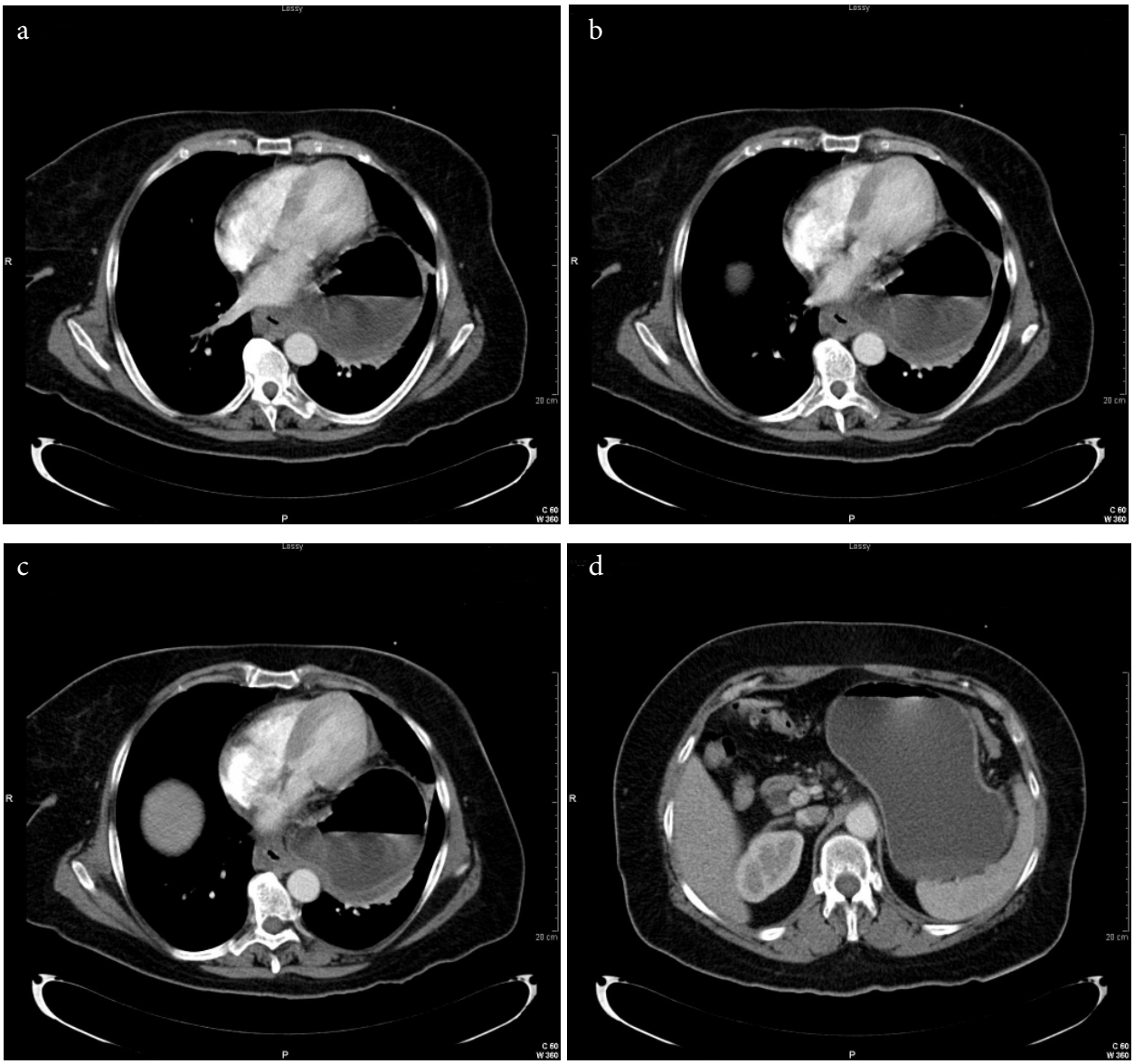

Figure 3: a) Horizontal section of the Computed tomography (CT) scan of the chest showing a large hiatal hernia **b)** Computed tomography (CT) scans of the chest showing a large hiatal hernia, a horizontal view. **c)** Computed tomography (CT) scans of the chest and abdomen showing a large hiatal hernia (Horizontal view). **d)** Horizontal Computed tomography (CT) scan of the abdominal area showing a hiatal hernia.

Due to the possibility of mortality with hiatal hernias, it is important for clinicians to recognize the various factors that may contribute to their development. These include: trauma, an inherent weaknesses in the surrounding muscles, straining during heavy weight lifting, having an unusually large hiatus from birth, or persistently intense pressure on the surrounding muscles, which may occur with vomiting or straining during a bowel movement. Additional risk factors include age (>50 years), obesity, pregnancy, and smoking (12).

Patients with hiatal hernias vary widely in their experience of symptoms. They are usually related to the development of GERD, which may often occur before or after the development of the hernia. These symptoms may include heartburn, gastric discomfort, chest pain, increased belching, hoarseness, throat irritation, dysphagia, haematemesis or malaena. However, it is also very common for patients to be completely asymptomatic. As in the case presented above, it is worth noting that the severity of symptoms does not necessarily correlate with the severity of the hernia.

A diagnosis of a hiatal hernia and gastric volvulus may be suspected based on clinical presentation, however, a thorough workup

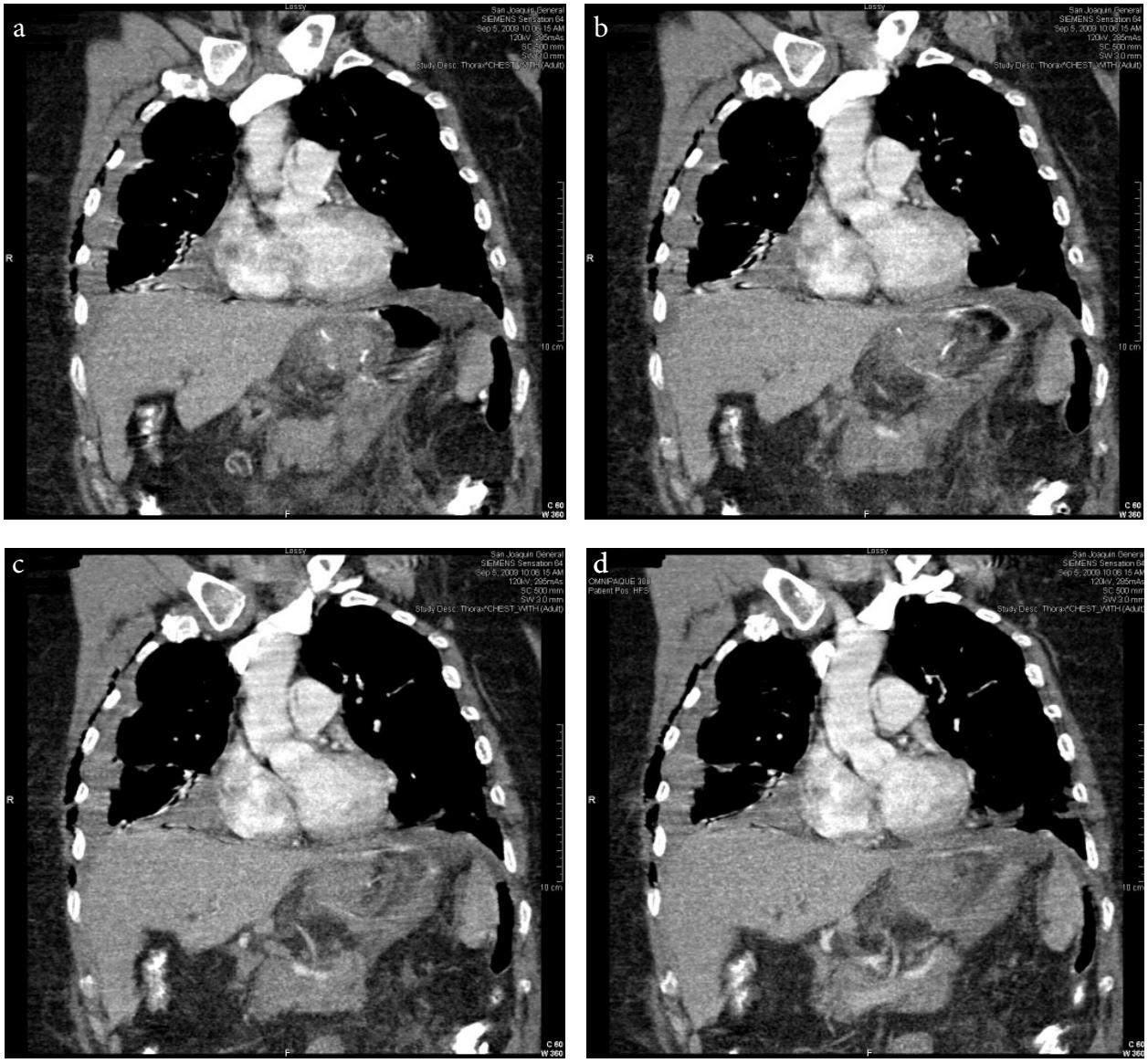

Figure 4: a) Thoraco-abdominal vertical view of the CT scan obtained after the surgical treatment confirmed resolution of the gastric volvulus and hiatal hernia. **b)** Thoraco-abdominal vertical view of the CT scan confirmed resolution of the gastric volvulus and hiatal hernia after the procedure. Post surgical changes are also apparent. **c)** Thoraco-abdominal vertical view of the CT scan confirmed resolution of the gastric volvulus and hiatal hernia after the procedure. Stomach is apparent in the abdominal cavity after primary gastropexy. **d)** Complete esolution of the gastric volvulus and hiatal hernia is shown in the CT scan, vertical view. Signs of primary repair with gastropexy and pyloromyotomy are also apparent upon close evaluation.

including imaging studies of the chest and abdomen with barium upper gastrointestinal series should be ordered. Radiological signs of gastric volvulus include a double air-fluid level on upright films, inversion of the stomach with the greater curvature above the level of the lesser curvature, positioning of the cardia and pylorus at the same level, and downward pointing of the pylorus and the duodenum (13). In addition, chest radiography may reveal a retrocardiac air-filled mass and abdominal films may reveal an increased soft tissue density in the upper abdomen consistent with a distended fluid filled stomach (2). The barium studies are both sensitive and specific and can confirm a diagnosis (2). It is important to rule out different etiologies including unknown masses and malignancies, which may be confirmed with endoscopic biopsy. Treatment depends on the severity of the hernia and can range from lifestyle changes to surgical intervention as seen in our patient.

Patients diagnosed with hiatal hernias should first be counseled on the importance of lifestyle changes to manage their condition. This includes a high fiber diet to decrease the amount

of straining during bowel movements and avoiding foods such as alcohol, chocolate, citric juice, and tomato-based products as these may decrease pyloric sphincter tone. Patients should also avoid eating large meals and eating too quickly as this stretches the stomach and relaxes the lower esophageal sphincter. Moderate exercise should be encouraged to maintain a healthy body mass index (BMI). Medications are also helpful in managing this condition and may include antacids, H-2 receptor blocking drugs or proton pump inhibitors. Prokinetic agents are also warranted in patients with mild symptoms but long term use is discouraged due to their potentially fatal complications. In some cases, endoscopic repair may be warranted before surgical intervention is necessary (14).

A minority of patients may require surgery. These patients have usually failed to improve even after aggressive proton pump inhibitor treatment and lifestyle modifications. Other groups may be those suffering from pulmonary complications such as asthma, aspiration pneumonia, chronic cough or hoarseness related to reflux disease. If the patient is found to have a gastric volvulus, surgical intervention is highly indicated as the mortality rate without it has been reported to be as high as 80% (15,16,17,18). In these cases, three types of surgical approaches may be performed. These include Nissen Fundoplication, Belsey (Mark IV) Fundoplication and Hill repair approach (19).

Our patient suffered a type IV paraesophageal hiatal hernia with organoaxial gastric volvulus. A unique discovery in this case was our ability to advance the NGT (20) which allowed more time for additional studies, thus sparing the patient from an emergent invasive surgical procedure. With additional time, we were able to adequately resuscitate the patient and provide comfort measures as well as optimizing the patient for surgery.

ABBREVIATIONS

ED-Emergency Department, CT-computer tomography, BMI-Body Mass Index, GERD-gastroesophageal reflux disease, NGT-nasogastric tube, EGD-esophagogastroduodenoscopy.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest

CONSENT

Written informed consent was obtained from the patient for publication of this case report and accompanying images.

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CASE REPORT

An Atypical Case of Myasthenia Gravis: Purely Bulbar in a Young Male

Muhammad Amer Saleem, Faizan Pervaiz, Anum Yousaf, Muhammad Amer Saleem

INTRODUCTION

Myasthenia Gravis (MG), an uncommon autoimmune syndrome caused by the failure of neuromuscular transmission, results from binding of autoantibodies to proteins that are involved in signaling at the neuromuscular junction (1). Acquired myasthenia gravis (MG) is an uncommon disorder (occurring in 200–400 cases per million people) (2).

Its symptoms are caused by a characteristic muscle weakness that worsens after repeated use. In most cases of MG, the initial sign is ocular weakness of any sort. The next most common sign is bulbar weakness (5) . In about two-thirds of patients, the extrinsic ocular muscles (EOMs) present with the initial symptoms. These symptoms usually progress to other bulbar muscles and limb muscles, resulting in generalized MG (gMG). In about 10% of MG patients, symptoms remain limited to the EOM, and this condition is termed ocular MG (oMG)(3,4). However in cases where weakening of other striated skeletal muscles occurs, this is referred to as generalized MG. We present a rare case of early onset Myasthenia Gravis affecting a young male with only and purely bulbar involvement.

CASE REPORT

A 22 year old male presented in the Ear Nose Throat out-patient department of Holy Family Hospital complaining of dyphagia and dysarthria and no significant past medical history. On examination, orophyrangeal edema was suspected, for which Coamoxiclav (Augmentin ® 625mg) and Citrizin (Sedil ® 10mg) Serratiopeptidase (denzin ® DS) were prescribed.

On the first week of follow-up, the symptoms of dyphagia and dysarthria had worsened and there was evidence of facial muscle weakening. The patient was referred to the neurology department. The patient had no significant past medical or surgical history. He denied smoking, IV drug abuse, alcohol abuse, and was sexually inactive. The family history was unremarkable as well. There was no history of fever, cough, cold, or recent upper respiratory tract infection. He had no known drug allergies and his current medications consisted of those prescribed for orophyrangel edema.

On physical examination, the patient was alert, awake and oriented, and his blood pressure, heart rate, respiratory rate, SpO2, and temperature were within normal limits. On neurological examination the patient showed signs of bulbar weakness, however, there were no other signs and symptoms to direct a diagnosis. There was no external ocular weakness, motor weakness, muscle wasting, sensory deficits, or sphincter dysfunction. He was diagnosed with a rare descending form of Gullian barre syndrome and an NCS was ordered to confirm the diagnosis. The NCS was negative for Gullian Barre syndrome. However, decremental response was seen in the proximal muscles at 3 Hz, suggesting Myasthenia Gravis (MG). To confirm MG, an acetylcholine receptor antibody titer was ordered and found to be 60nmol/L (where a measurement of less than 0.25nmol/L is negative). Despite this significant elevation, no signs of generalized myasthenia were detectable.

The patient was treated with acetylcholin-

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esterase (AchE) inhibitor, Pyridostigmine (Amygra ® 360 mg per day) and steroids, Prednisolone (Delta Cortef ®) over a period of 4 weeks. The patient was unable to talk, chew, swallow, or demonstrate proper facial expressions. However, there were no signs of ptosis, diplopia, difficulty seeing, double vision, dizziness, unsteady gait, fatigue, or any difficulty maintaining balance. The patient's condition did not improve much with Acetylcholinesterase (AchE) inhibitors and steroids. However, he was able to ingest liquids, consume a soft diet, and speak a few sentences after medication.

The patient's complete blood count was normal with no eosinophilia. His electrolytes were normal as was his thyroid function test, liver function test, coagulation profile, pulmonary function test. His chest CT scan with contrast showed no evidence of thymoma. At follow-up visits, the patient remained otherwise healthy with no evident development of other myasthenic signs except bulbar weakness. This case is atypical since bulbar onset MG does not usually persist with complete absence of other myasthenic signs and symptoms (of the generalized form), especially if it is an early-onset MG.

DISCUSSION

Myasthenia Gravis is a rare neurological disorder involving neuromuscular junctions and most commonly affects young females or older men6. Those having history of some autoimmune disorder are at higher risk for MG (7).

The most common initial presentation of MG is ocular weakness (5,8). Ocular weakness most commonly manifests itself as ptosis in 90% of cases. However an accommodative/vergence insufficiency or a concomitant or noncomitant oculomotor paresis may also be seen (9). Generalized MG eventually develops in 50% of those who manifest an ocular sign, whereas others only retain the ocular weakness and are thus considered as cases of ocular MG (3,4). The second most common presentation of MG is bulbar weakness. However, bulbar weakness usually progresses to generalized myasthenia gravis (3,4,5). Fatigue is the hallmark of any kind of myasthenia (10). Although fatigability of peripheral skeletal muscle is the hallmark of the disease, it can be absent in the bulbar forms. Isolated bulbar presentation is common in late-onset MG and may be confused with diseases of the oropharynx and other neurological conditions (11,12,13). MG that develops after the age of 50 is said to be late onset MG (14).

In the case of early onset MG, isolated bulbar presentation and its persistence are not commonly seen. In the present case report, the patient was a 22 year old male with an unremarkable past medical or family history, and as such, was unlikely to develop MG. Before a diagnosis of MG was made, orophyrangeal edema and descending gullian barre syndrome were also suspected. Diagnosis of MG was confirmed on the basis of a laboratory workup, which showed a significant elevation of the for acetylcholine receptor antibody. However, there were no signs and symptoms of fatigue, nor were there ocular signs and symptoms. The most widely accepted classification of MG is based onthe Myasthenia Gravis Foundation of America's Clinical Classification (15):

Class I: Any eye muscle weakness, possible ptosis, no other evidence of muscle weakness elsewhere.

