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UTMJ

University of Toronto Medical Journal

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UTMJ

University of Toronto Medical Journal

University of Toronto Medical Journal, 1 King's College Circle, Room 2260, Medical Sciences Building, Toronto, Canada M5S 1A8
E-mail: editors.utmj@utoronto.ca • http://www.utmj.org • Phone: 416-946-3047 • Fax: 416-978-8730

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Preface from the Editors

Dear Reader,

We are pleased to present you with the first issue of the 94th volume of the *UTMJ*. While a large spectrum of human disease has been discussed in previous editions of the *UTMJ*, our current theme of Paediatric Health has remained largely out of the spotlight. Our understanding of the interacting roles of genetics and environment in paediatric development, health, and disease is beginning to unfold. The impact of paediatric health on future healthcare outcomes, including those extending into adulthood, cannot be understated. Despite major advances in research and health care, however, close to six million children in the world under the age of five die every year.[1]

We are thrilled to feature original research, reviews, commentaries, interviews, and book reviews that encompass a variety of topics pertinent to paediatric health. In his review, Dr. David Malkin provides a thorough discussion of cancer predisposition syndromes and their implications. We are also proud to feature an interview with Dr. Michael Apkon, President and CEO of the Hospital for Sick Children, who is leading a new era of change and helps to illuminate some of the challenges encountered in paediatric healthcare.

This is an exciting time for paediatric health, with new battles being won and new challenges being overcome every day. It is with this same sense of duty and optimism that the 2016-2017 *UTMJ* team has endeavoured to compile this issue. We would like to express our appreciation for the dedication and hard work of our team of section reviewers, copy editors, associate editors, the interview team, cover artist, and web developers. We are grateful for ongoing patronage of the journal by our sponsors. Finally, we would like to thank you - the reader; we hope you enjoy reading this issue!

Sincerely,

Mark Shafarenko
Ahmad Mousa

Editors-in-Chief, UTMJ

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1. World Health Organization

Inuit Children's Health Shaped by Their Environment

Carla Jeantin, French Baccalaureate, MD student[1]

[1]Laval University Québec

Over the past years, Inuit child safety has been set as a priority in our health system in order to ensure equitable access to health care services. Not too long ago, I was offered the opportunity of doing a clinical observership in Nunavik, Québec. I came prepared with knowledge regarding their culture but little did I know about the reality to which I would be exposed.

Children account for more than half of the Inuit population and many Inuit children live in unsanitary conditions. Representing the community's future, they begin their lives with poorer health than other children in Canada.[1] This discrepancy is highly correlated with social determinants such as nutritional inadequacy,[2] family and social condition, and household income.[3] Housing conditions are the focus of this article as it is a specific social determinant at play that I was able to witness during my internship. It is a public health concern that should be brought to attention, and the reality of this issue concerns not only Nunavik but also other aboriginal communities across Canada. Early exposure to environmental pathogens can impact their health in the short term – for example: infections – as well as in the long run with chronic diseases.

Housing security's impact on health is an issue that is known and recommendations exist which guide regional housing authorities and help the prosperity of communities. WHO[4] recommendations help evaluate the burden of the environment on our health. In their guide, they expose the correlation between household crowding and tuberculosis, second-hand smoke and respiratory diseases, and indoor dampness and asthma onset in children. Other conditions have been described but these particular ones are the most represented in the Inuit population.

During my internship, I participated in home-visit services with a nurse and I was struck by the way the Inuit were living. The indoor air was damp and polluted with cigarette smoke. As the average number of children per family is around four or more,[5] household crowding is very common. Children are exposed to forgotten dirt, moisture, and dwellings that need repair.

These alarming conditions are compromising the health of Inuit youth and can lead to chronic diseases such as ischemic heart disease, asthma and lung cancer in adults.[5] Indoor air pollution from second-hand smoke is linked to respiratory disease. In many of the Inuit family's homes, smoking is a habit as 58% of Inuit in the North smoke cigarettes and 46% of the Inuit started smoking at age 14 or younger.[6] Hence, Inuit children are frequently exposed to second-hand smoke. It creates indoor pollution, which increases not only the risk for infections but also respiratory disease. In a damp and polluted environment, children are more prone to develop allergies and asthma.[4] The pollution creates inadequate ventilation, which is also correlated with a higher risk for infectious disease transmission such as tuberculosis.[4,5] Tuberculosis is an important cause of premature mortality and is much more prevalent in the North[7] than in southern territories in Canada.