Class II: Eye muscle weakness of any severity, mild weakness of other muscles

- Class IIa: Predominantly limb or axial muscles
- Class IIb: Predominantly bulbar and/or respiratory muscles

Class III: Eye muscle weakness of any severity, moderate weakness of other muscles

- Class IIIa: Predominantly limb or axial muscles
- Class IIIb: Predominantly bulbar and/or respiratory muscles

Class IV: Eye muscle weakness of any severity, severe weakness of other muscles

- Class IVa: Predominantly limb or axial muscles
- Class IVb: Predominantly bulbar and/or respiratory muscles (Can also include feeding tube without intubation)

Class V: Intubation needed to maintain airway.

In all classes, eye muscle weakness is standard along with varying weakness of limb, axial, bulbar or respiratory muscles. In the presented case study, only bulbar weakness not responsive to standard medications for MG was present. Although the bulbar form of MG is usually seen in cases of late-onset myasthenia, the presented case study provides an interesting example of bulbar weakness in a case of early onset MG.

CONCLUSION

It is evident from the case report that early onset MG can present in strictly bulbar form as well, which has not been reported elsewhere up until now. Therefore, in the case of any bulbar weakness with no signs and symptoms of fatigue, limb weakness, and ocular involvement, MG should not be ruled out. The prognosis for this patient does

not seem hopeful given his non- responsiveness to therapy. Further study is required to find out the cause of therapeutic failure in this case. The continued absence of ocular weakness, fatigue, and generalized symptoms in his six month follow-up visit is astonishing, as far as early onset myasthenia is concerned. Further follow-up of three years or more is indicated for this patient since previous reports show increased risk of developing the generalized form of the disorder during this time period.

ACKNOWLEDGEMENTS

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CONSENT

Written informed consent was obtained from the patient for publication of this case report.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest

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REVIEW ARTICLE

Email in Medical Practice: A Critical Review

Alysha Nensi and Natasha Chandok

ABSTRACT: Email between patients and physicians can be an effective means of communication and health care delivery, but concerns over security, privacy, feasibility, and legality prevail. This paper reviews the limited literature in this area, highlighting our current understanding of the prevalence of email in clinical practice, patient attitudes toward email communication, and the impact of email communication on patient outcomes. While there is a paucity of data on the role, benefits, and risks of email communication, patients and physicians alike should consider secure email as a convenient tool for communication. Physicians require further guidelines on appropriate uses of email in clinical practice to best enhance patient autonomy, preserve patient confidentiality, and comply with current medico-legal standards.

Key-words: Physician Patient Relationship, Communication, Electronic Mail, Ethics, Medical, Delivery of Health Care

INTRODUCTION

The patient-physician relationship is fundamental to the practice of medicine and medical ethics. A physician has an ethical obligation to deliver health care in a manner in which the dignity and privacy of their patients is upheld. While modern medicine rests on the four pillars of non-maleficence, beneficence, autonomy, and justice, our society places increasing value on patient autonomy. Communication is at the heart of patient autonomy; it allows for the exchange of information and empowers patients to be active participants in their own care. Communication between both patient and physician is enhanced when both parties share mutual respect, knowledge, trust, and values.

A number of issues, however, complicate the patient-physician relationship. In busy ambulatory clinics, for example, health care providers may not have the ability to spend a sufficient amount of time with each patient. Physicians may need to see too many patients in a given time frame, and are typically burdened with extensive paper work and other documentation that takes time away from face-to-face patient-physician encounters. Different settings of health care may add further complexity to the patient-physician relationship. For instance, in the hospital ward or intensive care unit setting, a number of other individuals may be involved in the care of a patient, including relatives, friends, nurses, social workers and other specialists. With multiple participants, it may be difficult for patients and their families to assimilate information and identify the most responsible physician. Another barrier to communication is classism; patient and/or physicians may perceive physicians as superior on the basis of education, expertise and socioeconomic status. Likewise patients may be perceived as inferior to their doctors on the basis of their physical or emotional suffering, and potential lack of knowledge and lower socioeconomic status. These types of barriers make it difficult for patients to ask questions and receive the information they need to be active participants in their own care.

The communication between patients and physicians faces new challenges in this information era, where patients are more educated and involved

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with their health care and have access to a wealth of medical knowledge at their fingertips because of the internet. With email and other communication interfaces on the internet, patients can also reach self-help and support groups and medical experts from around the world. Despite major advancements in communications, many patients and physicians do not communicate with one another via email, and medical laws have not kept pace with changes in communication technologies for the delivery of health care.

Email offers a number of potential advantages to enhancing the patient-physician relationship. For example, patients and physicians can connect more efficiently with one another, unlike telephone encounters where both parties need to be available at the same time. Email also offers the opportunity for patients to receive more education and general advice, which may be restricted in a face-to-face or telephone exchange where obstacles such as shortages of doctors, and time restraints on clinic appointments, are all too common. As such, email communication may improve patient satisfaction, compliance with therapy, minimize preventable errors, and could potentially be cost-effective. Email may also foster a patient's personal involvement in their own care and encourage self-care. To date, the impact of email on the therapeutic relationship between the physician and patient has not been thoroughly studied.

Physicians and patients need guidelines on the appropriate role of email in health care delivery. Email is likely a suitable forum through which a patient can make an appointment, ask a question or clarify an instruction, receive education, receive reminder for appointment, and enable a health care provider to monitor progress while undergoing treatment. However, it is important to note that email should not serve in a capacity which jeopardizes the delicate balance of the patient-physician relationship. As such, email should not substitute a face-to-face encounter where complicated or abnormal tests are reviewed, or a diagnosis, prognosis, or treatment information is shared with a patient.

Issues of security and confidentiality are primary concerns of patients and physicians who communicate with one other via email. Exposure of confidential health information to a patient's employer, another family member, marketer, or insurance company can have personal ramifications for a patient, and result in litigation against a physician. Ideally, patients should have a dedicated email address for the exchange of medical information with their doctor, and data containing a patient's health information should be encrypted. For example, an email interface could help triage messages through the use of a drop down menu to indicate the level of urgency of the message. An email interface can automatically instruct a patient to call their doctor's office rather than submit an email for an urgent health care matter, and interfaces can limit the number of words included in a health care message so that physicians do not need to spend an elaborate amount of time on each email. Thus, in light of these issues, individual health care institutions and medical societies may need to consider developing training protocols and general policies to protect a patient's privacy.

There are a number of potential pitfalls to email communication between patients and their doctors as well. For example, it is unknown whether email may lead to an increase health care utilization, and how time intensive email communications will be for health care providers in busy practices. There are also possible medico-legal ramifications if physicians do not respond in a timely manner, or if advice dispensed over email is unclear for patients. Another important concern is that email communication could lead to health care disparities between patients of higher versus lower socioeconomic status, or patients who do not speak English fluently and, therefore, may not be able to compose an email their physician.

For a myriad of reasons, some patients and physicians are reluctant to embrace email as a means of communication. That being said, email may potentially offer an opportunity to improve patient satisfaction with health care and enhance communication in the patient-physician relationship. The purpose of this paper is to review the current understanding of the impact of email between patients and physicians for the delivery of health care.

METHODOLOGY

Using MEDLINE with no date limits, a literature search was conducted using the medical subject headings: "electronic mail", 'physician patient relationship", "ethics", "communications", and "delivery of health care". Studies were screened upon review of their title and abstract. After a review of the article, studies were included if they met the following inclusion criteria: the article was written in English; the patient population was

greater than or equal to 18 years of age; outcomes included patient use, satisfaction or interest with electronic mail as a means for communication; or outcomes included the impact of electronic mail on medical management. Editorials and clinical review articles generated from the search were excluded but nevertheless reviewed for their content and reference lists, which were examined to identify any original articles which fulfilled inclusion criteria not found on the original search.

RESULTS

The search yielded 10 studies that fulfilled the inclusion criteria. Three studies examined the prevalence or patient attitudes of email usage in clinical practice. In a cross-sectional cohort study of all adult patients at an integrated health-care delivery system, Ralston et al. found that only 14% of 25,075 patients exchanged one or more e-mails with their primary or specialty care provider over a 14 month period (1). Factors associated with an increased likelihood of exchanging secure email included female gender, greater overall morbidity, and the health care provider's use of email with other patients (1). Less secure email use was associated with patient age over 65, and Medicaid insurance rather than commercial insurance (1). In a second cross-sectional study in 2005 from a large multispecialty group practice, investigators found that while 58.3% of 186,000 patients had email access, only 5.8% reported ever using email to communicate with their physician(s) (2). Patients were most willing to use email to obtain cholesterol and blood sugar tests, but were less keen on receiving emails containing medical imaging (e.g. computed tomography scan) test results (2). A third study from 1994, albeit now outdated, found that 46% of patients in an internal medicine practice regularly used email, and 89% reported email use only at work (3). 51% reported that they would use email all the time or most of the time if it was available as a means of communication with their health care providers (3).

Three studies examined patient use of email, and attitudes toward incorporating email into their health care delivery strategy. In a 2008 study in an outpatient rheumatology clinic, 74.5% of patients reported that they had internet access, and 72% of the 127 patients stated they would want to communicate with their rheumatologist with email, while only 28% reported a complete lack of interest in email communication (4). 41% of respondents identified privacy as a major concern with email (4). Younger adults and patients whose insurance would cover email communications (as opposed to paying out of pocket) were more likely to desire email communication with their rheumatologist. In this study, interest in emailing their rheumatologist or having access to the internet was not associated with a patient's education, income, or gender. In a third study, a randomized controlled trial from the University of Colorado, investigators examined the impact of an internet-based patient portal on patient satisfaction with access to their clinical care versus standard-of-care telephone communications (5). Patients in the "portal" group, who had access to secure emails to their health care providers, reported improved communication (44% versus 12%, $p<0.001$) and higher satisfaction with their overall health care (59% versus 48%, $p=0.04$) as compared to the control group (5).

One study examined the content of emails by health care providers and health care staff, providing insight into the proportion of emails a primary care practice composes to specifically communicate with patients and their families. In a diabetes care clinic at an American academic medical center, 27,061 emails exchanged over a 6 month period in 2003 between health care providers and staff caring for a cohort of 639 patients were analyzed to determine their content (6). Stiles et al. found that 47.2% of emails were done to communicate with patients, families, and other providers; the remainder of the emails were done between clinic staff for a variety of reasons such as documentation, logistics, and support functions (6).

One study investigated the use of unsolicited email from patients or their families who were seeking medical advice from expert physicians who published their research on the internet, on the only internet site in 1995 with a primary focus on cardiac arrhythmias (3). This study documented 70 unsolicited emails from 39 patients and 20 family members over a 12 month period; 22 inquiries received specific follow up advice (3). This study demonstrates that some patients and their families are capable of and interested in seeking subspecialty medical advise over email, and that physicians require guidelines on the appropriateness of dispensing recommendations over email (3).

Two studies investigated the role of email in enhancing patient care outcomes. In a trial of 83 adults with type 2 diabetes mellitus, Ralston et al. randomized patients to receive usual care plus web-based care versus usual care alone (7). In this study, the web-based care included patient access to medical records, secure email with providers,

email feedback on blood glucose readings, and an interactive online diary to enter health care information such as diet and exercise (7). Patients who received access to secure web communications had a statistically significant improvement in their glycemic control (hemoglobin A1C decline of 0.7%, 95% CI 0.2 – 1.3) as compared to patients who received standard of care only (7). In a second study focusing on email in an addiction medicine clinic, Collins et al. found that email communications between patients and their specialist can enhance treatment for substance dependency through a variety of means (8). For example, with the free ability to email their providers, patients can share daily self-assessments and receive continual encouragement and advice to amplify their odds of maintaining sobriety (8).

DISCUSSION AND CONCLUSION

The technology exists for secure, efficient electronic communications between patients and their health care providers through a variety of means, including email. While issues of concern over patient privacy must be discussed between the patient and health care provider, it is clear that many patients are interested in incorporating email communication into their health care experience. Email holds the potential to significantly improve health care delivery by facilitating communication between patients and their providers, thus enhancing the patient-physician relationship and improving patient satisfaction. Furthermore, email communications can also lead to improved clinical outcomes for patients.

Unfortunately, there is a paucity of data examining the role of email, and the impact of email on health care and patient outcomes. The assessment of the literature on this topic conducted for this review generates a number of questions, including the role of patient gender, socioeconomic status, and computer literacy on email preference for health related communications with practitioners. Further studies are needed to assess these important questions, as well as the cost-effectiveness and broader role of email in clinical practice.

Additionally, data is needed to guide expert panels in the development of guidelines for practitioners on the appropriateness and use of email in clinical practice. It is particularly imperative that the adoption of email in standard communications between physicians and patients not impinge upon the patient-physician dynamic or generate health disparities among patients of lower socioeconomic status. Despite the many challenges in establishing email as a widespread standard adjuvant practice in health care delivery, email has the potential to aid in health promotion and disease prevention.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

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ORIGINAL ARTICLES

Me and my "benign" brain tumor: Musings of a patient

Brigitte Rieger

I was in constant state of severe pain. After undergoing many tests, I was diagnosed with a brain tumor. The assessment at that time was that the tumor was benign, so it sounded like there was nothing to worry about. The tumor was operable but surgery would carry some risks, and it was thus recommended that the tumor be monitored.

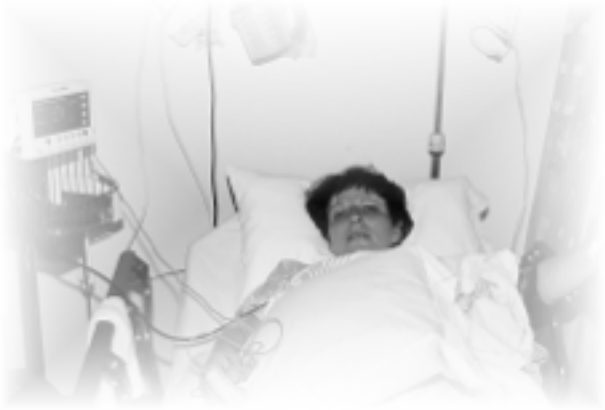
However, the reality of my benign brain tumor led to drastic changes. Not only was my life turned upside down, but suddenly I felt like I was having conversations in a foreign language. All of a sudden, I felt that this thing in my head was terrorizing me and that it wasn't fair. I felt cheated out of the chance to fulfill my dreams and to live the life I wanted.

I was embarrassed and ashamed, but as an energetic, independent and very strong woman who was successful in a male-dominated industry, I was determined to handle the situation all by myself. I really didn't want anything from anybody, and I refused to let anyone be a part of my life as it was. In my mind, I thought that if I could tough it out and pretend everything was fine, no one would worry about me. I refused to cope with my tumor and didn't want to know anything about it. I chose to put a wall around myself that kept me completely alienated from my own feelings, emotions and pain. My philosophy was that, basically, my life was not going to change.

However, my situation went from bad to worse, and my constant severe pain only intensified. It felt as though I was losing everything: my independence, my dignity and my health. Everything that could go wrong went wrong—one thing after another. It seemed it would never stop—like being on a runaway train. Worst of all, I felt like I was going insane from all the pain.

Finally, I came to a point where I didn't want to live anymore. I no longer cared about anything. It was the first time in my life that I was willing to give up on myself.

On one occasion, I had the most severe pain attack I have ever experienced—it really felt like I was being stabbed in the face with an ice pick. Combined with the headaches, it felt like my eye was being pushed out of its socket.



I thought I was having a stroke and my body was shutting down. Up to this point, I had always been able to hold on to whatever piece of furniture I could find to keep from hitting the floor, but this time I did end up hitting the floor and passing out.

After that point, my thoughts grew desperate and I just wanted to check out of this world, not because I wanted to die, but because it was the only way I was able to control the pain. I didn't think that a human being could possibly suffer through this kind of pain and survive. It was at that time that I experienced a personal disaster: it was a catastrophic defeat.

On the other hand, at that moment I felt totally encouraged and inspired by my role models, the former and active members of the

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German Federal Police Elite Special Forces Unit, the GSG 9. I gained my strength from their personalities, courage and expertise as well as the unit's unwavering dedication to every job they undertake – viewing their work as a calling. The duties and operations of the GSG 9 range from rescuing hostages and combating terrorism and organized crime, to saving people's lives in cases of particularly serious violent crimes. Actually, at that very moment the former and active members of the GSG 9 challenged my way of thinking and empowered me step-by-step to believe in myself and to believe, once again, in life in general.

I will tell you how the positive inspiration of the GSG 9 empowered me to turn my hopeless situation around. Actually, some people who know me personally would rather compare me with Mohandas Karamchand Gandhi or Mother Teresa, than with the GSG 9 - for them my personality seems a real contradiction. But it isn't. Very early in my life I realized that evil is real and is all around us. During my childhood and teenage years, I was looking at it from the outside, so to speak: I witnessed violence against family members and at the age of 10 the Munich Massacre, followed by Germany's most evil and violent murders since the Nazi Regime: those committed by domestic terrorists, who were responsible for slaughtering, injuring, victimizing or traumatizing numerous people and carrying out hundreds of bomb attacks, acts of arson and other aggressive and violent attacks, like kidnapping, terrorizing, humiliating and intimidating innocent people. Then as a young adult, I saw it from the inside, when I decided to get out of an abusive relationship. The very first time the situation got out of control, I confronted evil and made it known that I would not tolerate such violent behavior. But at the very moment when I challenged my abusive partner's perceived level of total control and misunderstood power, it became a violent attack. Realizing that evil exists and what evil is eventually capable of doing triggered the power within me to take control of my actions by pushing through fear, in order to get myself to do what I wanted to do –it meant successfully escaping this violent attack at gunpoint.

Please don't get me wrong. I can't physically "wrestle a bear to the ground", so to speak - but I did find meaning in the whole event, afterwards. My strengths are not in fighting physically but in learning from events and living in a centered and harmonious way. I think at this point it is important to note that even in extreme survival situations, it's not the physically strongest who usually survive, the ones that are the most centered, with the mental ability to go beyond their physical ability. Gaining that centeredness and mental strength, the power within me, is my joy in being alive.

The GSG 9 was founded following the Munich Massacre, the so-called Black September in 1972, when Palestinian terrorists used the Summer Olympic Games to kidnap 11 Israeli athletes, resulting in the tragic deaths of those athletes and one policeman. After this unthinkable tragedy, which no-one was prepared for, the GSG 9 was founded under the leadership of Ulrich Wegener. The GSG 9 has proven itself in more than 1500 operations. The unit became known world-wide especially through the release of the hostages from the Lufthansa aircraft "Landshut" on October 17th 1977 in Mogadishu, the capital of Somalia.

I believe that the members of GSG 9 were a natural choice to be my role models. Consciously and unconsciously throughout my teenage years and, of course, my adulthood I modeled my beliefs and activities on their bravery, courage, and unwavering dedication to saving lives that seemed impossible to save. I developed a kind of guide to my own behavior towards violence and victimization. I believe that it is not only what we say but more importantly the life that we lead that shows what each of us is made of: Having the courage to speak one's opinion, to stand up for what is right, to face tough issues head on, to pick someone up after an injustice, and to not necessarily do as everyone else does. As a result, I have tried to take leadership on the issues I believe in, an approach which is built on integrity, self-respect, self-worth and love for myself and others, as well as respect for the rights of others. Mahatma Gandhi stated, "When I despair, I remember that all through history the way of truth and love has always won. There have been tyrants and murderers and for a time they seem invincible, but in the end, they always fall — think of it, always."

Since my initial diagnosis, my fear of the unknown and my denial of the facts had blinded me to the fact that I was living my life in a totally primitive, helpless and hopeless position. This kept me powerless and vulnerable. My sense of security and control was taken away, and my ability to feel anything or make sense out of life's experiences was gone. Through this denial, I created more pain and frustration. I was literally using all my power to protest and fight against the "benign" tumor. I was trying to wrestle "a bear" to the ground, but I wasn't able to defend myself very well. The outcome was physically as well as mentally losing this self-

created battle: my personal catastrophic defeat. In actual fact, since my initial diagnosis I had made myself a victim of my own actions - I who believed that victimization would never ever happen to me!
Since my initial diagnosis, I had chosen to be a bystander to my own life - I asked myself why it was necessary to be engaged in such a powerless and vulnerable fight with a "bear" at all. The fact is that when I turned 40, I felt that my life was under attack, as no one is prepared to receive the diagnosis I had been given. At the time, the easiest way was to listen to and believe the negative voices inside and outside my head, the voices which were telling me, "It's all over - this is a death sentence on the tumor's terms". Gradually I realized and I was able to admit that I was the victim of a tumor which was ruling, terrorizing and taking advantage of me and my life.

Acknowledging that felt like a powerful explosion, which triggered my ability to get myself to do what I wanted to do – at that very moment to reach out and to face the reality of the "benign" tumor– I knew one thing for a fact: if I stay quiet, I can pretend nothing ever happened: if I talk about it, it will become real. With that inside I knew I had to take some positive steps to change my life: going from feeling and being treated like a victim to being a victor. Learning from the event and gaining back my centeredness and my strength, the power within me - my joy in being alive. I decided to dare to be an active participant in my present life; I chose to win back my life!
As I look back over my past, I clearly see the truth of "What goes around comes around". In my case it was from my role models the former and active members of the GSG 9 and from the people I was possibly meant to meet during my compassionate and satisfying life path, as I always strove to be an anchor and a voice for those in desperate need. I've dedicated a part of my life to being an advocate on behalf of victims of crime and abuse through helping them to rebuild their lives. I feel I've been doing good things for the right reason, and I do think there is a special gift you get back from giving: a satisfaction, centeredness and a feeling of fulfillment. Giving is really strengthening; it motivates you and gives you peace of mind. At the most difficult time in my life, both my role models' powerful inspiration and my modeled "guidelines", gained from my dedicated life path, gave me the confidence to push through the fear. I very quickly began to recognize what a negative impact the wrong attitude and fear could have on my mind and thoughts. I believed that change was possible, but that I also had to make a personal effort to get my life under control.

Since my initial diagnosis, I had forced myself into living a life with an underlying fear of "what if I tell someone what is going on …what if I let them know about the pain that has suddenly gone from making some kind of sense to making no sense at all …who would believe me … possibly no one and I would end up in a mental institution" running through my head. My mind was totally controlled by these fearful, negative feelings and as a result, I had limited myself. Realizing these mental limitations in fact prevented me from being in control of my actions, I finally found the courage to confront the underlying fear, and eventually I overcame it. I began to face the "what if" I had worked so hard to avoid, since my brain tumor had always been benign anyway. As a result, I reached out to my husband, my friends and my medical team and let them know about the pain that had suddenly gone from making some kind of sense to making no sense at all. I soon received clarification about my pain condition; I denied being depressed and I learned that my constant burning and stabbing facial pain and my severe pain conditions were real and were caused by my misleading labeled "benign" brain tumor; in fact, "benign" is relative and only refers to the infiltration because the tumor cells do not invade the surrounding tissues.

This event in my life has taught me valuable lessons, as unexpected life circumstances of different kinds happen to all of us. At the end of the day, it doesn't matter if the "tumor" is a benign or malignant i.e., a cancer diagnosis or - is a person who is bullying his way through life, perhaps a terrorist, a parent, or in some cases even a person who you consider a friend. We can't change unexpected and sudden life circumstances resulting from all kinds of "tumors" - but we do have a choice in terms of how we respond.

They are like scars, and these scars remind us of where we've been, but they don't have to dictate where we're going …….

Having a physical limitation resulting from a "benign" brain tumor is one aspect; having the mental ability to go beyond these "limitations" is a completely different aspect – a quite challenging one – but it was the beginning of proactively living my life for the first time since my initial diagnosis.

I realized that just because I have to live with this tumor, it doesn't mean I am weak or vulnerable. In fact, it is just the opposite: it speaks to the strength inside me, and I'm forced to become stronger because of it.

The label brain tumor is not a "death sentence" nor is it that the tumor is ruling my life or terrorizing me. It is quite the opposite: it is a "life sentence"- that every day is going to be more valuable and we should live every day as fully, responsibly and proactively as we can. The quality of life for people with a brain tumor is extremely important. In that regard, I often use the analogy of a rescue operation: people suddenly find themselves in an unexpected and unwanted situation. Then they are rescued, the rescuer brings them to safety, and they get medical help. Still, they are shaken up and traumatized from the fearful event - they need care and psychological help, as well as many other types of support, motivation and encouragement.

At a time when my world was shattered, my husband, my friends and my very skilled and dedicated medical team immediately responded to my need to heal. They treated me with dignity and respect - and as an individual. I felt that they listened to me, believed in me, and trusted me. Everyone offered to help me in my healing process and supported me unconditionally in adapting to my new affliction. My medical team immediately implemented a chronic - pain management model (featuring one-on-one counseling with emergency care access and opportunities to address pain concerns between visits), a variety of medication trials, therapies and techniques, combining Western and Anthroposophic Integrated medicine with forms of alternative medicine, such as homeopathy, Chinese medicine and acupuncture, as well as intensive patient education and advocacy. In fact, we created a unique patient-centered approach to establish my goals and treatment plan, which takes into account all aspects of my psychological, physical and social needs.

In the aftermath of this diagnosis, I faced the challenge of reconstructing my life and, when exposed to triggers, coping with my constant and severe pain condition. From that point on, the symptomatic pain, which will remain for years to come, became my most significant concern. I suffered from many of the problems experienced by people living with a symptomatic pain condition—my case being what is probably the most painful condition known to mankind. It makes me almost immobile and unable to do any activities until the pain subsides. I have had my share of experiences with overusing painkillers, including narcotics (in reality all they ever did was dull the pain), antidepressants and several frustrating trials with anticonvulsants, which were either ineffective or intolerable.

My life was difficult enough before I got sick, but it became much more difficult when I had to leave the "old me" behind. Mentally as well as physically, I couldn't just turn my back on the independent, active, responsible, rewarding and satisfying life that I had been living until this time. But I certainly understood my desire to heal and, from the moment I accepted my new lot in life, I had the power to work towards this desire and need to heal. Step by step, guided by the various training materials of my mentors, the former members of the SAS (the SAS is a British Army Elite Special Forces Unit, the members of which are the best and most highly trained experts in surviving extreme situations, such as torture) whose survival skills and techniques in extreme situations enabled me to develop a mental ability and strategies with respect to how I want to react to this kind of "torture" in my future, even if I'm not in the hands of the enemy. Assimilating their professional advice, expertise and knowledge, I was able to train my mind to stop paying attention to my constant pain and worked very proactively and responsibly towards dealing with the frequency and severity of my pain attacks. I educated myself on the severity of my pain condition, and learned to be more understanding and more patient in accepting some of the limitations caused by this condition. With ongoing inspiration, encouragement, support and understanding, I have adapted well to my new situation.

As many great philosophers have noted, with great loss comes the possibility of many gains. For people like me who are living with constant symptomatic pain, the challenge is how to make our lives worth living and find a sense of purpose and hope when there aren't any cures, when the root of what causes this symptomatic pain cannot be treated, or when death isn't likely in the near future.

At times, my life feels like a bitter pill to swallow. I can't function 100% of the time, I'm mostly confined to my home, and I'm unable to work. This "benign" brain tumor has taken a lot from me.

Living year after year with the label "benign," whether consciously or unconsciously, has had an impact that goes far deeper than my physical pain. The biggest challenge I have faced in adapting to this misleading label was dealing with feelings that were, at times, beyond anger. However, my anger was possibly the energy that has driven me to "let the tumor go", forgive myself and move on. I realized that if I fixated only on the misleading label and on the tumor in general, I would disappear! Letting the tumor go doesn't mean I was actually surrendering to it or that I had given up fighting. It

meant that from the moment I "let the tumor go," I had the power to work towards my need to heal, instead of making the same mistakes I had made earlier, when I used all my power to protest and fight against it. Indeed, these experiences had a great effect: I recognized the mistakes and wrong decisions I had made since my diagnosis.

I knew they were valuable experiences because I learned the most from the things I had confronted since finding out about my new life circumstances. Until this time, I had always denied that I was taking any risks because I had incorrectly interpreted a risk as being a physically dangerous act or an act that infringes on the rights of other people. In my opinion, these types of acts are not really empowering. Neither integrity nor the love for oneself or others is behind these acts, so that's why I hesitated and denied that I take risks. Now I was ready to take the risk of accepting myself because this "risk" was, in fact, built on integrity, self-respect, self-worth and love for myself and others, as well as respect for the rights of others.

Throughout my journey, I often sensed a kind of frustration and skepticism wearing down both the afflicted person and the health care professionals. No one is prepared to receive the diagnosis I was given. I had difficulty pronouncing or spelling it. Nine years ago my inner voice spoke up and tried to tell me that something was wrong. Five years later, my inner voice spoke up again, but this time it was an urgent wake up call to listen to my body's physical and mental signals and to learn what my body was telling me. At the end of the day I knew one thing for sure: I had nothing to lose but much to gain in the future—a new outlook, so to speak. The idea of the holistic approach was introduced to me—a unique patient-centered approach to establish my goals and treatment

plan, which takes into account all aspects of my psychological, physical and social needs—helping me to think in a proactive and responsible way about my future and how to make my future turn out the way that I want it to be. It's a challenging outlook I have to admit, but as a matter of fact, this new outlook introduced me to my healing process and it was the key to my success. I achieved what I had once believed was impossible: to lead a "normal life" again. In maintaining a healthy balance of realism and cautious optimism, I am now able to manage and to understand what I need in order to live with my tumor and the resulting symptomatic pain.

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My success and my achievements are gratefully dedicated to the memory of Thomas Hafenecker, Michael Newrzella and Tobias Retterath and are a tribute to the rare and special people who have

inspired me, kept me optimistic, and cheered me on. They are my hero of a husband, my role models, my mentors, my dear friends, my extremely skilled and dedicated medical team and members of the community. They never gave up on me - or gave me the sympathy I was looking for; rather all of them kept encouraging me to change my attitude and supported me unconditionally in my healing process, in adapting to my new affliction and in achieving what I once believed was impossible: leading a "normal life" again, in which no one knows I'm in constant pain if I don't tell them so — for these special gifts I'm thankful beyond words.

My heartfelt and special thanks to my cheering squad– you really pushed me to my limits and out of my comfort zone by encouraging me to go public with my story.

ABOUT THE AUTHOR

Brigitte Rieger (age 49) was in a constant state of severe pain, after undergoing many tests; she was diagnosed in 2002 with a brain tumor. The assessment at that time was that the tumor was operable but surgery would carry some risks, and it was thus recommended that the tumor be monitored. Due to her severe pain, her medical condition was re-evaluated, showing that her brain tumor had increased in size by 5 mm. To stop the tumor from growing, she was treated in 2006 with the Gamma Knife Radiation Treatment. In 2007 on top of her constant state of severe pain, she experienced the most severe pain attack. She reached out to her husband, her friends and her medical team and let them know about the pain that had suddenly gone from making some kind of sense to making no sense at all. After undergoing many tests and talking to several highly specialized experts in the field, she received clarification about her pain and medical condition and was diagnosed with occipital neuralgia, symptomatic trigeminal neuralgia and left hemi-cranial pressure resulting from a benign brain tumor (a meningioma, which is affecting the left trigeminal nerve, acoustic-facial bundle and is mildly compressing the middle cerebellar peduncle) in the left cerebellopontine (CP) angle and with chronic daily headaches. A resection of her lesion is possible, however the risks of having surgery includes death, stroke, heart attack, bleeding, infection and CSF leak and the surgical risks of removing her cerebellopontine (CP) angle meningioma includes facial nerve palsy, facial numbness, hearing loss, gait & balance problems and double vision. A unique patient-centered approach to establish her goals and a treatment plan were created, which took into account all aspects of her psychological, physical and social needs. With ongoing inspiration, encouragement, support and understanding, Brigitte has adapted well to her new situation - Brigitte's assessment of her medical condition is that her meningioma appears to be stable. Her symptomatic pain has been under control with various therapies, and she currently does not require any specific treatment in that regard. Her chronic daily headaches were consistent with medication overuse. They have fully resolved and require no further intervention.

"There is no formula for success except perhaps an unconditional acceptance of life and what it brings." - Arthur Rubinstein

ORIGINAL ARTICLE

Privatization in Canada? Not Yet

Anthony Bozzo

From 1975 to 2005, the proportion of medical expenses financed privately grew by 25% (1). In 2005, the Canadian Supreme Court issued a ruling in Quebec that legalized private delivery of core medical services (2). Shortly thereafter, the CMA endorsed a motion supporting the right to have private insurance for core medical services (3). Dr Brian Day, head of the CMA from 2007-2008, is litigating the unconstitutionality of Medicare within the British Columbia Supreme Court with the goal of increasing both private funding and private delivery of medical services (4). These facts could lead one to believe that medical practice within Canada is on the fast track to privatization. However, in this paper I will argue that despite certain suggestive initiatives, the privatization of hospitals and core medical services is unlikely in the foreseeable future and therefore presents limited implications for my future practice.

Canada's position on universal healthcare – the provision of core hospital and physician services independent of social status, age, gender, or race, was a reflection of our value of the equality of all citizens. Today, the public healthcare system, which has stood for 50 years, is under attack not due to changes in Canadian ideology, but for other reasons: efficiency and economy. A mixed public-private system is being touted as advantageous for the patient by lessening patient queues within the public system (2,5). There is already an increased private presence within our medical system, and this has occurred slowly and almost inconspicuously in three primary ways.

Firstly, within the publicly funded portion of Quebec healthcare, private companies have been allowed to compete to be the providers of certain goods (4). The government's aim in this regard was to generate lower end prices by increasing competition. This is one important example of the difference between public funding and public delivery of healthcare. Secondly, private interests have gained lasting footholds in our health care system through a change in the way large-scale health projects are financed. Whereas governments used to pay up-front for the construction of hospitals, provincial governments of Quebec, Ontario, and BC have all entered public-private partnerships (P3s) in which a private team of construction companies and project managers assume the building costs while governments provide ongoing payments in the future. The P3 financiers are then usually given lasting decision making power normally exclusive to hospital board members (4). Thirdly, and perhaps most significant, is the ruling in the Chaoulli case of 2005. After a patient's life was put in jeopardy while he waited futilely within the public system for a hip replacement, the Supreme Court ruled that it was a violation of Quebec's charter of rights to refuse this patient's private operation elsewhere (5,6). Since this ruling, patients have been able, for the first time ever, to seek private insurance for core hospital services, but only if those publicly funded services fail to meet certain medical benchmarks.

Today, only around 70% of Canadian health expenses are publicly funded. However, public funding of hospital care and physician services has always been close to 100% and it is newly emerging health care categories such as in-vitro fertilization and cosmetic surgeries, services rendered outside of hospitals (long-term home care, ambulances), and prescription drugs which are mostly, or in some cases completely, financed by private funds. Furthermore, while the publicly financed proportion dropped from 75.6% in 1975 to 69.6% in 2005, it has remained steady at that level since then with the public percentage being 70.6 in 2007 and 70.2 in 2009 (1,4). In light of the aforementioned events, will Canada continue on the trend towards privatization?

While some physicians in high positions have been accused of supporting private healthcare

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out of self-interest (higher salaries, etc) (6), the requisite government support and the legislation required for shifting to privatization will only occur if private medicine is shown to improve patient's access to care. The question then becomes, has private care been shown to improve patient outcome in the countries that have it and lessen wait times in public hospitals in countries with mixed public-private healthcare?

Tellingly, studies in Australia, Britain, and New Zealand have found that having a parallel private system does not reduce or eliminate wait times in a public system (7,8). In fact, areas with higher rates of private insurance were correlated with higher wait times in their public sectors (7). Perhaps most striking is the finding in several countries that patients in the private system do not have a better quality of life or live longer than patients in the public system (9,10). A similar trend is seen when observing our neighbors to the south: the private US system's per capita spending ($5635) is almost double the largely public Canadian spending ($3003) without any significant advantages in patient outcome or quality of life (5,7).