Moreover, household crowding is correlated with an increased prevalence of tuberculosis, as the crowding increases the frequency and duration of contacts among individuals, which helps spread the disease.[5,8] Thirty-six percent of Inuit children are living in a crowded environment (more than one person per room) and 29% live in dwellings requiring major repair.[4] The health of Inuit children aged from two to five is especially related to housing conditions.[4]

We need ongoing monitoring in Inuit communities or large population-based studies to better manage the health of Inuit children. More research needs to assess not only the diseases induced by poor housing but also the impact it has on the development of Inuit children. In 2016, the regional housing authorities are still in need of financial help to address this issue.[9]

This housing crisis endangers a generation of Inuit children. Too many children are affected by poor housing security and the impact it has on their health is critical. This problem has been going on since the creation of Inuit sedentary communities and we need to keep our promise of health equity among children in Canada. If it is not remedied now, Inuit children will not have a fair chance of thriving in Canada's future because of the consequences of poor housing conditions on their health.

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Addressing the Needs of Canadian Children with a Social Paediatrics Approach

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Increasingly, the need to address the social determinants of health in clinical practice is being recognized.[1] In the realm of community paediatrics, focus on the social factors that influence child development and health is known as "social paediatrics". This article will explore social paediatrics, its history, educational training opportunities, and various initiatives that have been undertaken.

The History

The term "social paediatrics" stems from the establishment of the European Society of Social Paediatrics and Child Health (ESSOP) in Sweden in 1977 by paediatricians who believed it was essential to consider social context in child health.[2] The ideas endorsed by the society stem from physician reformers, particularly Abraham Jacobi (1830–1919), who is considered the father of social paediatric medicine.[2] ESSOP defines social paediatrics as "a global, holistic, and multidisciplinary approach to child health", which considers the "health of the child within the context of their society, environment, school, and family."[2] In Canada, social paediatric initiatives began to gain ground in the early 2000s, and as of 2013 every Canadian medical school offers electives that fit within the scope of social paediatrics, such as Aboriginal, immigrant, or refugee child health, or the impact of environmental factors on child health.[3]

Medical Education in Social Paediatrics

Canadian medical schools generally offer elective opportunities during undergraduate and post-graduate training to further educate students on social determinants of health, through first-hand experiences with disadvantaged children and families. Trainees are exposed to medical care in new settings – including schools, community centres, clinics for the uninsured, and patient homes – and they work with skilled multidisciplinary teams and specialists.[4] These programs demonstrate the challenges faced by disadvantaged children and youth, and how these can influence childhood development and contribute to subpar life trajectories. At the end, students may be asked to write a reflective report on their experience.[4]

Reflective Report

The reflective reports written by trainees have been published in major journals and in the media, and have helped shed light on some of the most poignant issues in our communities. "How did you sleep last night? Have you eaten today?" published in *Child and Paediatric Health* speaks about an elective student's experience of asking those questions on a home visit to a teenage mother, opening up a dialogue about a whole host of issues including safe housing, literacy, education, safe sex, and prenatal care.[5] In "Antibiotics without food" published in the *Canadian Medical Association Journal*, another student is about to advise an 18-year-old patient in a group home to take antibiotics with food, before realizing that the patient may not have food to take with their medication.[6]

Another student's experience was published by *The Evidence Network* and was featured in the *Toronto Star, Huffington Post*, and *Ottawa Life*. She wrote:

> *"When a doctor regularly meets patients who face poverty, food insecurity, lack of safe housing and psychosocial stressors, it reinforces the necessity to ask about their social and living conditions. We don't know unless we ask. And we don't ask unless we understand those living in poverty."*
>
> *"Medical schools teach a lot about patient-centered care. But there's a need for more exposure to the daily struggles of disadvantaged families."*
>
> *"I wish more of my fellow medical students could share this experience of immersion into a culture of medical practice where a deep understanding of the experiences of marginalizes groups influences not only the questions asked, but the treatment strategy and approach"*[7]

Raising Awareness

A large part of social paediatrics is educating stakeholders and the public about issues related to child health, and advocating for improvements through editorial and commentary publications in medical journals and major newspapers.

Dr. Dennis Daneman, the former Chief of Paediatrics (2011–2016) of the Hospital for Sick Children (SickKids), has been active in publishing on the topic of social paediatrics. Under his leadership, the 16 Paediatric Chairs at Canadian medical schools published an article revealing Canada's mediocre results on a 2013 child well-being UNICEF report and

advocating for a robust child health advocacy strategy and integration of the social paediatrics approach into medical curricula.[3] Since then, he has published updates on the state of child well-being in Canada, keeping these issues at the forefront of the medical community.[8,9]

The Evidence Network has also become a popular platform for experts to offer their opinions on a range of issues. For example, Dr. Lee Ford-Jones, a paediatrician at SickKids, has written extensively on the issue of child poverty, as well as vision screening and the affordability of corrective lenses.[10]

Social Paediatric Initiatives

A wide range of social paediatric initiatives has been undertaken by healthcare practitioners to address the disparities faced by at-risk children in our communities. Some examples include clinical screening tools, collaborations with legal professionals and community health centres, and new sites for healthcare delivery.