There is also a lack of evidence indicating clear benefits in the use of P3s in building hospitals. While data from the UK indicates that P3 projects are more often completed on time and within budget, this efficiency was shown to come at the expense of facility "quality" and design flexibility. Oftentimes the layout of the facilities was said to be optimal for the construction team rather than for the patients that would eventually take up residence4. Furthermore, P3 contracts are typically finalized many years in advance and the government would incur severe penalties for any changes, thus limiting the potential use of new technologies (4). The local implications of our new MUHC superhospital being a P3 with both SNC-Lavalin and a British firm are beyond the scope of this paper.

It is worth noting that the "most controversial Supreme Court of Canada decision to date"4 (Chaoulli) did not open up the option of private practice to droves of Canadian physicians. For one, the ruling within Quebec could not be readily applied to other provinces due to slightly different wording of the relevant clause within their respective charters. Within Quebec, the only noticeable short term effect was a positive outcome within the public system as the government adopted strict benchmarks of a six month maximum wait for hip replacements and a provision that the government would pay for treatment outside the province if wait times exceeded this (5).

Furthermore, there are signs that governments are beginning to more effectively police Canadian physicians who try to charge patients for core services – a practice outlawed by the Canada Health Act. The most prominent example is the auditing of the practice of Dr Brian Day, a former CMA head, by the British Columbia Medical Services Commission. They are investigating this vocal proponent of medical privatization for unlawful billing practices such as charging patients for core services – a clear violation of the Medicare Protection Act (4). Taken together, there are signs that our government will not passively accept private practice while the legislation supports public medicine.

Today, fewer than 1% (158/16000) of Quebec physicians are practicing privately (1). Doing so would require opting out of the public system entirely and they would therefore not be assured of any revenue. This is one of many obstacles which has deterred physicians from working privately in the past and will continue to do so until core services become privatized, therefore providing a larger potential pool of patients. I believe that until there is evidence to back the claim that a private system will strengthen the existing public system, the CHA ban on private coverage of core services will not be amended and will consequently continue to limit private medical practices in Canada to fringe specialties like IVF and cosmetic surgery.

Public funding in Canada has remained stable at 70% since 2005 and the Chaoulli ruling did not result in the introduction of mass private healthcare in Quebec. There is a lack of the requisite evidence that a mixed public-private system would reduce wait times and improve patient outcomes needed to push significant changes at the government level. While private financing may continue to increase in fringe medical markets such as IVF and cosmetic surgery, there is no indication that the core services offered by physicians will be privatized in Canada anytime soon. As such, only medical students considering a specialty choice in one of the aforementioned narrow fields are likely to encounter a scenario in which a privatized practice is an option.

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ORIGINAL ARTICLE

Appreciating the global impact of cleft lip and palate at the medical school level

Youssef Tahiri, Saoussen Salhi, Hani Sinno, Mario Luc

INTRODUCTION

Medical schools take on the responsibility to teach future physicians the basics of cell biology, biochemistry, physiology, genetics, pathology, pharmacology and during the last years, introduce medical students to the clinical application of these subjects.

However, at the end of medical school, most, if not all students are unable to appreciate the global, societal and personal impact diseases and illnesses can have.

Orofacial clefts represent the second most frequent congenital anomaly and the most common congenital anomaly at the level of the craniofacial region (1, 2). An orofacial cleft can affect the lip, or palate or both, and can be unilateral or bilateral, depending on which step of facial development has been disrupted (3). Worldwide, the problem is significant with an incidence that ranges from 1:500 to 1:2500 children each year, varying with geographic location, ethnic group and socioeconomic conditions (1). This problem is indeed more common in developing countries, especially those in Asia with an incidence of 1:500 (3), compared to an incidence of 1:800 in the United States (4). The reason for this discrepancy remains unknown, but it is hypothesized that the lack of prenatal care, genetic inheritance and poor nutrition are all contributing factors (5).

This article doesn't aim at being exhaustive on the subject of cleft lip and palate. Rather, it aspires at inviting medical students to gain an awareness of the global impact of orofacial clefts. First, we will provide a brief overview of the pathophysiology of clefts and expand on its epidemiology and the humanitarian organizations involved in correcting clefts on a global scale. Then, we will present the areas that, in our view, need improvement to ultimately correct more clefts in the best way possible.

PATHOPHYSIOLOGY AND ETIOLOGY OF CLEFT LIP AND PALATE

What is a cleft lip or palate? A simple way to explain it would be that it is a congenital malformation that starts as a disruption in the foetal development resulting in an abnormal anatomy and function at birth.

Embryologically speaking, the development of the face takes place between the 4th and 10th weeks of gestation. It occurs by the development and fusion of five prominences: the frontonasal prominence, the two maxillary prominences and the two mandibular prominences (6).

A cleft lip has been attributed to failure of the mesenchyme of the maxillary prominence and medial nasal processes (derived from an invagination on the frontonasal prominence) to develop adequately (6). This hypoplasia of the maxillary prominence and two nasal processes subsequently results in failure of their fusion (6). This fusion normally leads to the formation of the intermaxillary process which later develops into the philtrum and primary palate containing the four incisors (6). Therefore, the abnormal fusion can lead to a cleft that may range in length from a minor notch in the vermilion border of the lip, just lateral to the philtrum, to a cleft that completely separates the lateral lip from the philtrum and nasal cavity (6). The depth of clefting also varies: a cleft can involve just the soft tissue of the lip or divide the lateral portion of the maxillary bone from the premaxillary portion (that bears the incisors). These latter clefts result in deformed, absent or supernumerary teeth (6).

On the other hand, the palate development starts around the 7th week of gestation, when the medial

walls of the maxillary prominences produce a pair of thin medial extensions called the palatine shelves. These shelves first grow downward and at the end of the 7th week, rotate upward into a horizontal position before fusing with each other and with the primary palate to form the secondary palate. Failure of these palatine shelves to fuse results in a cleft palate (6).

The etiology of these two anomalies appears to be multifactorial. First, if a parent was born with a cleft, the offspring will in turn be affected in 7% of cases. Moreover, if in addition to a parent, there is also a sibling affected, then the child will have a cleft in 14% of instances (2). This reflects the genetic inheritance of these anomalies. However, if a child suffers from a cleft, the chance of his monozygotic twin also having a cleft is only 60%. This suggests that there are other nongenomic factors (3). Some of these include environmental factors, such as drugs (valproic acid, thalidomide, phenytoin...), maternal alcohol and tobacco use, dioxins and other herbicides, and possibly high altitude (3). Chromosomal and nonchromosomal syndromes are also associated with clefting (e.g. Stickler and Treacher Collins syndromes) (3, 6).

The treatment of cleft lip and palate is surgical closure. The timing of cleft lip repair is controversial, but the general agreement is to perform the repair between 6 weeks and 9 months of age. The ultimate goal of the repair is to establish symmetrical nostrils, alar bases, natural philtrum columns and central dimple, as well as the Cupid's bow and vermilion tubercle (2).

In terms of cleft palate repair, many surgeons now prefer earlier closure by 6-12 months of age to preserve adequate speech development. The various cleft palate repairs are designed to reorient the musculature of the palate, close the cleft and lengthen the palate (2).

IMPACT ON A GLOBAL SCALE

A cleft palate is associated mostly with complications relating to speech. A competent palate is necessary for normal speech production. It elevates and meets the posterior pharyngeal wall during speech and also during swallowing. A cleft palate impairs this function causing the speech to become hypernasal or incomprehensible, as well as difficulty in swallowing (2). As mentioned above, an early repair is essential for normal speech development. Indeed, a later repair is associated with a more difficult regain of normal speech function (7).

Moreover, in patients with a cleft palate, the muscles of the palate are abnormally arranged around the Eustachian tube's opening into the pharynx causing recurrent otitis media. Almost all of these children would require myringotomy tubes to avoid long-term hearing problems (2).

A cleft lip, on the other hand, is usually not associated with any such complications. The "only" reason why a cleft lip is repaired is for the sake of appearance (2). It may certainly seem like a trivial reason to not only perform surgery on a child but also mobilize resources to perform it on children of developing countries where other problems may seem more urgent and worthy of those resources.

An orofacial cleft results in disfigurement that alone can cause affected children to be socially isolated especially by their peers in school (7). Furthermore, as mentioned above, the clefts occur with a higher incidence in developing countries, where it is not unusual to encounter strong cultural and religious beliefs especially in the most remote villages (7). For instance, in Togo where Voodoo remains an important belief system, it is seen as a curse to be born with a cleft. If the cleft is too disfiguring, it may be decided to sacrifice the child (7). Thus, it seems that in the best case scenario, a child with a cleft ends up as a social outcast, hidden away by his family, and does not attend school either because he cannot speak properly or because he is rejected by his peers (7).

HUMANITARIAN ORGANIZATIONS

A few humanitarian organizations travel to developing countries to attend to children with craniofacial deformities including orofacial clefts. The most popular of these organizations is probably Operation Smile International (OSI). This is a non-governmental organization that provides reconstructive surgery for children and young adults around the world born with cleft lips, palates and other craniofacial deformities (8). It was founded in 1982 by a plastic surgeon Dr. William Magee Jr. alongside his wife Kathleen, a nurse and clinical social worker (8, 4). Since then, OSI has provided free surgeries to more than 140,000 children in 50 countries (9). A medical mission team assembles plastic surgeons, anaesthesiologist, nurses, a paediatrician, a dentist, a speech pathologist, a child life specialist and a biomedical technician (8). In a typical two-week mission, from 300 to 500 children are screened to determine whether or not they are candidates for repair (8). If a child is too young, malnourished or is otherwise judged unable

to sustain the stress of surgery and anaesthesia, he/she will not be operated on (10). Furthermore, the cases requiring prolonged anaesthesia and complicated postoperative follow-up are also avoided since a postoperative team remains at the host site only for three days (5). In the end, about 100 to 150 children are surgically treated. Each surgery takes from 45 to 60 minutes (8)

The team brings along supplies, instruments and equipment. However, the host sites are required to provide specific necessities such as oxygen, beds, electricity, and water. Moreover, the hosts are asked to advertise to the countryside about the patient screening. This is most commonly accomplished through schools, churches and mission groups since mass media is often absent (5).

An important ally to OSI is The Flying Hospital Inc., another non-profit humanitarian organization. It is a jumbo jet equipped with a twelve-bed preoperative and postoperative suite, three-position surgical suite, two-position dental, ophthalmologic, and otorhinolaryngologic areas, sterilization station, nurses' station, and scrub area. It also contains on-board oxygen generation, nitrous oxide, a medical air system, medical vacuum, and a water purification system. The jet's lower level houses a pharmacy, patient check-in and waiting areas that also serve as classrooms for patient education and on-site physician training (4).

Another goal of OSI is for the on-site health care professionals to learn the procedures and become familiar with the new equipment brought along by the visiting team. Dr. Magee indeed explained "it is our hope that, after we've left, the medical training and technology donations will help people in these countries become more self-sufficient" (4).

Nevertheless, this aspect of OSI could be seen as an area to improve (7). Indeed, Dr. Pavi, a paediatric plastic surgeon, member of another non-governmental organization (NGO) called "la chaîne de l'espoir", pointed out the "flaw" of OSI. They bring with them new equipment and their own jet fully equipped, teach the on-site doctors how to use the new equipment and then leave with their jet. If the host sites run out of the equipment brought along by the OSI team, the hosts are back to square one, where they don't have the capacity to operate on children with orofacial clefts (7).

Unlike OSI, "la chaîne de l'espoir" is a smaller NGO. On a mission to Togo that lasted two weeks, Dr. Pavi and Dr. J.Moren, an anaesthesiologist, performed four surgeries per day, amounting to a number of about 40 children operated on for cleft lip or palate. This number is much smaller than the OSI one. However, when Dr. Pavi and Dr. Moren arrived in Togo, they did not bring any equipment because their objective is to teach the on-site doctors how to perform the procedure with the equipment available at the host site. Thus, during each operation, Dr. Pavi teaches two on-site surgeons the procedure, with equipment that will be available to them even after the team has left the site (7).

CHALLENGES TO IMPROVEMENT

From what has been said before, it appears that there is significant room for improvement. A compromise between adapting the teaching of the host-site health care professionals to the type of equipment that is available to them and operating on a maximum of children has to be reached. Indeed, the ultimate goal of these types of organizations should be to make their help no longer a necessity to developing countries which should become autonomous in their capacity to operate on children with orofacial clefts (7).

However, even if the on-site surgeons acquire the expertise, there is still the problem of the cost of these types of surgeries. In Togo for example, a single cleft lip or palate repair costs about 450 dollars, exceeding the monthly salary of the surgeon performing the procedure (7). So why is the surgery so expensive? The answer is that in developing countries such as the countries of West Africa, in order to have a surgery, a patient must pay for all the supplies needed including the antibiotics, the compresses, the sterilizing agents... Moreover, even if the patient is able to afford those supplies, the pharmacies often lack them (7). Therefore, it seems that as long as developing countries have poor economies, the NGOs mentioned above will be needed, if only to help in terms of funding.

Another problem faced by developing countries is that doctors from these countries usually leave to study medicine in Europe or North America. There they have access to well-equipped hospitals and the newest medical technologies and therefore seldom return to their home countries where they are needed the most. These surgeons should be encouraged to return home once their medical training is completed or at least actively participate in humanitarian missions (7).

Furthermore, as with any surgery, there can be complications associated with cleft lip or palate repair. Identification and correction of these complications would require follow up for longer than what the teams spend in each country. Team

participants should be audited for their performance and a system that measures surgical outcomes should be implemented (1). Such a system should take into consideration the degree of disability that persists despite or as a result of the surgery: defects in nasolabial appearance, palate integrity (fistulas) and function (speech and swallowing), hearing, dental development and psychosocial adaptation (1). Among all of these factors, nasolabial appearance is the only outcome that can be properly and reliably assessed within 1 year of the operation. The other elements would require a longer follow-up period (1). This outcome measurement was thought of by OSI and attempted during the "World Journey of Smiles" in November 2007: during a period of 10 days, at 40 simultaneous mission sites, high quality digital images were collected during screening and under anaesthesia before surgery, immediately after surgery while still under anesthesia and at a 1-week, 6-month, and 1-year follow-up visits organized by local foundations. With these elements, an outcome evaluation chart was created for each patient (1). A plastic surgeon member of the International Outcomes Council scored the results using a standardized evaluation system. The final feedback reports were sent to respective surgical teams, in-country executive and medical directors as well as to each surgeon listing which patients they had operated on (1).

This is a major advancement that should be added to any NGO. Indeed, it is only fair that their activities be reported not only by the number of procedures performed but also procedural outcomes. However, quality images can only assess symmetry and aesthetics. Indeed, the current system is still unable to evaluate speech, hearing and feeding abilities postoperatively. Moreover, there remains the problem that the majority of patients do not come back for follow-up visits. This is often due to their inability to travel to the follow-up sites mostly because they generally live in remote geographical areas. Parents also tend to think that a follow-up visit is unnecessary if they do not see a complication. A way to address this last obstacle is to stress to parents, during their first visit, the importance of follow-up as a way to identify those children who need further treatment to complete their care (1).

Finally, NGOs could also add to their programs education for the inhabitants of the host countries regarding the meaning of orofacial clefting. This could be done by trained medical personnel brought along on missions. This could help affected children become accepted in the society they live in, even prior to surgical repair (4).

CONCLUSION

Orofacial clefting is a major problem worldwide, more prevalent in developing countries for poorly understood reasons. Unfortunately these countries lack the appropriate financial, medical, and technological resources to address this very common condition. As a result, several children worldwide are left to live with disfiguring facial malformations that cause them to quickly become social outcasts hidden away by their families.

Several humanitarian organizations travel to these countries to perform free operations on these children every year. Although the work accomplished is significant, there is still room for improvement when one looks at the number of children who receive the surgery versus the children who are turned down for reasons mentioned earlier.

To teach the on-site surgeons how to operate on cleft lips and palates with on-site equipment rather than new expansive supplies that the host countries will never be able to afford, should become a primordial priority to these NGOs. Moreover, surgeons from developing countries, who train in developed countries, should be encouraged to return home after their training is completed in order to make their knowledge and expertise available to children who need it most.

Furthermore, a system to evaluate surgical outcomes should be implemented by these NGOs for two reasons: first, so surgeons can receive feedback on their operating skills and improve on them accordingly and second so children who require additional treatment can be identified.

Despite all of this, developing countries will still need financial support to afford the basic supplies needed for surgeries (compresses, antibiotics...).

Meanwhile, the help of these NGOs is still needed, and it seems that a simple way to have more children operated on during a mission is to have more people participate in these missions. Therefore, we encourage all interested medical students and residents to participate either in their future careers or in academic activities to help improve the care of orofacial clefting worldwide.

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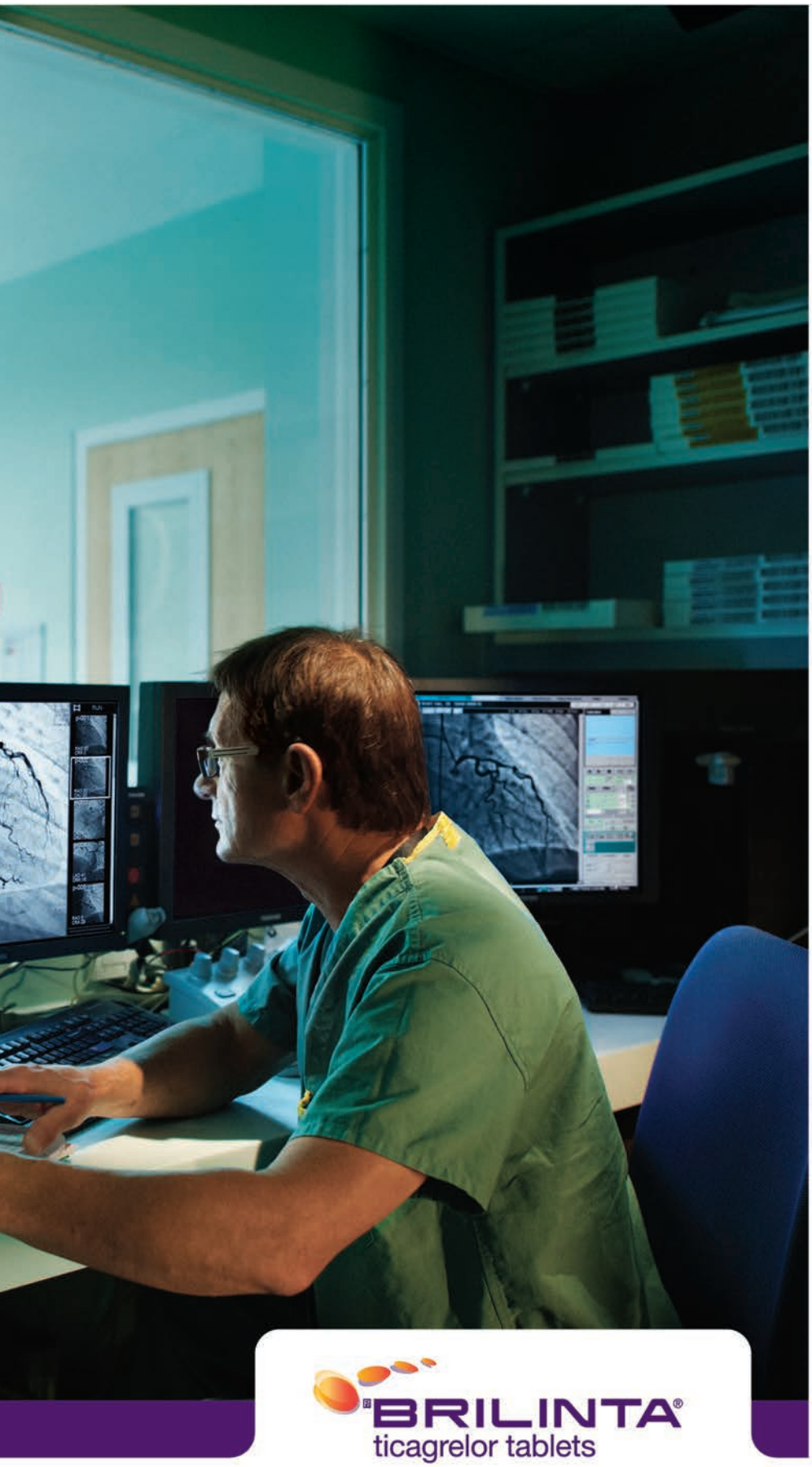
"OPINION
IS GOOD.
BUT EVIDENCE
IS BETTER."*



BRILINTA (ticagrelor), co-administered with acetylsalicylic acid (ASA), is indicated for the secondary prevention of atherothrombotic events in patients with Acute Coronary Syndromes (ACS) (unstable angina [UA], non–ST elevation myocardial infarction [NSTEMI] or ST elevation myocardial infarction [STEMI]) who are to be managed medically, and those who are to be managed with percutaneous coronary intervention (PCI) (with or without stent) and/or coronary artery bypass graft (CABG).

Based on a relationship observed in PLATO between maintenance ASA dose and relative efficacy of BRILINTA compared to clopidogrel, BRILINTA is recommended to be co-administered with low maintenance dose ASA (75-150 mg daily).

BRILINTA is contraindicated in patients who: are hypersensitive to this medication or to any ingredient in the formulation, have active pathological bleeding such as peptic ulcer or intracranial hemorrhage, have a history of intracranial hemorrhage, have moderate to severe hepatic impairment or are also taking strong CYP3A4 inhibitors.

BRILINTA should be used with caution in patients with a propensity to bleed (e.g., due to recent trauma, recent surgery, active or recent gastrointestinal bleeding, or moderate hepatic impairment) and in patients requiring oral anticoagulants (e.g., warfarin) and/or fibrinolytics agents (within 24 hours of BRILINTA dosing). Caution should also be used in patients with concomitant administration of medicinal products that may increase the risk of bleeding (e.g., non-steroidal anti-inflammatory drugs [NSAIDs]). Co-administration of BRILINTA and high maintenance dose ASA (>150 mg daily) is not recommended.

In the PLATO study, bleeding events associated with BRILINTA vs. clopidogrel included total major (11.6% vs. 11.2%) and combined total major + minor (16.1% vs. 14.6%). When minor bleeding was included, combined PLATO-defined major and minor bleeding events were significantly higher on BRILINTA than on clopidogrel (p=0.0084). There were few fatal bleeding events in the study, 20 (0.2%) for BRILINTA and 23 (0.3%) for clopidogrel. The most common adverse events associated with BRILINTA vs. clopidogrel were dyspnea (12.0% vs. 6.5%), headache (6.5% vs. 5.8%) and nosebleed (6.0% vs. 3.4%).

See the Product Monograph for full contraindications, warnings, precautions, dosing and administration.

Reference: 1. BRILINTA® Product Monograph. AstraZeneca Canada Inc. May 26, 2011.

*Fictitious quote. May not be representative of all healthcare professionals.

BRILINTA® ticagrelor tablets

AstraZeneca

Member R&D PAAB BR032E 08/12

See prescribing summary on page

BRILINTA®
ticagrelor tablets

Prescribing Summary

Patient Selection Criteria

THERAPEUTIC CLASSIFICATION: Platelet Aggregation Inhibitor

INDICATIONS AND CLINICAL USE: BRILINTA (ticagrelor), co-administered with acetylsalicylic acid (ASA), is indicated for the secondary prevention of atherothrombotic events in patients with Acute Coronary Syndromes (ACS) (unstable angina [UA], non–ST Elevation Myocardial Infarction [NSTEMI] or ST Elevation Myocardial Infarction [STEMI]) who are to be managed medically and those who are to be managed with percutaneous coronary intervention (PCI) (with or without stent) and/or coronary artery bypass graft (CABG).

Based on a relationship observed in PLATO between maintenance ASA dose and relative efficacy of BRILINTA compared to clopidogrel, BRILINTA is recommended to be co-administered with low maintenance dose ASA (75-150 mg daily).

Pediatrics (<18 years of age): The safety and efficacy of BRILINTA in pediatric patients below the age of 18 have not been established. Therefore, BRILINTA is not recommended in this population.

CONTRAINDICATIONS: BRILINTA (ticagrelor) is contraindicated in:

- Patients who are hypersensitive to this medication or to any ingredient in the formulation
- Patients who have active pathological bleeding such as peptic ulcer or intracranial hemorrhage
- Patients with a history of intracranial hemorrhage
- Patients with moderate to severe hepatic impairment
- Patients who are also taking strong CYP3A4 inhibitors (e.g., ketoconazole, clarithromycin, nefazodone, ritonavir and atazanavir), as it may lead to a substantial increase in exposure to ticagrelor

SPECIAL POPULATIONS:

Pregnant Women: The safety of BRILINTA during pregnancy has not been established, as no clinical study has been conducted in pregnant women and limited clinical data on exposure to BRILINTA during pregnancy are available. Women of childbearing potential should use appropriate contraceptive measures to avoid pregnancy.

Nursing Women: It is not known whether this drug is excreted in human milk, as no clinical study has been conducted in lactating women. Studies in rats have shown that ticagrelor and its active metabolites are excreted in milk. Therefore, the use of BRILINTA during breastfeeding is not recommended.

Geriatrics (≥65 years of age): In PLATO, 43.1% of patients were ≥65 years of age and 15% were ≥75 years of age. The relative risk of bleeding was similar in both treatment and age groups. No overall differences in safety or effectiveness were observed between these patients and younger patients.

Pediatrics (<18 years of age): The safety and efficacy of BRILINTA in pediatric patients below the age of 18 have not been established. Therefore, BRILINTA is not recommended in this population.

Hepatic Impairment: Use of BRILINTA is contraindicated in patients with moderate or severe hepatic impairment.

Renal Impairment: No dose adjustment is necessary for patients with renal impairment. No clinical study has been conducted in patients on renal dialysis. Ticagrelor is not thought to be dialyzable. Appropriate caution should be used in patients requiring renal replacement therapy. Creatinine levels may increase during treatment with BRILINTA. The mechanism has not been identified. Renal function should be monitored in the course of patient management.

Uric Acid Increase: In PLATO, patients on BRILINTA had a higher risk of hyperuricemia than those receiving clopidogrel. Caution should be exercised when administering BRILINTA to patients with history of hyperuricemia or gouty arthritis. As a precautionary measure, the use of BRILINTA in patients with uric acid nephropathy is discouraged.

Safety Information

WARNINGS AND PRECAUTIONS:

General

Bleeding Risk: As with other antiplatelet agents, the use of BRILINTA (ticagrelor) in patients at known increased risk for bleeding should be balanced against the benefit in terms of prevention of thrombotic events.

If clinically indicated, BRILINTA should be used with caution in the following patient groups:

- Patients with a propensity to bleed (e.g., due to recent trauma, recent surgery, active or recent gastrointestinal bleeding, or moderate hepatic impairment). The use of BRILINTA is contraindicated in patients with active pathological bleeding, in those with history of intracranial hemorrhage, and moderate to severe hepatic impairment.
- Patients requiring oral anticoagulants (e.g., warfarin) and/or fibrinolytics agents (within 24 hours of BRILINTA dosing). Such agents confer an independent bleeding risk as they function in a distinct and complementary mechanism of hemostasis compared to BRILINTA. The combination of BRILINTA with either of these classes of drugs has not been studied.
  - **Warfarin Therapy:** Due to an increased propensity to bleed, caution is advised in patients taking warfarin during BRILINTA therapy. A specific drug-drug interaction study with warfarin has not been performed.
- Patients with concomitant administration of medicinal products that may increase the risk of bleeding, e.g., non-steroidal anti-inflammatory drugs (NSAIDs).

No data exist with BRILINTA regarding a hemostatic benefit of platelet transfusions; circulating BRILINTA may inhibit transfused platelets. Since co-administration of BRILINTA with desmopressin did not decrease template bleeding time, desmopressin is unlikely to be effective in managing clinical bleeding events.

Antifibrinolytic therapy (aminocaproic acid or tranexamic acid) and/or recombinant factor VIIa may augment hemostasis. BRILINTA may be resumed after the cause of bleeding has been identified and controlled.

Maintenance Dose Acetylsalicylic acid (ASA): Based on a relationship observed in PLATO between maintenance ASA dose and relative efficacy of BRILINTA compared to clopidogrel, co-administration of BRILINTA and high maintenance dose ASA (>150 mg daily) is not recommended.

Cytochrome P450 3A4 Strong Inhibitors: Co-administration of BRILINTA with strong CYP3A4 inhibitors (e.g., ketoconazole, clarithromycin, nefazodone, ritonavir and atazanavir) is contraindicated as co-administration may lead to a substantial increase in exposure to ticagrelor.

Peri-Operative Considerations

Surgery: If a patient requires surgery, clinicians should consider each patient's clinical profile as well as the benefits and risks of continued antiplatelet therapy when determining when discontinuation of BRILINTA treatment should occur.

To minimize the risk of bleeding, if a patient is to undergo elective surgery and antiplatelet effect is not desired, BRILINTA should be discontinued 5 days prior to surgery.

Respiratory

Dyspnea: In PLATO, approximately 13.8% of patients randomized to BRILINTA, versus 7.8% for clopidogrel, reported dyspnea, including dyspnea at rest, exertional dyspnea, paroxysmal nocturnal dyspnea and nocturnal dyspnea. The dyspnea is usually mild to moderate in intensity and often resolves during continued BRILINTA treatment. The mechanism has not yet been elucidated. If a patient reports new, prolonged or worsened dyspnea this should be investigated fully and if not tolerated, treatment with BRILINTA should be stopped.

ADVERSE REACTION SERIOUSNESS AND INCIDENCE:

Adverse Drug Reaction Overview: The commonly reported adverse events in patients treated with BRILINTA (ticagrelor) were dyspnea, headache and epistaxis and these events occurred at higher rates than in the clopidogrel treatment group (see Table 1).

Table 1: Summary of Adverse Events (Regardless of Causality) Reported for ≥1% of Patients in Either Group (PLATO)

Adverse Event (System Organ Class)	BRILINTA (%) N=9235	Clopidogrel (%) N=9186
Blood and Lymphatic System Disorders		
Anemia	1.9	1.7
Cardiac Disorders		
Atrial fibrillation	4.2	4.6
Bradycardia[a]	2.9	2.9
Cardiac failure	2.3	2.6
Ventricular tachycardia	2.0	2.1
Palpitations	1.2	1.1
Angina pectoris	1.2	1.1
Sinus bradycardia	1.1	0.8
Ventricular extrasystoles	1.1	1.1
Ventricular fibrillation	0.8	1.0
Ear and Labyrinth Disorders		
Vertigo[b]	1.5	1.3
Gastrointestinal Disorders		
Nausea[b]	4.3	3.8
Diarrhea[b]	3.7	3.3
Vomiting[b]	2.5	2.3
Constipation[b]	2.2	2.6
Dyspepsia[b]	2.0	1.8
Abdominal pain upper	1.9	2.0
Abdominal pain[b]	1.5	1.2
General Disorders and Administration Site Conditions		
Non-cardiac chest pain	3.7	3.3
Fatigue	3.2	3.2
Chest pain	3.1	3.5
Pyrexia	2.9	2.8
Edema peripheral	2.3	2.5
Asthenia	2.0	2.1
Hemorrhages or bleeding		
Epistaxis[b]	6.0	3.4
Contusion	3.9	2.0
Hematoma	2.2	1.3
Post-procedural hemorrhage[b]	2.1	2.0
Vessel puncture site hematoma	1.7	1.1
Ecchymosis	1.5	0.6
Infections and Infestations		
Urinary tract infection	2.0	1.8
Hematuria	1.9	1.6
Nasopharyngitis	1.8	1.6
Pneumonia	1.4	1.9
Bronchitis	1.3	1.4
Metabolism and Nutrition Disorders		
Diabetes mellitus	1.2	1.1
Dyslipidemia	1.0	1.0
Hypercholesterolemia	1.0	0.9
Hypokalemia	1.6	1.5
Musculoskeletal and Connective Tissue Disorders		
Back pain	3.6	3.3
Pain in extremity	2.1	2.3
Musculoskeletal chest pain	1.5	1.4
Musculoskeletal pain	1.5	1.5
Arthralgia	1.5	1.4
Myalgia	1.4	1.6
Nervous System Disorders		
Headache[b]	6.5	5.8
Dizziness[b]	4.5	3.9
Syncope	1.1	0.8
Psychiatric Disorders		
Anxiety	2.2	1.9
Insomnia	1.7	2.0
Depression	1.1	1.1
Renal and Urinary Disorders		
Renal failure	1.0	0.7
Respiratory Disorders		
Dyspnea[a,b]	12.0	6.5
Cough	4.9	4.6
Dyspnea exertional	1.9	1.4
Skin and Subcutaneous Tissue Disorders		
Rash[b]	1.8	1.7
Pruritus[b]	1.0	1.0
Vascular Disorders		
Hypertension	3.8	4.0
Hypotension	3.2	3.3

a Several MedDRA PT combined.
b These events have also been reported as Adverse Drug Reactions (possibly or probably related to BRILINTA).

DRUG INTERACTIONS: Cytochrome P450 (CYP) 3A4/5 are the major enzymes responsible for the metabolism of BRILINTA (ticagrelor) and the formation of the active metabolite. Clinical pharmacology and *in vitro* data show that there is a complex interaction between ticagrelor and CYP3A4/5. Indeed, depending on the substrate, ticagrelor and its active metabolite are shown to weakly inhibit or weakly activate CYP3A4/5 (see DETAILED PHARMACOLOGY). Therefore, co-administration of BRILINTA and CYP3A4/5 substrates with narrow therapeutic indices is not recommended. CYP enzymes 1A2, 2C19 and 2E1 do not contribute meaningfully *in vitro* to ticagrelor metabolism. BRILINTA is also a p-glycoprotein (P-gp) substrate and a weak inhibitor of P-gp.

You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by one of the following 3 ways:

Report online at www.healthcanada.gc.ca/medeffect
Call toll-free at 1-866-234-2345
Complete a Canada Vigilance Reporting Form and:
Fax toll-free to 1-866-678-6789, or
Mail to: Canada Vigilance Program
Health Canada
Postal Locator 0701C
Ottawa, ON K1A 0K9

Postage-paid labels, Canada Vigilance Reporting Form and the adverse reaction reporting guidelines are available on the MedEffect™ Canada website at www.healthcanada.gc.ca/medeffect.

Administration

Recommended Dose and Dosage Adjustment

BRILINTA therapy should be initiated with a single 180 mg oral loading dose (two 90 mg tablets) and then continued at 90 mg twice daily. Patients taking BRILINTA should also take acetylsalicylic acid (ASA) daily, unless specifically contraindicated. Following an initial loading dose of ASA, BRILINTA should be used with a daily maintenance dose of ASA of 75-150 mg.

BRILINTA can be taken orally with or without food. In a study of healthy subjects, ingestion of a high-fat meal had no effect on ticagrelor C_{max} or the AUC of the active metabolite, but resulted in a 21% increase in ticagrelor AUC and 22% decrease in the active metabolite C_{max}. These changes are considered of minimal clinical significance. BRILINTA was administered without regard to food in PLATO.

Grapefruit juice interaction: A drug-drug interaction study with grapefruit juice has not been performed. Based on the pharmacokinetic data for ticagrelor, grapefruit juice is expected to increase ticagrelor exposure to a clinically insignificant extent. Therefore, BRILINTA can be taken with grapefruit juice.

Missed Dose

Lapses in therapy should be avoided. A patient who misses a dose of BRILINTA should take one 90 mg tablet (their next dose) at its scheduled time.

SUPPLEMENTAL PRODUCT INFORMATION

WARNINGS AND PRECAUTIONS:

Discontinuations: Patients who require discontinuation of BRILINTA are at increased risk for cardiac events. Premature discontinuation of treatment should be avoided. If BRILINTA must be temporarily stopped due to an adverse event, it should be re-initiated as soon as possible when the benefits outweigh the risks of the adverse event or when the adverse event has come to resolution.