New Tools for Clinical Use

Improving Identification of Needs, Linking to Community Services, and Accessing Additional Financial Resources

Canadian children who grow up in poverty are at higher risk of poor health and developmental trajectories. In response, a tool was developed using the mnemonic "ITHELLPS" to assist family physicians and community paediatricians with comprehensively covering social history and identifying families with unmet needs. The tool incorporates questions about income, transportation, housing, education, legal status, literacy, personal safety, and support.[11] Screening families for social problems allows for further assessment and referral to resources and programs.

Poverty tools developed by physicians in a number of provinces provide a comprehensive list of national and provincial specific resources and programs.[12] Physicians who identify any issues in the social history are able to easily connect families with programs or other community resources they may benefit from.

Screening and referral to programs within clinic and hospital settings has been investigated in a number of studies. These studies have shown improved outcomes, such as increased referral and better navigation of and access to community and government programs.[11]

Speech and Language Tool

Early speech and language delays can influence a child's early development and literacy skills. Unfortunately, children with speech and language delays may not get access to speech and language services in a timely fashion, due to late identification and significant wait times following referral. In response, paediatricians from SickKids worked with Toronto Public Health to develop a tool that helps primary care physicians identify speech and language delays in children early and accurately, refer to appropriate services as required, and offer effective home-based interventions in the interim period before referral is accessed.[13] Home-based interventions by trained parents have been shown to be equally effective to those offered by clinicians, and ongoing research will seek to validate this tool and determine its short and long term impacts.[13]

New and Enhanced Collaborations

Legal Advice

Families faced with social inequities that influence child health – such as inadequate housing, immigration challenges, and unstable employment – often benefit from legal assistance. Unfortunately, families may be ineligible for legal aid assistance and unable to afford legal counsel. In response, Pro Bono Law Ontario at SickKids was established to provide free legal help to economically disadvantaged families of children treated at the hospital. Over a one-year period, the program provided 360 consultations for issues including domestic violence, child support and custody, immigration law, disability and family welfare, and health insurance.[14] The program proves that many low-income families can benefit from the advice of a legal professional.

Community Health Centres

Given the difficulty that low-income children and families have with accessing conventional as well as multidisciplinary medical care, alternate models of healthcare delivery are needed. Community health centres (CHCs) are an excellent model, as they offer interprofessional care and engage the community on relevant priorities. CHCs work together with other community agencies to provide culturally appropriate care and address the specific needs of the community. CHCs are increasingly recruiting community paediatricians as consultants in order to offer high quality, multi-disciplinary care, and physicians have made a unified appeal to try to attract more paediatricians to community health centres.[15]

New Sites of Care

School-Based Clinics

Inner city families often face significant barriers in accessing healthcare, including issues with transportation, cultural and language barriers, lack of healthcare benefits, discrimination and stigmatization. School-based healthcare clinics have been proposed as a solution to improve children's access to healthcare services. The Toronto District School Board and St. Michael's Hospital launched the Model Schools Paediatric Health Initiative, which established a school-based clinic in an inner-city elementary school in Toronto. Two-thirds of families who qualified enrolled their children in the clinic, and one-third of those children attended. Three-quarters of patients seen at the clinic received a new diagnosis. In particular, developmental diagnoses were made in a large number of children.[16]

Clinics for the Uninsured

Paediatric residents at the University of Toronto initiated a paediatric consultation clinic for medically insured children and youth at the Scarborough Community Volunteer Clinic. The clinic provides care to recent Canadian immigrants or refugees and failed refugee claimants who are not covered by the Ontario Health Insurance Plan (OHIP).[17] During their six-month pilot project, a variety of paediatric cases were seen, including asthma, amenorrhea, developmental delay, and behavioural problems. Paediatric residents in Hamilton, Ontario, have also initiated similar programs.

Vision and Hearing Screening in Schools

Inner city children face significant barriers in accessing vision and hearing screening. In addition, families may lack financial resources for interventions such as prescription glasses or hearing aids. Lack of identification of vision and hearing problems can have long-term detrimental effects on educational attainment. As a result, the Toronto Foundation for Student Success began a program called the Gift of Sight and Sound that has provided free vision and hearing screening to nearly 10,000 students in Toronto model schools. If necessary, children receive free hearing assistance devices, complimentary optometrist services and glasses from corporate sponsors, and additional referrals.[18] In 2008/2009 the screening program identified and provided referrals for one in four children with potential vision problems and one in seven with potential hearing problems. In 2009/2010, 90% of children with an identified vision problem were followed up by a school-based optometry clinic.[18]

Future Implications

Many social paediatric initiatives have been developed based on best available evidence. Further research is necessary to determine and quantify their impacts. Many of the initiatives involve expanding the scope of practice within clinics and hospitals to address factors that have a known effect on child health such as poverty, delayed speech and language development, and inaccessibility of legal advice. These initiatives may require a multi-disciplinary approach with realms such as social work and law, where partnerships have been shown to improve health outcomes for at-risk populations.[19] Other initiatives involve offering medical care in new settings, such as community health centres and schools, which has been shown to empower communities and promote community investment.[18] Finally, programs that offer medical services to children without medical insurance ensure a standard of care for all children in Canada.[19] While these programs are not widespread, proof of their benefit through further research may lead to greater integration of these approaches into general paediatric care.

Conclusion

After 20 years, and in keeping with societal needs, social paediatrics in Canada has necessarily expanded. Training opportunities have taught healthcare practitioners about the factors that can negatively influence child health and well-being, such as poverty and limited access to healthcare, and how to utilize a social paediatrics approach to address these. Physicians have developed initiatives that work to improve the health of children in the community. Moving forward, the hope is that these programs can be expanded, new programs can be developed, and we can prove to the world that Canada is committed to caring for its children.

Acknowledgements

I would like to thank Dr. Lee Ford-Jones for her guidance and support in the creation of this article.

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Do Doctors Treat Communities, Too?

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"The doctor will see you now." This is what patients hear when they go to visit their healthcare provider. During this visit, the doctor may perform several examinations, order investigations, listen to the patient's narrative, write a prescription, provide patient teaching, follow-up with the patient, and so forth. Hopefully, by the end of the encounter the patient has received the care and guidance they need to feel better.

Utilizing their medical skills and knowledge to promote health and prevent illness is undoubtedly a major role for physicians. When physicians interact with patients, the clinical process may seem clear. A patient presents with an illness, a diagnosis is made, and a treatment plan is initiated. However, how does this apply to communities? Is it the same process?

A community can be defined as a group of people who share a common living space, certain interests, resources, and/or needs.

In this context, a community does not need to be restricted to a neighbourhood. In fact, communities can arise in and intersect between a variety of contexts including workplaces, schools, cultural centres, and groups of individuals. Therefore, when considering *whom* the physician is working with in a community, one must recall that communities do not need to have defined locations. For example, a group of single-parent mothers can be considered a community.

Physicians working closely with communities can be found in areas such as public health, medical clinics, community centres, and more. By understanding the role of physicians in the community, one can come to appreciate the influence of these interactions on the health of our patients. In a community context, physicians can still effectively listen to narratives, perform examinations, and prescribe treatments, but the methods and processes by which these activities are done may vary.[1] For example, consider the physician who is working with a school plagued by poverty. The children are tired and their health suffers because their parents cannot afford to pack healthy lunches, nor do they eat breakfast at home. What can a physician do? The first step should be to identify the issue. This can be done by listening to the children describe their problem and by observing the effects of the problem on the children (ex. fatigue, poor concentration, poor developmental growth, etc.). The next step should be to consider how one approaches or solves the problem, such as considering what needs to change so that the children can have healthy food to eat. The physician must use his or her knowledge, skills, and any available resources to create a care plan, the "prescription," that will be effective. Just like writing a prescription for a blood pressure pill or a new pain medication, the community physician in this case may consider "writing" a prescription that informs parents on food banks they can access for assistance. Alternatively, perhaps the physician will decide to provide free workshops to the parents on how to purchase and prepare healthy foods on a budget, in the process helping parents understand the importance of doing so. This is, in essence, equivalent to providing individual patient teaching and counselling on the treatment regime. Next, the physician ought to follow-up and monitor the progress of the community. Did the intervention work? Have the children eaten breakfast before coming to school and do they have healthy lunches? This is akin to monitoring the blood pressure status of a patient who has been prescribed a new pill, or tracking the blood test results of a patient who began taking iron supplements for iron-deficiency anemia.

Working with communities can have its own challenges. With a large population, it can be difficult to define priorities. The community may have a multitude of concerns, and determining what the physician will first work on can be overwhelming. Moreover, a lack of apparent resources complicates this process and makes it difficult for physicians to implement certain interventions. How does the physician overcome these obstacles? The answer seems to be that the encounter, similar to what occurs with individual patients, is to use what is available. When working with patients, physicians draw on their individual strengths and direct patients to resources that may be of assistance to them. The same ought to occur when working with communities. The astute physician will empower communities to identify the resources they have and to make use of them. Communities should be reminded that they are partners with the physician and that together they can work towards better health outcomes.[2] This provides the community with a sense of strength and unity. Furthermore, physicians can and should promote capacity building amongst the community. This is a process whereby communities are encouraged to continuously identify their needs and make plans to address them as a group. This strengthens relationships between members, but also provides communities with opportunities to make partnerships with other organizations, healthcare teams,

and so forth. Thus, it is clear that the work of a physician with a community is a circular, collaborative process.[3]

Examples of physicians working in the community are numerous. Consider the role of public health physicians, who monitor infections, outbreaks, diseases, and responses to treatment. These physicians look at communities as a whole and aim to prevent health crises from occurring. One should also consider family physicians who may see patients with a host of concurrent medical issues. Of course, these patients cannot be treated without first understanding the contexts in which they live: their communities. By exploring the community context, understanding the risk factors inherent in the neighbourhood, and highlighting the strengths of the community, the physician can better help the patient and the community. For example, through open communication and discussion, a physician may realize that a certain community lacks adequate housing, and that this predisposes the citizens to respiratory infections. By knowing this, the physician can treat a patient presenting with a respiratory illness correctly, but can also take this further and advocate for change in the community. Therefore, the interaction of the physician with the community has the potential to impact not only the health of individual patients, but also of communities.