Cardiovascular

Patients at Risk for Bradycardic Events: Due to observations of mostly asymptomatic ventricular pauses in an earlier clinical study, the Phase III study (PLATO) excluded patients with an increased risk of bradycardic events (e.g., patients who have sick sinus syndrome, 2nd or 3rd degree AV block or bradycardic-related syncope and not protected with a pacemaker). Therefore, due to the limited clinical experience, BRILINTA should be used with caution in these patients.

In addition, caution should be exercised when administering BRILINTA concomitantly with drugs known to induce bradycardia. However, no evidence of clinically significant adverse interactions was observed in the PLATO trial during concomitant administration with one or more drugs known to induce bradycardia: in PLATO, 96% of patients took beta-blockers, 33% took diltiazem or verapamil (calcium channel blockers) and 4% took digoxin.

Neurologic

Effects on Ability to Drive and Use Machines: No studies on the effects of BRILINTA on the ability to drive and use machines have been performed. BRILINTA has no or negligible influence on the ability to drive and use machines. During treatment for Acute Coronary Syndromes, dizziness and confusion have been reported. Therefore, patients who experience these symptoms should be cautious while driving or using machines.

Peri-Operative Considerations

In PLATO patients undergoing CABG, BRILINTA had a similar rate of major bleeds compared to clopidogrel at all days after stopping therapy except Day 1 where BRILINTA had a higher rate of major bleeding.

Because of the reversible binding of BRILINTA, restoration of platelet aggregation occurs faster with BRILINTA compared to clopidogrel.

In the OFFSET study, mean Inhibition of Platelet Aggregation (IPA) for ticagrelor at 72 hours post-dose was comparable to mean IPA for clopidogrel at 120 hours post-dose. The more rapid offset of effect may predict a reduced risk of bleeding complications, e.g., in settings where antiplatelet therapy must be temporarily discontinued due to surgery or trauma.

Adverse Drug Reaction Overview

In PLATO, a total of 6762 patients with Acute Coronary Syndromes (UA, NSTEMI and STEMI) were exposed to BRILINTA (180 mg loading dose followed by a 90 mg twice daily maintenance dose) for at least 6 months and up to 12 months for 3138 of them.

Serious adverse events were reported in a similar frequency between BRILINTA (20.2%) and clopidogrel (20.3%) treated patients. The most frequent serious adverse events observed were cardiac failure (1.1% vs. 1.0%), non-cardiac chest pain (0.9% vs. 0.9%) and dyspnea (0.7% vs. 0.4%).

The rate of study drug discontinuation because of adverse events was 7.4% for BRILINTA and 5.4% for clopidogrel. Dyspnea was the most common adverse event leading to study drug discontinuation for BRILINTA (0.9% for BRILINTA and 0.1% for clopidogrel).

Clinical Trial Adverse Drug Reactions

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

Bleeding Events: The primary safety endpoint in the PLATO study was the composite endpoint of 'Total Major' bleeding, which consisted of the components of 'Major Fatal/Life-threatening' and 'Major Other'. Table 2 shows the 12-month rates of patients experiencing bleeding events in the PLATO study (PLATO-defined).

Table 2: Analysis of Overall Bleeding Events – PLATO-defined

	BRILINTA (%) N=9235	Clopidogrel (%) N=9186	*p*-value*
Primary Safety Endpoint			
Total Major	11.6	11.2	0.4336
Secondary Safety Endpoints			
Major Fatal/Life-threatening	5.8	5.8	0.6988
Combined Total Major + Minor	16.1	14.6	0.0084
Non-procedural Major	3.1	2.3	0.0058
Non-procedural Major + Minor	5.9	4.3	<0.0001
Non-CABG Total Major	4.5	3.8	0.0264
Non-CABG Major Fatal/Life-threatening	2.1	1.9	0.2516

*Nominal *p*-value not corrected for multiple testing.
Major Fatal/Life-threatening: Clinically apparent with >50 g/L decrease in hemoglobin or ≥4 red cell units transfused; or fatal; or intracranial; or intrapericardial with cardiac tamponade; or with hypovolemic shock or severe hypotension requiring pressors or surgery.
Major Other: Clinically apparent with 30-50 g/L decrease in hemoglobin or 2-3 red cell units transfused; or significantly disabling.
Minor: Requires medical intervention to stop or treat bleeding.

There were few fatal bleeding events in the study, 20 (0.2%) for BRILINTA and 23 (0.3%) for clopidogrel. When minor bleeding was included, combined PLATO-defined Major and Minor bleeding events were significantly higher on BRILINTA than on clopidogrel.

Location of 'Total Major + Minor' Bleeding (BRILINTA vs. clopidogrel): Intracranial 0.3% vs. 0.2%, pericardial 0.1% vs. 0.1%, retroperitoneal 0.03% vs. 0.03%, intraocular 0.02% vs. 0.04% and intra-articular 0.02% vs. 0.01%. Other common locations were in rank order of event frequency: gastrointestinal 1.8% vs. 1.5%, epistaxis 1.3% vs. 0.7%, urinary 0.5% vs. 0.4%, subcutaneous/dermal 0.5% vs. 0.4% and hemoptysis 0.1% vs. 0.08%.

Non-procedural Fatal Bleeding: There was no difference with BRILINTA compared to clopidogrel for overall non-procedural fatal bleeding. There were numerically more 'Major Fatal/Life-threatening' intracranial non-procedural bleeding events with BRILINTA (n=27 events, 0.3%) than with clopidogrel (n=14 events, 0.2%). Of the intracranial non-procedural bleeding events, 11 bleeding events with BRILINTA and 1 with clopidogrel were fatal. 'Major Fatal/Life-threatening' gastrointestinal bleeding was the same with BRILINTA and clopidogrel, with numerically more fatal events for clopidogrel (5) than for BRILINTA (none).

Bleeding in Subgroups Patient Population: Baseline characteristics including age, gender, weight, race, geographic region, medical history, concurrent conditions and concomitant therapy were assessed to explore any increase in risk of bleeding with BRILINTA. No particular risk group was identified for any subset of bleeding.

Table 3 shows the overall rates of TIMI-defined bleeding events.

Table 3: Analysis of Overall Bleeding Events – TIMI-defined

	BRILINTA (%) N=9235	Clopidogrel (%) N=9186	*p*-value
Major	7.9	7.7	0.5669
Major + Minor	11.4	10.9	0.3272
Non-CABG Major	2.8	2.2	0.0246
Non-CABG Major + Minor	4.5	3.6	0.0093

TIMI Major: Clinically apparent with >50 g/L decrease in hemoglobin or intracranial hemorrhage.
TIMI Minor: Clinically apparent with 30 to ≤50 g/L decrease in hemoglobin.

Additional clinical Adverse Drug Reactions that were reported as possibly or probably related to BRILINTA are listed below by body system:

Common (≥1% to <10%)
- *Skin and subcutaneous tissue disorders:* subcutaneous or dermal bleeding
- *Gastrointestinal disorders:* gastrointestinal hemorrhages
- *Renal and urinary disorders:* urinary tract bleeding

Uncommon (≥0.1% to <1%)
- *Nervous system disorders:* intracranial hemorrhage (may be fatal or life threatening), confusion, paraesthesia
- *Gastrointestinal disorders:* gastritis, retroperitoneal hemorrhage
- *Eye disorders:* eye hemorrhage (intraocular, conjunctival, retinal)
- *Respiratory, thoracic and mediastinal disorders:* hemoptysis

Rare (≥0.01% to <0.1%)
- *Musculoskeletal connective tissue and bone:* hemarthrosis

DRUG INTERACTIONS:

Drug-Drug Interactions

Effects of Other Drugs on BRILINTA

Ketoconazole (Strong CYP3A4 Inhibitors): Co-administration of ketoconazole with ticagrelor increased the ticagrelor C_{max} and AUC equal to 2.4-fold and 7.3-fold, respectively. The C_{max} and AUC of ticagrelor's active metabolite were reduced by 89% and 56%, respectively. Other strong inhibitors of CYP3A4 (clarithromycin, nefazodone, ritonavir and atazanavir) would be expected to have similar effects and are contraindicated with BRILINTA.

Diltiazem (Moderate CYP3A4 Inhibitors): Co-administration of diltiazem with ticagrelor increased the ticagrelor C_{max} by 69% and AUC by 174% and decreased its active metabolite C_{max} by 38% and AUC was unchanged. There was no effect of ticagrelor on diltiazem plasma levels. Other moderate CYP3A4 inhibitors (e.g., amprenavir, aprepitant, erythromycin, fluconazole and verapamil) would be expected to have similar effects. These exposure changes are not considered clinically significant, and therefore can as well be co-administered with BRILINTA.

Rifampin and Other CYP3A4 Inducers: Co-administration of rifampin with ticagrelor decreased the ticagrelor C_{max} and AUC by 73% and 86%, respectively. The C_{max} of its active metabolite was unchanged and the AUC was decreased by 46%. Other CYP3A4 inducers (e.g., dexamethasone, phenytoin, carbamazepine and phenobarbital) would be expected to decrease the exposure to ticagrelor as well and may result in reduced efficacy of BRILINTA.

Others: Clinical pharmacology interaction studies showed that co-administration of ticagrelor with heparin, enoxaparin and acetylsalicylic acid (ASA) did not have any effect on ticagrelor or its active metabolite plasma levels. Co-administration of ticagrelor and heparin had no effect on heparin based on activated partial thromboplastin time (aPTT) and activated coagulation time (ACT) assays. Co-administration of ticagrelor and enoxaparin had no effect on enoxaparin based on factor Xa assay.

Effects of BRILINTA on Other Drugs

Simvastatin: Co-administration of ticagrelor with simvastatin increased the simvastatin C_{max} by 81% and AUC by 56% and increased simvastatin acid C_{max} by 64% and AUC by 52% with some individual increases equal to 2- to 3-fold. Consideration of the clinical significance should be given to the magnitude and range of changes on the exposure to patients requiring greater than 40 mg of simvastatin. There was no effect of simvastatin on ticagrelor plasma levels. BRILINTA may have similar effect on lovastatin, but is not expected to have a clinically meaningful effect on other statins.

Atorvastatin: Co-administration of atorvastatin and ticagrelor increased the atorvastatin acid C_{max} by 23% and AUC by 36%. Similar increases in AUC and C_{max} were observed for all atorvastatin acid metabolites. These increases are not considered clinically significant.

Tolbutamide: Co-administration of ticagrelor with tolbutamide resulted in no change in the plasma levels of either drug, which demonstrates ticagrelor is not a CYP2C9 inhibitor and unlikely to alter the metabolism of other drugs metabolized via CYP2C9.

Warfarin: A drug-drug interaction study with warfarin has not been performed. As with other oral antiplatelet therapy, there is a potential for increased risk of bleeding, therefore, warfarin and BRILINTA should be co-administered with caution.

Oral Contraceptives: Co-administration of ticagrelor and levonorgestrel and ethinyl estradiol increased the ethinyl estradiol exposure approximately 20% but did not alter the PK of levonorgestrel. No clinically relevant effect on oral contraceptive efficacy is expected when levonorgestrel and ethinyl estradiol are co-administered with BRILINTA.

Digoxin (P-gp Substrate): Concomitant administration of ticagrelor increased the digoxin C_{max} by 75% and AUC by 28%. Therefore, appropriate clinical and/or laboratory monitoring is recommended when giving narrow therapeutic index P-gp dependent drugs like digoxin concomitantly with BRILINTA.

Other Concomitant Therapy: In clinical studies, BRILINTA was commonly administered with ASA, heparin, low molecular weight heparin, intravenous GpIIb/IIIa inhibitors, proton pump inhibitors, statins, beta-blockers, angiotensin-converting enzyme inhibitors and angiotensin receptor blockers as needed for concomitant conditions. These studies did not produce any evidence of clinically significant adverse interactions.

DOSAGE AND ADMINISTRATION:

General

The PLATO trial data suggest the efficacy of BRILINTA (ticagrelor) relative to clopidogrel is associated with ASA dose during maintenance therapy. Patients receiving a low maintenance dose of ASA benefit more than those receiving a high maintenance dose of ASA. Because the data from patients receiving high maintenance dose ASA (>300 mg daily) do not provide conclusive evidence of the efficacy of BRILINTA compared to clopidogrel, high maintenance dose ASA (>150 mg daily) is not recommended for maintenance dual antiplatelet therapy with BRILINTA. There is no conclusive evidence regarding the underlying biological mechanism. Based on analysis of the available clinical data, it is recommended that BRILINTA be used with a daily low maintenance dose of ASA (75-150 mg).

Furthermore, no safety and efficacy data is available on the use of BRILINTA beyond one year treatment duration.

Recommended Dose and Dosage Adjustment

Switching from clopidogrel to BRILINTA: Patients can be switched from clopidogrel to BRILINTA without interruption of antiplatelet effect. This results in an absolute inhibition of platelet aggregation (IPA) increase of 26.4%. Conversely, switching from BRILINTA to clopidogrel results in an absolute IPA decrease of 24.5%. Clinicians who desire to switch patients from clopidogrel to BRILINTA should administer the first 90 mg dose of BRILINTA 24 hours following the last dose of clopidogrel.

Dosing Considerations in Special Populations

Geriatrics (≥65 years of age): No dosage adjustment is required in elderly (≥65 years) patients.

Patients with Renal Insufficiency: No dosage adjustment is required in patients with renal impairment. No clinical study has been conducted in patients on renal dialysis. Ticagrelor is not thought to be dialyzable. Appropriate caution should be used in patients requiring renal replacement therapy.

Patients with Hepatic Insufficiency: No dosage adjustment is required in patients with mild hepatic impairment. BRILINTA has not been studied in patients with moderate or severe hepatic impairment.

OVERDOSAGE:

For management of suspected drug overdose, contact your regional Poison Control Centre.

Treatment

There is currently no known antidote to reverse the effects of BRILINTA (ticagrelor), and ticagrelor is not expected to be dialyzable. Treatment of overdose should follow local standard medical practice. The expected effect of excessive BRILINTA dosing is prolonged duration of bleeding risk associated with platelet inhibition. If bleeding occurs, appropriate supportive measures should be taken.

ACTION AND CLINICAL PHARMACOLOGY:

Pharmacodynamics

Inhibition of platelet aggregation (IPA) mediated by ticagrelor increases with increasing plasma concentrations of ticagrelor and its active metabolite (AR-C124910XX), until almost complete inhibition is attained. The inhibition of platelet aggregation gradually decreases with declining plasma ticagrelor and active metabolite concentrations, as the IPA mediated by ticagrelor is reversible. Since ticagrelor reversibly binds to the $P2Y_{12}$ receptor, the recovery of platelet function is expected to be dependent on the plasma concentrations of ticagrelor and the active metabolite and not on the replacement of irreversibly inhibited platelets as with thienopyridine antiplatelet agents.

The IPA of ticagrelor is generally independent of factors such as race, hepatic or renal disease or co-administered ASA, heparin and enoxaparin.

Pharmacokinetics

Ticagrelor demonstrates linear pharmacokinetics. Exposure to ticagrelor and its active metabolite are approximately dose proportional.

Date of Preparation: May 26, 2011

The Prescribing Summary provides the most current information at the time of printing. For access to the most up-to-date information, view the full Product Monograph (prepared for health professionals) by visiting www.astrazeneca.ca or by contacting AstraZeneca Canada Inc.

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CROSSROADS

Cultural Competency in Haitian-Serving Community Health Centers in South Florida

David Campbell

ABSTRACT: The purpose of this research was to explore the perspectives of health care administrators, practitioners and patients regarding the role and operationalization of cultural competency in their organizations. This work was conducted in three Haitian-serving Community Health Centers (CHCs) in South Florida. CHCs were established in the United States to provide services to underinsured individuals. In recent years cultural competency discourse has become prominent in these institutions through the establishment of federal regulations mandating these programs. The data was collected primarily through ethnographic methods: interviews and participant observation. Conversational interviews were held with the following groups of informants: staff, patients and members of the community at large. Semi-structured interviews were held with 15 physicians and administrators of the centers. Unexpectedly, institutions largely devalued cultural competency and were able to sidestep federal regulations by hiring Haitian staff. However, through interactions with patients, it was discovered that aspects of cultural competency were in fact important to them. The qualities they most desire in physicians are: accessibility, linguistic proficiency, and the ability to treat them as individuals within their cultural context."Cultural humility" is proposed as the resolution to this dilemma. Cultural humility involves a redefining of medicine's understanding of culture. It does not involve complex training programs or the hiring of physicians who are similar to the patient population, but is patient-centered medicine, practiced reflexively. This approach is proposed to improve communication without the undesirable assumptions and effects of the cultural competency paradigm.

INTRODUCTION

The Public Health Agency of Canada has published what they feel to be the 12 key determinants of health (1). Over the years there has been an important debate about the relative importance of each of these to overall health status. Through medical and academic discourse of these determinants, several medical experts have posited that culture is a major contributor to the health of immigrant populations (2-4). It has been postulated that minorities have poorer access to health care because of cultural incompatibilities with the health care system and with their individual providers. This spawned the notion of "Cultural Competency" – the idea that medical practitioners can tailor their care for a given cultural group if they gain an adequate understanding of the culture.

The notion of cultural competency became popular among physicians and administrators who work in clinics in large urban centres with significant minority groups. Many of these clinics have targeted members of particular communities by claiming to provide culturally competent services for that specific group. Cultural competency gained importance in highly Haitian-populated areas of South Florida, as cultural incompatibility is a frequently-cited barrier

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to health care for this population (5-6). It has been proposed that increasing cultural competency among practitioners could effectively address this barrier to adequate health care (7).

Two authors (8) have traced the appearance of the term "cultural competency" in medicine to a single publication by psychologist Paul Pedersen in 1988 (9). In the decade that ensued, many articles were published in both medical and anthropological journals, attempting to define cultural competency, and stressing its importance. In order to provide culturally competent care, it is requisite to define what is understood by the term culture. The medical understanding of culture is drastically different from that used in anthropological circles. Anthropologists feel that clinicians and medical researchers are prone to simply culture to distil it to a list of beliefs held by a given ethnic group. This definitional discrepancy has caused a debate between anthropologists and clinicians with regards to the importance of cultural competency and how it should be practiced and institutionalized.

Context

This research explored the notion of cultural competency, as embodied in several Community Health Centers (CHCs) that serve Haitian immigrants in South Florida, through an anthropological lens.

Haitians comprise one of the largest ethnic minority groups in South Florida. The area most densely populated with individuals of Haitian descent is Little Haiti – a neighbourhood just north of Downtown Miami with a population of 33,908 (10). The two counties located immediately north of Miami-Dade: Broward and Palm Beach, are also known to have sizeable Haitian populaces.

The majority of Haitian immigrants in this area are uninsured or underinsured (6). In recent decades, several publicly funded CHCs have been created to improve the provision of medical care and other vital social services to the uninsured and medically underserved populations in highly Haitian-populated areas of South Florida. These CHCs are distinct from one another in many ways; however each of them treats many indigent Haitians, and claim to provide culturally appropriate care for this population.

Community Health Centers provide an interesting site to examine the use of cultural competency in clinical settings. The CHC program was initially set up to establish a network of "safety-net providers" for patients with no alternative source of primary care (11). It was thought that this would improve access to preventive services and thereby decrease costly visits to public hospitals' emergency rooms. Susan Shaw, medical anthropologist specializing in culturally appropriate healthcare programming, has written about how the increasing preoccupation with cultural competency has caused CHCs' main objective to shift from being "providers of last resort" towards being "providers of culturally appropriate care" (12). This assertion has substantial implications for the effectiveness of CHCs and their ability to serve their designated purpose as safety-net providers. Anthropologists have questioned the erroneous assumptions that guide the clinical application of cultural competency, as such assumptions may result in unintended negative outcomes.

REVIEW OF THE LITERATURE

Support for Cultural Competency

Several medical anthropologists were instrumental in developing the idea of cultural competency. These applied anthropologists were involved in clinical medicine by "helping health care providers understand cultural differences in health behaviours" (13). These scholars focused on improving medical care through enhancing the physician-patient relationship. This is purportedly accomplished by "translating the understandings of anthropology for health professionals so that their services to patients can be more humanistic, holistic or culture-sensitive" (14).

Arthur Kleinman explains the differences between subjective patient experiences and the objective view of the medical profession through the Explanatory Model of Illness (EM) approach (15). Both patients and providers have individual explanatory models with regards to a given illness episode. Kleinman states that "the interaction between the EMs of patients and practitioners is a central component of health care" (16). These EMs may in some cases be drastically different, which Kleinman proposes can cause problems in the medical interaction. The incompatibility of patient and practitioner EMs, and the repercussions of such, lends support for cultural competency in medicine.

Journals of public health, nursing, psychiatry and clinical medicine are rife with publications that lend support to the further development of cultural competence in these diverse medical settings. Studies show that culturally appropriate care has been positively correlated with better disease outcomes (17) and may encourage proper use of vaccine programs (18).

Culture has often been cited as the reason patients fail to comply with the instructions of medical professionals. It is thought that if patient and practitioner EMs are dissonant this will negatively affect patient compliance: "the degree of 'match' or 'mismatch' between the patient's expectations and the care the patient receives will ultimately play a substantial role in the patient's compliance with and response to the treatment plan" (19). It is commonly believed that a physician who is trained in cultural competency will understand the particular qualms that might be troubling patients and be able to resolve them, which will in turn improve compliance. Cultural competency has figured prominently in discussions of quality of care within the medical professions over the past 15 years. They have advanced a strong case for the institutionalization of cultural competency.

Critiques of Cultural Competency

Critical medical anthropology is defined as "the work of anthropology turned upon our own society" (20). Many critical medical anthropologists have analyzed the assumptions made by the promotion of cultural competency models. These assumptions include: the static and isolated nature of culture used in this concept; the ability to define a culture by a certain set of beliefs or practices; and the homogeneity of individuals deemed to be of the same culture. Also important to consider are the repercussions of focusing on such programs.

In order to promote culturally competent care, the medical institution must first define "culture". This is very difficult, as "culture is what various people conceive it to be, and different people perceive it in different ways for different ends" (21). The way in which medicine has used "culture" has been one of the most prominent critiques of the cultural competency movement. Cultural competency frameworks were built upon outdated anthropological definitions of culture – where it is seen to be static and essentialist (22). While medical professionals have been devising strategies to increase knowledge of various cultures, anthropological discourse has produced a more nuanced and complex understanding of culture (23). Taylor states that "what 'culture' is taken to mean in these [clinical] contexts is generally quite distant from, if not actually at odds with, the current state of discussions of 'culture' within anthropology" (24). The most current understanding of culture in anthropological circles is one that "draws on diverse sources, depends on borrowings, and is in flux" (25). It is "a dynamic, ongoing process and an emergent product of human interaction" (26).

The definition of culture may be seen to be trivial in the context of medicine. However, it is tremendously important as this definition leads to another crucial assumption upon which the policies and practices of cultural competency are built: that cultures are distinct entities with their own definable 'beliefs and practices'. It then becomes possible to delineate the qualities of a given culture. These characteristics can be taught to clinicians thereby producing "culturally competent practitioners". Kleinman states that "cultural competency becomes a series of "do's and don'ts" that define how to treat a patient of a given ethnic background" (22).

The definition of "culture" used in this discourse includes the fallacious assumption that culture is equally and universally shared by all those who are known by a given cultural label. Dreher and MacNaughton claim that "although individuals may belong to the same cultural group, the assumption that they are, in fact, the same is an ecologic fallacy" (27). One's ethnicity is among several factors that can influence beliefs and actions.

The building of cultural competency on a foundation of fallacious assumptions is a serious matter, as emphasizing this type of essentialist cultural distinction can, in fact, disfavour minorities and increase health disparities through the practises of: ethnic risk grouping, victim blaming, covering up the socio-economic roots of health disparities, and leading to decreased patient-provider communication through cultural generalizations.

One rationale for the necessity of culturally competent care is that certain ethnic groups are deemed to be at higher risk for certain diseases. This technique of ethnic risk grouping has been heavily supported by epidemiologists. According to Ian Hacking (28), statistics related to humans must always be preceded by the classification of individuals into definable risk groups. Anthropologists are critical about such categorization and purport that 'cultural risk grouping' can essentially pathologize ethnicity (29). Viewed in this way, culture is a risk factor that a physician may check off alongside smoking or engaging in unprotected sex. A very well documented example of this practice and the ensuing marginalization is the classification of Haitians as a risk group in the American AIDS epidemic. (30). The pathologizing of ethnicities can ultimately lead to victim-blaming: when patients are blamed for their own illnesses due to culturally-determined behaviours. This can be seen as a means of absolving practitioners and institutions of the responsibility to provide the best possible

care to minority patients, as negative outcomes can simply be attributed to cultural factors. In this light, it could be argued that cultural competency does not improve the provision of health care, but rather, detracts from quality of care.

One of the most harmful effects of victim-blaming is that the true root causes of health disparities can be overshadowed. Statements such as: "Culturally competent healthcare systems have the potential to reduce racial and ethnic health disparities" (31), have generated considerable controversy. Health disparities are distributed predictably along the lines of class and socio-economic status (32-33). Emphasizing the cultural reasons for disease and morbidity can detract attention from true causes of inequalities. Farmer terms this "the conflation of structural violence and cultural difference" (34). Training culturally competent physicians is resource intensive (35). Critics of cultural competency argue that these resources would be better used to support initiatives that reduce socio-economic barriers to health care rather than building up programs that could potentially place blame back onto those affected by poverty and disease.

Finally, it can be argued that cultural competency could be paradoxically detrimental to physician-patient communication. This is illustrated through the Foucauldian notion of the "medical gaze" (36). This can be described as physicians "seeing a 'case' or 'condition' rather than a human being" (37). This concept is intimately tied to issues of power. The medical gaze is defined by Foucault as "the eye that knows and decides, the eye that governs" (38). This means that physicians are endowed with the authority to treat patients however they see fit, according to scientific principles, and patients are often denied a voice in their care. In the medical profession, it is generally acknowledged that gazing is an undesirable habit in medical practise (Davenport, 2000). Yet how cultural competency facilitates gazing is rarely acknowledged. This can happen as a practitioner gains the impression that he has become sufficiently familiar with ailments commonly affecting a given cultural group. Rather than taking the time to talk patients through their concerns, diagnoses can be made hastily since the physician is 'competent' in culture-bound illnesses. The physician is placing his own understanding of the cultural group's explanatory model on the person, rather than exploring the individual's EM in order to provide the quality personalized care that we claim is deserved by each patient, regardless of ethnicity or culture. A cultural competency model that is simplistic and utilizes the "dos and don'ts list" approach, can lead to more gazing in the medicine, and paradoxically, work contrary to its objective of improved clinical communication.

Cultural competency is an issue that is hotly debated with strong arguments both in support and opposition of these programs. Many clinicians and administrators argue that these programs will strengthen physician-patient relationships thereby improving compliance and ultimately producing better disease outcomes (39). Many critical social scientists are of the opinion that these programs are based on overly simplistic and fallacious assumptions about culture and its role in peoples' lives and may in fact result in poorer service provision to these cultural groups (40).

METHODS

Open-ended qualitative methods were preferentially chosen over preformed questionnaires in this study for several reasons. The strength of qualitative methods is that they are able to explore patient responses in rich detail. A preformed questionnaire is too restrictive in exploring the perceptions and beliefs that were the goal of this research: "Qualitative methods can be used to obtain the intricate details about phenomena such as feelings, thought processes, and emotions that are difficult to extract or learn about through more conventional research methods." (41)

Data for this ethnographic study were gathered during 6 weeks of fieldwork in South Florida. The primary methods of data collection were participant observation and interviews. The researcher volunteered at several CHCs and was able to observe the administrative aspect of the organizations' operations. The researcher also spent time in waiting rooms observing and conversing with patients. Semi-structured interviews were conducted with clinic administrators and physicians. Conversational interviews were conducted with clinic patients. Interviews and fieldnotes were transcribed and analyzed qualitatively by examining for common themes and codes.

All patient interviews were conducted in Haitian-Creole. Verbal consent was obtained from all informants who participated in the study. This study was approved by the research ethics board of the University of Edinburgh's School of Social and Political Sciences and followed all recommended procedures.

RESULTS

The research revealed that shared views

of cultural competency were non-existent – this supports the point that culture is much more complex than the medical profession portrays. The notion of cultural competency and how it is embodied both in individual practitioners and within institutions was explored. Each individual physician that was interviewed had unique and diverging understandings of what it meant to be culturally sensitive or competent in the given context.

Surprisingly, the most commonly recurring theme in cultural sensitivity expressed by individual practitioners was that culture was not of primary importance. Several practitioners reduced the importance of cultural differences to linguistic differences. These physicians claimed that if an individual speaks Creole (or if they have a translator) then they are adequately equipped to be equally as effective as a Haitian doctor or one who 'knows' Haitian culture. One physician in particular said that culture or ethnicity is not important but that success was entirely dependent upon the doctor's ability to speak Creole and build a relationship with his patients through empathy and compassion. He said: "they come to me because I make them feel at ease. They are not only my patient but they are my friend. It is only because of that relationship that there are many things that I can gather, that others may not, not because I am Haitian".

A diverging idea that was expressed was the importance of having a basic knowledge of Haitian culture. Individuals who claimed this believed that it helps them to make sense of patients' clinical presentations which differ from those of other Americans. Some said that it also gives them better perspective on how to increase compliance in their patients: "it helps you come from a perspective where you can actually get them to take what you want them to take".

Most physicians who believed in the importance of culture also believed in a "tolerance" approach to Haitian medical beliefs and expressed concern that trying to correct them may engender hostility and resistance. They expressed that they try to be understanding of people's individual beliefs while strongly encouraging people to follow their recommendations. By contrast, one Haitian physician expressed a "corrective" approach. He claimed that his knowledge of Haitian culture and medical beliefs allowed him to rectify peoples' misinformed etiologies and ineffective treatments. He stated that "you can't make them understand unless you speak to them in their language" – he defined "language" as something much deeper than simply words – he meant having an understanding of folk beliefs and how these are verbalized. Essentially, his mastery of this "language" permitted him to translate patient presentations in Creole into a medical diagnosis and he could then provide education and a prescription in the patient's language.

The institutionalization of the federally mandated program of Cultural and Linguistically Appropriate Services (CLAS) in these CHCs was also explored. The researcher expected to find centralized training programs and institutional emphasis on cultural competency. Surprisingly, no trace of such institutional trainings was found. Some informants claimed that this was because cultural competency could only be learned by those who were truly interested in immersing themselves in Haitian culture, not by occasional trainings and corporate slogans. It was also expressed that this type of training would require significant amounts of time and resources.

Instead of investing in training personnel in cultural competency, the researcher found that these centers tended to prefer a 'quick fix' solution to the CLAS standards;in many cases this accomplished through the hiring of Haitian clinical and support staff. This way CHCs are able to claim to provide culturally competent care without having to do any extra administrative or educational work. This solution is fraught with problems and misguided assumptions. It assumes that because a provider is Haitian his culture is automatically compatible with that of Haitian patients'. This is certainly not necessarily true; many factors could make this unlikely, including education & socioeconomic status, religion, and length of time in the United States. Many classic ethnographies and social histories of Haiti describe the great divide between educated wealthy citizens and the peasants and slum-dwellers (42). One Haitian physician noted that he often sees this embodied in the actors in the CHC setting: "they [the Haitian physicians] want to be like French, they are acting like they are above the people they are serving". Clearly, if this is the case, hiring more Haitian physicians is not an adequate response to demands for increased quality of care for patients.

Religion is another factor that could cause a Haitian physician to be less culturally sensitive than a foreign doctor. The traditional religion of the Haitian peasantry is Catholicism coupled with Vodoun (42). The Haitian elite has been characterized as being naive or hostile when it comes to knowledge about Vodoun: "They know

very little about vodou which they dismiss as odd superstitions of the mass and are sensitive about the subject... They feel that vodou has given a bad name to Haiti" (43). Even if they are familiar with patients' folk beliefs and treatments, a physician who belongs to the elite class may have class or religion-based Anti-Vodoun sentiments and would be more likely to have a personal bias against these beliefs than a foreigner who has no moral ties to this worldview.

The amount of time that one is in the United States also affects the ability of someone labelled Haitian to be culturally sensitive. An example of this is one of the Medical Assistants at a CHC who serves as a translator for the non-Haitian physicians. In her role as translator, she is expected to be a cultural broker between the patient and the physician. She had immigrated to the US when she was young. When asked about times when patients present with supernatural illnesses she openly admitted that most of the time she has no idea what they are talking about. As the conversation went on, it became apparent that the researcher's knowledge of "cultural illnesses" surpassed hers, even though she was deemed culturally competent simply due to her ethnicity.

Beyond physician conceptions of cultural competency, it was important to find out whether patients had any concept of this issue and whether it was important to them. Approximately 80% of participants stated that they would rather see a Haitian doctor than a white doctor. Most of the others said that that they had no preference so long as there was a translator present, and a minority stated that they would rather see a non-Haitian physician. Those who would rather see a Haitian physician used certain catch phrases and proverbs to explain why this was important to them: "Jan pa yo se pa jan pa nou" – their ways are not our ways, "lè ou manje manje ou, ou rekonet gou, men lè ou manje manje ou pa konnen ou pa konnen ki gou l genyen" – when you eat your food you recognize the taste, but when you eat food you are unfamiliar with you don't know what taste it has: "genyen maladi ki sèlman nan ras nou" – there are illnesses that are only in our race.

Patient informants were often very passionate about the issue of cultural sensitivity. This was surprising, especially in light of the disregard for CLAS from administrators and some physicians in each of the CHCs. One of the CHCs was interesting in that despite 40% of their patient base being Haitian, there is only one full-time physician who speaks Creole. This physician told me that nearly all the Haitian patients request to see him. He is saddened because his schedule is so full and he can no longer accept any new patients. Since he was hired he has been trying to convince the administration to hire more Haitian or Creole-speaking physicians. However, he expressed that they just are not particularly concerned with this issue and feel that the patients are fine seeing American or Hispanic physicians with a translator. These interviews left onewondering why if having a culturally competent physician is so important to Haitian patients, why it is neglected by the physicians and CHC administrators who serve them.

DISCUSSION

The researcher intended to take a critical approach to the application of cultural competency in these CHCs whose primary focus was supposed to be to function as a 'provider of last resort'. However, the position on this issue gradually changed over the course of the research as a result of interactions with CHC patients and staff. In fact, as a critical medical anthropologist whose role is "to position ourselves squarely on the side of human suffering" (20), the author took on a role of advocacy on behalf of increasing cultural competency, due to the significance of this issue in the eyes of patients and the widespread triviality of it to administrators.

This ethnographic research suggests that cultural and linguistic competency is important in clinical practice, at least for Haitian patients of South Florida CHCs. These clinics' response to CLAS standards – the hiring of a handful of Haitian physicians – seems insufficient to meet patient demands. Shaw states that there is a need to "move beyond straightforward ideas about [physician-patient] resemblance to develop more complex ways to modify systems of care to better respond to diverse patients (12). It is easy to understand the anthropological critiques of the "list of dos and don'ts" view of cultural competence but it is also important not to ignore the voice of patients who demand some form of cultural consideration. Several solutions to this dilemma have been proposed by anthropologists and clinicians. The resolution that is proposed in this article is a move towards Cultural Humility.