Winston Churchill once said, "Healthy citizens are the greatest asset a country can have." This can only occur when physicians begin to treat communities, not just individual patients. Working with communities can be extremely rewarding for physicians as it not only allows physicians to make a difference, but it also creates special partnerships and therapeutic relationships.[4] For communities, benefits include having their concerns addressed, receiving support and guidance, and feeling that they are not alone. Communities also benefit by becoming empowered to change their lives and to promote their own health, just like what occurs during a physician-patient encounter.

"The doctor will see you now." This is what communities ought to hear when they require assistance, empowerment, intervention, and guidance. These physician-community encounters are what define community health promotion.

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Interview with Dr. Michael Apkon

UTMJ Interview Team (Sarah Kanji, Nicole Kim, Aidan McParland, Austin Pereira, Shubham Shan)

Dr. Michael Apkon

Dr. Michael Apkon, MBA, MD, PhD, was appointed President and CEO for The Hospital for Sick Children (SickKids) in January 2014.

Dr. Apkon has a BSc degree in Biomedical Engineering from Northwestern University, as well as MD and PhD degrees from Washington University School of Medicine in St. Louis and an MBA from the Yale School of Management.

Prior to coming to SickKids, Dr. Apkon was senior vice president for Medical Affairs and the chief medical officer for the Children's Hospital of Philadelphia (CHOP) and professor of Anesthesiology and Critical Care at the University of Pennsylvania, as well as a practicing paediatric intensive care specialist.

Dr. Apkon also served in leadership roles at Yale University School of Medicine and Yale-New Haven Health System, including executive director for Yale-New Haven Children's Hospital, and as a faculty member for Yale School of Medicine and the Yale School of Management.

As a healthcare executive, Dr. Apkon has led systems development and improvement to drive high quality and safe care, improve clinical operations, and promote an integrated approach to healthcare across a continuum of services. His academic interests include using technology to enhance safety and the application of operations management tools to enhance performance.

UTMJ: Could you tell us a little about yourself, your career trajectory and your transition into an executive capacity?

MA: I was educated first as a Biomedical Engineer, and engineers think about systems from the standpoint of how different components are selected and connected together. I believe in the proposition that every system is perfectly designed to give exactly the performance that you observe. This is a mechanical view of the world and how things work. After completing my undergraduate degree, I trained as a scientist. Scientists believe that there are explanations for observations, although they may remain to be discovered, and they work through hypothesis generation and testing to develop models that explain those observations. In some ways, they are trying to figure out the system design by probing it from the outside. Scientists will acknowledge that all models are flawed, but some models are useful and help communicate a way of thinking about the world. I also have been trained as a physician and have been moved and inspired by the promise and capability of modern medicine and by the caregivers that bring commitment and passion for making a difference at the bedside. At the same time, I have also been frustrated that systems of care are sometimes inadequate and can even fail tragically. Those failures drive us to find new clinical solutions and improve those systems. For me, it led me to move to more of a health administrative role over my career and to pursue a more formal management education by obtaining a Masters of Business Administration (MBA) degree.

What I learned over my administrative career is that organizations are complex systems and their behaviour is hard to explain in engineering terms. However, the process of improvement requires recognizing that complexity and inspiring people to pursue a common goal; to align and direct energy to make the system better.

My educational trajectory has been mirrored in the healthcare roles I've had. I'm a Paediatric Intensivist. The Intensive Care Unit (ICU) is an interesting and important example of a clinical microsystem – a relatively self-contained clinical system, where different people come together to do complex things. My thinking of critical care has evolved from worrying about how well I could perform the life-saving procedures like resuscitation, intubation, making the right diagnosis and doing the right things to treat critically ill children, to now thinking more holistically about how to optimize a child's functional outcome as they move through the ICU. The broader my thinking, the more I came to recognize the number of people who contribute to those outcomes and the more apparent the challenges in coordinating their contributions. As I've taken on expanded roles, my thinking has evolved to consider a broader team and to think about the boundaries between professions, disciplines, and different components of the healthcare system. I have been fortunate to have professional experiences that allow me to have a broader scope and to work across many boundaries.

UTMJ: Just as a follow up, what influenced your choice to pursue Paediatric Intensive Care?

MA: I think it reflects my being a systems thinker from the beginning. As a pre-medical and engineering student, I focused on physiologic systems and how they operate. Most medical specialties are organized around one organ system or another. If you look at the field of intensive care medicine (especially paediatrics), you work as an applied systems physiologist across all physiologic systems. In intensive care, you need to have an understanding across most specialties and the interactions between the organ systems each specialty is responsible for. In some ways, it allowed me to be involved with all disciplines of medicine. Another thing that drew me to intensive care was being a member of a complex team where you end up as a sort of a quarterback across many different specialties. You are responsible for getting a child through critical condition or illness, such as helping them through the post-operative care after cardiac surgery, or their recovery from a major trauma.