Cultural humility has been proposed as a solution to the cultural competency debate (44). Cultural humility is defined as "an ongoing, courageous, and honest process of self-critique and self-awareness"

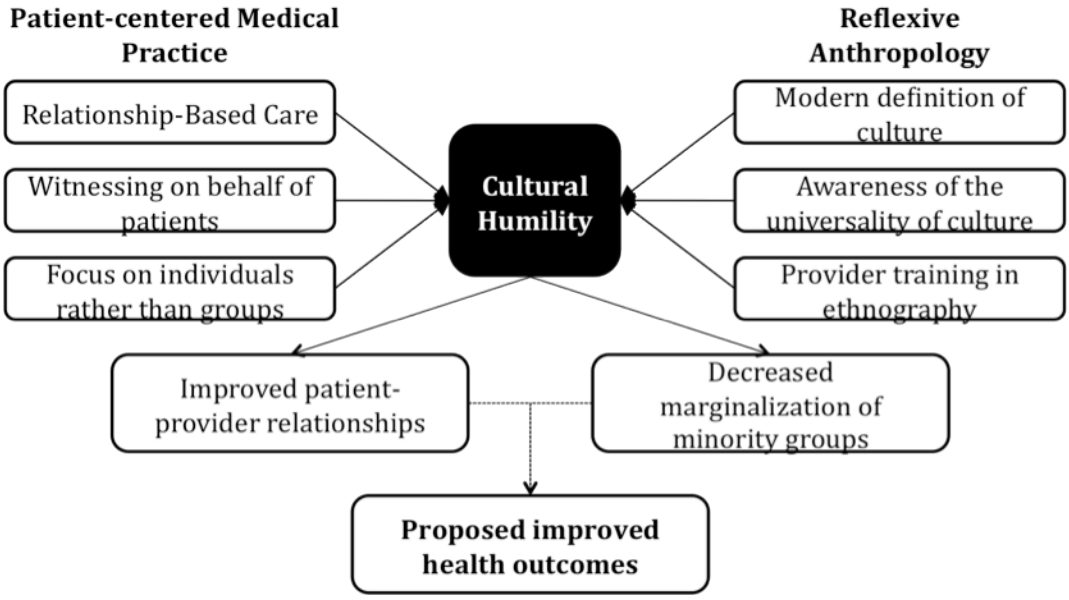

Figure 1: Conceptual Model of Cultural Humility

on the part of medical practitioners (44). The findings of this study show that cultural humility is what patients really demand. They were not looking for a specially trained culturally-competent physician, but were rather looking for a physician who practices medicine in a reflexive manner – cognizant of their own culture and open to diverging beliefs of others.

Cultural humility encompasses both the beneficial principles of patient-based medical care and encompasses the suggestions from discussions elicited in modern critical anthropology (See Fig. 1).

The first issue that needs to be addressed is a modernization of the "culture" used in medicine to bring it more in line with contemporary anthropological understandings of the term. This means that culturally humble medical practice recognizes that cultures are not static and are unable to be mastered in such a way as is idealized by the concept of cultural competency. This modern definition of culture also recognizes that cultures are not comprised of a homogenous set of beliefs and practices, and that there is significant and important variation in each member of any given culture. It is imperative that culture be recognized as a universal concept that affects the behaviour of all people: "cultural information is, in fact, embedded in the illness events of all of our patients, not just our "ethnic" patients" (27) and "culture is not just what patients have: clinicians also participate in cultural worlds" (22).

Clinical reflexivity can reduce the power-fraught notion of Foucault's medical gaze (Iedema, 2005, SSM). "Witnessing" has been proposed as the opposite to gazing, defined as: "acknowledging the whole lives of the population [physicians] serve" (37). Witnessing only becomes possible through cultural humility of the medical practitioner, or the willingness to relinquish his gaze and his position of power and authority. One of my physician-informants spoke of this cultural humility:

"Cultural competency is SO difficult to describe. I mean, what does that mean to anybody? How competent can you be in a culture that's not your own? I don't think you need to have that. I think that sensitivity is more important. Willingness to say "ok, they have a different way of seeing things, I'm willing to work with that, not totally oppress or impress my own cultural beliefs on it".

Humility and redefinition of culture can also function to improve the communication between physician and patient as it will lead to an "openness and willingness to seek clarification when patients present with unusual or unfamiliar complaints" (26). By employing a humble approach to culture, medical practitioners are forced to see patients as individuals rather than resorting to generalizations about them based on learned cultural stereotypes. One doctor explained that when you have a relationship with your patients and can communicate with them in their own language, you can understand their personal complaint rather than stereotyping them with your "cultural knowledge". This improved

communications approach that is facilitated by cultural humility has been termed "relationship-based care". This care is characterized by physicians who understand that "when compassion and care are conveyed through touch, a kind act, through competent clinical interventions or through listening and seeking to understand the other's experience, a healing relationship is created" (45).

It is proposed that the application of cultural humility to the medical system would enhance patient-provider relationships and potentially result in improved health outcomes. If engrained in medical professionals early, these practitioners would not require special training for each individual culture with whom they interact. One proposed method of increasing cultural humility in medical practitioners is to train clinicians in the art and methods of ethnography (22). One of the most effective places to implement this change would be to incorporate such teaching in undergraduate medical curricula. This would mean an increase in emphasis on subjective aspects of the medical interview and on the importance of listening to patients. While many medical curricula already teach these aspects of ethnography, basic instruction in reflexivity is rarely found in the objectively-driven field of western medicine (46). Young medical trainees need to be taught to acknowledge their limitations and biases and to recognize what implications these have on their ability to interpret data from the patient interview. If done effectively, this teaching would allow trainees to gain an appreciation for "the importance of understanding the natives' point of view… appreciating and humanly engaging with their foreignness" (22).

Cultural humility is proposed as the answer to the debate about the importance and effectiveness of the notion of cultural competency. There are significant complexities in medical interactions between individuals of different cultural backgrounds. However, many of these difficulties persist in interactions between providers and patients within the same cultural group. Cultures are not bound, static entities with clearly demarcated features. Attaining a level of competency in another culture is therefore not a realistic expectation. Cultural humility accepts a modern concept of culture and emphasizes relationship-based care where providers acknowledge and consider their own biases. This type of care is proposed to lead to strengthened patient-provider communication and relationships which have been correlated with improved health outcomes.

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CROSSROADS

When can you conclude death?

Evan Watts

How do we define human death? Is it a threshold in life or a catastrophic point of no return? Or is death simply a product of biological fact? What is your philosophy?

Over the course of human history, it is estimated that smallpox has claimed the lives of 300–500 million people; more than the Black Plague and the Great World Wars combined. Even as recently as 1967, this deadly killer was responsible for the deaths of approximately 2 million people each year. However in December of 1979, the World Health Organisation certified the eradication of smallpox; a day that proclaimed that no person shall die from the virus again.

The elimination of smallpox has ultimately challenged the very concept of death. Smallpox was a known killer in the 19th century and Edward Jenner's discovery of a vaccine (1) meant that science offered a way to defy death. It can be speculated that this discovery marks a critical point in science and perhaps even in the evolution of humankind. All of a sudden, humans seemed to be in control of their own destiny. Which meant that, in the century that followed, humankind took aim at prolonging life and in some respect, even manufacturing it. Nobel Prizes in science such as, insulin, stem cell research and organ transplantation were products of our obsession to provide a means to live longer and healthier. Even today, public focus continues to strive towards preventative and curative medicine with slogans of, "beating the fight against cancer", "saving lives" and "finding the cure for disease." The recent choice of wordage is nothing more than a positive spin on the concept of delaying death. If there is one thing for certain that has and will remain the same throughout time; you, me, and everyone – we will die; and yet we aim to prevent it.

With a growing focus on the concept of death, how is it medically defined? For example, is it merely an instance, or end product, of organismic death? Or, perhaps, does it hold a religious significance? This purpose of this article is to search deep into the philosophy of death; defining the known mechanisms and parameters that distinguish it from life. By the end of this, you should be thinking of your own definition and how it will apply to your clinical practice.

Understanding the concept of death is simple if you consider it as a fact; defined as the outcome to the end of life, or a condition as the result of life. The difficultly lies in understanding what constitutes the process of death; viewing death as an event. The medical community attempts to classify the event of death as the product of specific mechanisms. To fall into one of the different categories, a person's death has to exhibit resemblance to others that have followed similar mechanisms to the fact of death. The premise of this methodology assumes that the underlying mechanism of death is a biological fact (i.e., a specific system in the body has undergone irreversible damage, and has caused death). It also assumes that individual deaths are universal (i.e., the event of death from all cases of colon cancer are identical).

If we are going to assume that death is due to biological breakdown then we must investigate life as an assortment of biological factors that prevent death. This concept is related to the idea of maintaining internal harmony (i.e., preventing death), which in the body is a process known as homeostasis. Homeostasis, by definition, describes how disturbances to the internal environment are

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normally kept within narrow limits via automatic processes that are recruited to prevent wide oscillations within the body (2). For example, physical properties such as temperature, oxygen saturation, blood pH, organ perfusion, blood glucose levels etc., are restricted to unique ranges of values that are in place to ensure our livelihood as a biological unit. The significance of regulating these constituents is not only important at the level of the whole organism (the individual) but at every level of our biology, including organs, tissue, and at the cellular level. It is using these levels of organization that we can begin to see how the loss of homeostasis can ultimately lead to death. The best way of describing this is to look at an example. For instance, in myocardial ischemia, disturbances in blood flow to the heart results in its starvation of essential oxygen (3-4). The cause of ischemia is most commonly triggered by an increased demand on the heart (i.e., work) and/or the presence of an atherosclerotic plaque in one of the epicardial coronary arteries. In an attempt to restore the reperfusion rate in an ischemic heart, a series of homeostatic cascade mechanisms are automatically activated to increase oxygen to affected areas (5-6). However, under certain conditions these compensatory mechanisms fall short (i.e., myocardial infarction) and the affected tissues of the heart undergo a process of irreversible damage. The consequence of this process is collectively called cellular necrosis, or tissue death (7-8). At the very extreme, necrosis of the heart destroys its electrical or mechanical function; predisposing to fibrillation and/or cardiac arrest. If the heart was to arrest, or there was ventricular fibrillation, the down-stream consequence of reduced cardiac output would involve the brain receiving an inadequate supply of blood. This would most often manifest as a loss of consciousness and would start-off the countdown before the onset of irreversible brain damage (9-10). As the functionality of the brain decreases, brain-stem activity concurrently dampens; ceasing respiration. At some point after the loss of consciousness and the capacity to breathe, there is an evidential transition from life to death. Was it the loss of brain function that ultimately defined death?

To examine this idea, we must go back to the second premise of the organismic theory of death, which describes individual death as universal. If this proves to be true, this raises the question if people exist only when the brain is functioning? To begin to answer this question, we must first look for a mechanism of death that does not involve the underlying destruction of the brain. Firstly, we could identify organs in the body that are described as vital; as vital organs are essential to the succession of life. The problem with this approach is that the loss of a vital organ, for example the liver, will provide a description of dying, but it will not define the event of death. Even so, the loss of liver function will create a series of pathophysiologies that result in death. For example, hepatic encephalopathy from detoxification failures can create susceptibility to the onset of human coma (11). This occurs either when the liver function fails or when the liver is bypassed in cases where portal circulation shunts intestinal venous blood into the systemic circulation. Liver dysfunction may also cause portal hypertension and loss of clotting factors. These may produce oesophageal varices, which can rupture and induce hypovolemic shock (12). The underlying cause of death from the loss of liver function (i.e., brain damage, respectively) in these examples has been documented as a series of downstream mechanisms that cause the cessation of brain function (13). But, how does brain dysfunction link to other vital organs? The paradigm of loss of brain function and death can be applied to the lungs, another vital organ, for example. With irreversible damage, the loss of effective oxygen diffusion at the lungs results in central cyanosis. In this scenario, the brain is receiving adequate blood perfusion; however the composition of arterial blood has changed, i.e., ¯pH, ¬pCO2, and ¯pO2 (14-15). The consequence of this condition may cause electrolyte disturbances resulting in cardiac arrest or more likely causing brain anoxic-ischemia. Evidentially, the time sequence of such anoxic changes is correlated with the extent of brain injury (16-17). In experimental models, periods of severe hypoxemia (greater than 10 min) resulted in extensive ischemic cell changes in cerebral neurons, especially prominent in white matter, which increased with time. Clinically, brief anoxic-ischemic periods lasting only minutes have produced sufficient brain damage to cause death in humans, although these observations have varied from person to person and with clinical setting (18).

Although these examples represent two isolated, and simplistic, mechanisms of death, they show the product of their dysfunction will result in brain damage. And so it raises the next question, “Is the loss of brain function a definitive step in the event of death?”

To further investigate the importance of the brain in the event of death, we must look at the brain

and the body as separate and distinct mechanisms in the cessation of life. In this way, we can identify if brain dysfunction is the ultimate factor that causes death, or rather, if it is merely the evitable downstream product of bodily dysfunction. Traditionally, death was only viewed along the lines of bodily dysfunction, known as the cardio-pulmonary standard of death (19-20). When this method was used to determine if someone had died, the attending physician would look for signs of life, such as a pulse, breathing, or other indications that the heart and lungs had stopped working (i.e., chest movements and/or moisture coming from the mouth). If these physical characteristics were found to be absent, then the attending physician would confirm (in his professional opinion) that the patient had died. The significance of this methodology in the confirmation of death was experimentally first acknowledged in a study in 1938 (21). During this time, a prisoner in Utah, Arizona, U.S.A., was to be executed for the murder of an innocent businessman. In a gesture of atonement, the prisoner agreed to participate in an experiment to have his heartbeat recorded during his execution – the first of its kind. The intention of the experiment was to provide information of how soon death would occur, after the heart is wounded. During the execution, four bullets were launched into his chest. One bullet ripped directly into the right side of his heart causing it to spasm and then 15 seconds later, stop. Although his heart no longer beat, the prisoner had regular and steady breathing. After 135 seconds his breathing finally stopped and he was pronounced dead. Even today, this methodology is still practiced, i.e., the natural expiration of some people is determined by the cessation of the heartbeat and breathing. Does this conclude that death and brain function is really just a downstream event of bodily dysfunction?

Well, not long after the union between scientific technology and medicine did we begin to see the importance of brain function in the determination of death. Resuscitative technologies, such as mechanical respirators and defibrillators, were beginning to rescue patients after periods of asystole lasting up to several minutes (22). Next, the uses of cardio-pulmonary by-pass machines were allowing patient's heartbeat to cease for several hours with full recovery. Finally, mechanical ventilators were making it possible to maintain oxygen exchange in the lungs indefinitely, which was allowing comatose patients to sustain oxygen perfusion to the body and their viability as a whole (23). All of a sudden, these interventions were giving doctors the tools to restore life. Out of this was coined the concept of brain-stem death, which highlighted that the loss of neurological function and/or the lost of cardio-pulmonary function can result in the fact of death. If we shift our thinking back to the essential importance of the brain, it is really the loss of brain function that is coordinating the event of death (21,24). Therefore, if we are to consider the brain as vital to life, along with other organs, then we must also consider it as the essential element to life. And with that, we must understand that all roads to death will eventually involve some sort of brain dysfunction. But, this still does not answer the question of how the event of death is related to the brain? And, why is the brain so important?

A simple mechanism known to occur before the fact of death is the loss of consciousness. Consciousness by definition is the state of awareness of self and the environment. It is well known that consciousness is a product of the brain as disorders in consciousness have been correlated with a wide spectrum of brain dysfunction (25). The range of human consciousness is rich and variable, which includes a baffling number of terms have been applied, such as "vegetative state", "akinetic mutism", "delirium", "sleep", etc. Understanding the degree of consciousness is important in determining when it exists and when it is lost. Consciousness is based on two physiologic components, namely, arousal and content (26). Arousal is the behavioural aspect of consciousness, which is closely related to the appearance of wakefulness. Content is the other aspect of consciousness that represents both cognitive and affective mental functions. To use these in an example, a lesion to the brain may result in the inability to comprehend language (Wernicke's aphasia) although the patient is fully awake and aware of self and environment. But it raises the question: With so much variability in consciousness, how does this tie into the event of death?

It is important to stress that any impairment, reduction or absence of consciousness does not imply the presence of death. Death is a limit of consciousness that describes the permanent and total loss of external awareness, with the lack of any potential to regain responsiveness, even if externally stimulated (26-27). Death also describes a process where normal conscious function has been irreversibly replaced by a state of non-function. In this condition, the brain has undergone damage so extensive that it can no longer maintain the body's internal functioning as well as the ability to elicit any transmission of neuronal signals. Clinically, com-

plete cerebral ischemia in humans can cause the loss of consciousness in 8-10 seconds. Not surprisingly, the exact cause or sequence of molecular events that underlie the transition from first functional changes in the brain to brain death, is not fully understood. Some experimental studies have shown that reduced blood flow (oligemia) to the brain or oligemia plus hypoxemia produces initial neuropathic changes in unique regions of the brain, after insults as brief as 2 minutes (28-29). These initial changes begin with mitochondrial swellings in the hippocampus that progress to wide spread injury affecting more distal areas of the brain. Evidence also suggests that ATP levels play a vital role in the vitality of brain tissue. It was shown that following functional changes such as hypoxia, ischemia, hypoglycemia or hyperammonia, if ATP levels remained within normal cellular limits then the insulted brain tissue could restore its functional capacity. If damage is located to both the cerebral hemispheres and brainstem, this results in the loss of internal homeostasis aforementioned. By contrast, the irreversible loss of consciousness seen in a permanent vegetative state describes a process where the cerebral hemispheres are extensively damaged, but the brainstem is largely intact (30-31). These individuals have undergone permanent loss of the ability to maintain connection with the external environment but they have retained enough brainstem function to continue with unassisted respiration and heartbeat.

The difficultly in determining the status of an unresponsive patient is that the confirmation of death does not rely on a single laboratory test or screening procedure. Diagnosing death requires a general agreement that brain death has ultimately occurred and that requires one to exclude all discernible evidence that either the cerebral hemispheres or vital centres in the brainstem are functioning, and equivocal evidence that they may begin to function in the future. Traditional thinking has death as the final state to life. The problem with this viewpoint is that death does not always follow tradition. Death is unique in that it is not solely based on an outcome. The process of dying can be long, painful and questionable. How will you truly know when someone has died? And by looking at the event of death, can this pathway be inhibited to prolong life?

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