UTMJ: What is possibly the greatest misconception the public has about paediatric health care?

MA: Probably it is just thinking about kids as small adults and thinking about their needs as being simply scaled down. This extends to people often thinking that the common conditions that kids and adults suffer from can be treated in the same way. There are a couple of differences between paediatric and adult health care. One is that kids suffer from different conditions and even when they suffer from the same ones, the presentation can be very different. It takes a certain degree of specialization to recognize and manage those conditions and the benefit of specialization is very clear. There is a technical expertise when caring for kids that can have a considerable impact. Because children make up only 20% of the population and are healthier than adults on average, most adult-oriented caregivers, even those with a general practice such as general surgery, will not see many kids and won't get many opportunities to treat sick kids. The benefits of technical expertise focused on children is significantly underappreciated. Another difference is that kids experience their injury or illness during a period of their most profound development: cognitive; psychosocial; and motor development. They are also evolving at a time when they are developing attachments to parents and siblings, as well as trying to make sense of the world. It is hard for us to convey the rationale around the discomfort of medical care or the separation from their parents that is sometimes required during treatment. How a child is helped through that experience has a significant impact on their emotional wellbeing and, ultimately, their overall health. Paediatric care is specialized to help a child through that experience in ways that recognize their developmental level and unique needs. The importance of that is also underappreciated. Being child-centered isn't about having the right artwork on the walls. Rather, it is about helping the child through the experience of a painful procedure, managing their anxiety, and helping them engage with their activities of daily living in ways that recognize their dependence on adults.

One other consideration in thinking about paediatric care compared with adult care stems from the fact that children are, by and large, healthy and their utilization of health care services is much lower than the per capita utilization of adults, particularly older adults. That means you don't need, relatively speaking, a lot of paediatric expertise to serve the paediatric population. That fact creates a different dynamic in terms of how care is concentrated for advanced pediatric care compared to advanced adult care. Children's care tends to occur in far fewer organizations than the care of adults with similar conditions. An example is the organization of cardiac surgery services in the province of Ontario. There are roughly a dozen hospitals that do cardiac surgery for adults and each hospital has a number of cardiothoracic surgeons, because that's what it takes to meet the demand of the population of Ontario and deliver high quality services. That also ensures that cardiac surgery is available relatively close to home for most of the province's adults. In contrast, for children, when you consider the number of surgeries a centre needs to do to operate with high quality, you find that the number of cardiac surgery cases only warrants one or two programs. Any more would compromise the ability of one or more of the programs to deliver high quality, because surgeons simply would not have enough training. Each of these serve a much larger geographic base than the comparable adult programs. This kind of differential scale has led to a super concentration of advanced services in only a few locations within the province. That means families will be more challenged by the choice of convenience vs. quality, and there will be a greater need to coordinate care among providers separated by greater geographical distances compared to the adult healthcare world.

UTMJ: How has the delivery of paediatric health care changed in the last 10-15 years?

MA: There has been a real evolution in the kinds of care that can be delivered in two ways. First, we have become better in preventing the common illnesses of childhood that previously would have led to hospitalization and morbidity. A good example of that is the development of the rotavirus vaccine, which was introduced roughly a decade ago and which led to approximately a 40% decrease in hospitalizations in community hospitals, since one of the most common reasons for paediatric admissions had been rotavirus-associated gastroenteritis. There have also been changes in emergency department management of diarrhea and vomiting in children, allowing for outpatient management and leading to more of a decrease in the number of hospital admissions. Second, our capability at the extreme end of the care spectrum has evolved considerably. As an example, the indications for bone marrow transplant, one of the more advanced therapies we offer, has expanded from the treatment of leukemias to treatment of sickle cell disease, immune deficiencies, and a variety of other conditions. This has led us to perform more complicated work. Refinement in living donor transplantation has meant we do more solid organ transplants as well. Advances in cardiac surgery have allowed us to advance from providing only palliative care for the most severe cardiac disease to complete surgical repairs or even relying on artificial hearts. This means children that would have passed away in infancy now survive into adulthood. The care delivered by these kinds of advances is highly specialized and happens in only a small number of centres. The result of both factors is that we don't need to do as much in community hospitals while we are doing more in highly specialized centres.

UTMJ: You have already mentioned a few, but what are some challenges you see in delivering health care to the paediatric population in the near future?

MA: There are two challenges that I see. One is spanning distance to address the problem created when you need access to highly specialized services, but where there is a low demand for those services. In Ontario, there are only 4 centres with paediatric intensive care units, but children requiring those units live all over the province. That begs the question as to how we connect children to critical care services and to those centres when needed. They will likely present to the closest emergency department of local health clinics, but for most of those sites, caregivers will have limited experience caring for critically-ill children. We need to be thinking about how to solve the geographic and capability gaps between the highly specialized and the more accessible local centres so that we build or preserve local competencies; hence, when those centres are called upon, they are able to provide high quality care in advance of transporting a child to a more specialized centre for definitive care.

The second challenge is that of coordinating care as our care delivery gets more specialized and complex. Now, we manage entire populations of people with very complex care needs, such as those that have major congenital abnormalities or that have undergone transplantation. It is wonderful that these people are able to survive conditions that they may not have in the past, but the complexity of their care creates other challenges. We are also taking a broader view of the outcomes we are trying to achieve through care, and that also creates challenges. For example, for children with congenital heart disease, we are no longer focused on survival from surgery or survival through infancy. Rather, we are increasingly oriented towards the best possible functional outcomes as a child grows and develops through childhood and into adulthood. Those challenges require a different mindset and a much larger team to weigh in and provide therapies over extended periods of time and to coordinate care across multiple venues, multiple professions, and multiple disciplines. This is a problem for all fields of medicine. As care becomes more specialized, care becomes more fragmented and requires coordination across those providers. This is not unique to paediatrics, but it is even more amplified in paediatrics due to the concentration of the experts and specialists at fewer locations. It is already an issue in adult oncology, cardiac care, and many different specializations, but it is more pronounced in the paediatric population.

UTMJ: You mentioned that many children are surviving complex conditions and growing into adulthood, so can you comment on the barriers to the transition from paediatric to adult care?

MA: The barriers are profound. The fundamental barrier is that there are not that many adult providers that have the expertise to continue providing care to children with rare diseases and there is a discontinuity in the caregivers' knowledge about a patient as they transition. Even if you did have competent caregivers, there is a handoff of an entire childhood of medical information that is quite complex in some cases. That transition can become very problematic. Oftentimes, the medical records stay at the original institution, particularly when you have electronic records. But the lack of expertise is often the bigger problem. In some areas, transitions work well. For example, for a child

with diabetes, there are quite competent adult endocrinologists that treat Type 1 and Type 2 diabetes. For those children, the challenge is a good hand-off and not finding clinical expertise, although there are some unique considerations in dealing with young people during that transition to adulthood where they need to take more responsibility for their own care. In other areas, it has been historically difficult to find adult-oriented specialists familiar with diseases of childhood. In some cases, there has been a very deliberate attempt to build that expertise. If I think about management of patients with cystic fibrosis (CF) for example, there hadn't been many adults living with cystic fibrosis until recently, so the experience among adult-oriented physicians was not that extensive. Children's hospitals like SickKids have sought out adult providers to become part of the care team, in order to develop that expertise and facilitate the transitions in care. Those kinds of programs have added a lot of value. Over time, as the numbers of adults living with CF has increased, that expertise has deepened and become more widely available. In other areas, it has been harder to build that expertise, particularly in some of the surgical disciplines where it takes a lot of training and practice to develop the expertise to address the abnormal anatomy of congenital anomalies.

Hospitals like SickKids have tried to identify partners on the adult side of the health care system and to work together to build effective transition approaches. For example, in congenital heart disease, our cardiac surgeons would go to University Health Network or St. Michael's Hospital and do cardiac surgeries on young adults with congenital heart disease if their expertise is needed. We run a joint program where we have pediatric cardiologists and adult cardiologists working together on the transition. This helps to build skill on the adult side and to bring the expertise of the pediatric cardiologists and develops a group of adult cardiologists that are comfortable with the complex anatomies of congenital heart disease. In fact, there has been an emergence over the last few years of specific training programs. There are programs now that take adult cardiology trainees to that train in a children's hospital program for some period of time to develop their skills.

UTMJ: We have talked a lot about new technologies and how often they are being introduced and, of course, paediatrics is no exception. What are your thoughts on the role that technology plays in the paediatric population, how can it influence the relationship between the physician and the patients as well?

MA: That is an interesting question. Technology is a broad term, so I can think of a number of ways that that fits in. Certainly, there are technological advances that let us do things at the bedside. In the last decade and a half, we have seen the refinement of extracorporeal life supports, Echo, heart-lung machines in the ICU, and artificial heart technology being able to save many kids that would have died because of their heart disease or following surgery. These have become a kind of a routine technology that have become more functional over time, and I expect it will continue to see those advances. Another example is the advances in robots that make it possible to operate in tiny spaces more effectively. I believe that we will continue to see technology kind of push us further towards reducing mortality and morbidity.

Technology is also likely to be a significant enabler of transcending geographic distance. There are so many untapped possibilities around tele-medicine and tele-health that could allow experts centralized to one centre to manage patients remotely and to help build capacity in the more distant communities.

A third application of technology may be the digital enablement of bedside care. As an example, the more robust use and deployment of electronic health records connected to decision support systems that leverages the promise of artificial intelligence could improve diagnostic accuracy and care in many ways. One worry is that the use of technology could create barriers between caregivers and patients At the same time, however, technology could actually be empowering, by allowing physician brain power and time to be more directed towards creating a more human connection to patients and their families, allowing for more of a healing relationship to develop.

UTMJ: In February of this year, a joint panel of MPs and senators tabled the 70-page report called: "Medical Assistance in Dying: A Patient Centred Approach". It suggested a two-phase approach, with an initial phase allowing doctor-assisted deaths for adults 18 years and older, and then expanding it to mature minors within 3 years. What are your thoughts on the role of medical assistance in dying in paediatric populations?

MA: I personally feel somewhat conflicted about the topic. Certainly, end of life care is a significant component of care in the ICU. I think that there is probably some blurring in the line between compassionate palliative care and medical assistance in dying. Some of the more emotionally difficult experiences I've had in the ICU have been related to end of life care and the sorts of moral dilemmas that such care can encompass.

The issue is probably more amplified by the difficulty in determining at what point it makes sense to allow a person to decide for themselves about their end of life care. Age 18 to me is an artificial milestone and, certainly, the ethical constructs that we use in paediatrics recognize that there are many things where minors do have the right to decide, as long as it respects the principle of informed consent. The challenge is figuring out when, and figuring out how to avoid a slippery slope where it becomes younger and younger, and the tests become less and less clear. If you said that the rules that we afford to an 18-year-old should be applied to 17-year-olds, if they meet certain criteria, I would probably have no problem accepting that from the standpoint of fairness and fitting within the ethical construct that we have. That doesn't mean I'm comfortable with medically-assisted dying; it means that I could accept it and believe that it has a role. If you told me a 3-year-old should be able to decide, I'd have a real hard time with that, as I am sure most people would. What I struggle with is what happens in between and I honestly don't know how to address it. I'm troubled by the cases where families have let very young children make decisions to reject care. Although those decisions are not necessarily the same as decisions about medical assistance in dying, I'm not sure there is a bright line between choosing medically-assisted dying and saying no to life-saving therapy. I'm troubled when that happens at a very young age, because I don't believe informed consent is possible and we know from a lot of developmental work individuals don't have a good way of balancing short-term priorities with the long-term, even in adolescence.

UTMJ: On a lighter note, who have been some of your biggest influences both inside and outside of medicine and what kind of impact have they had on your career?

MA: Outside of medicine, I look to my parents and my grandfather. My grandfather really stressed the importance of listening to people and making a good first impression, as well as engaging in productive, constructive business relationships and professional relationships. I think of my parents from the standpoint of the importance of service and making a difference. Some of my earliest memories are accompanying my father in some volunteer work that he was doing with disabled and handicapped young adults. Professionally, I've had the benefit of three exceptional mentors. The person I trained with in critical care at Yale taught me a lot about how to think about clinical problem-solving, as well as how to think about the relationship between a physician and families that they serve. He set a very high standard for quality and compassionate care, as well as for the intellectual rigor in thinking deeply about clinical medicine and physiology. From the two mentors I've had over my administrative career, I've learned a lot about leadership, how to think strategically, as well as how to think about influence in a way that doesn't rely on power as much as being able to bring people to a common vision.

UTMJ: Last question to wrap up, what advice would you give to doctors who are interested in entering the world of administration in medicine?

MA: I would suggest that you think beyond the role and work of physicians and really think about systems and interrelationships between professions, disciplines, and organizations. I'd also suggest trying to see things through the eyes of the people we are caring for. Administrative roles can be very rewarding. For me, it has been a means to an end, the end being better care. It's important to be clear on the role. There is a tendency for people, as they move into administrator roles, to view the role as an advocate for the group you are leading, and this is not unique to physicians. The reality is that leadership is about aligning those individuals so that they can more effectively contribute to an organization's success. With each succession up the administrative ranks, there is an even greater need to have a broader view and to think about how your constituencies relate to the others. As a physician executive, overseeing a group of physicians for example, it is easy to understand the perspective of being there to ensure that everybody else supports what is needed by the physicians to do their job. At the same time, I actually think the more important perspective is to be able to see what these other stakeholders need from the group I lead. That's not always an easy perspective to develop.

UTMJ: Is there anything else you'd like to add or mention?

MA: I hope people reading this interview appreciate the unique and powerful ecosystem that we have in and around the University of Toronto. This is an exceptional medical, education, and discovery ecosystem that is as advanced and productive as anywhere on the globe. The wonderfully collaborative environment gives us some unique opportunities for us to think collectively about addressing the greatest challenges in healthcare: the fragmentation in our Ontario health system and the need to mitigate the tradeoffs we make with more specialized and complex care delivery.

Assessing the Need for an Educational Intervention for Primary Care Practitioners on HPV-Related Oropharyngeal Cancer

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Abstract

Background and Objectives: Human papillomavirus (HPV) is causing an epidemic of oropharyngeal squamous cell carcinoma (OPSCC). Patients presenting with HPV-related OPSCC tend to be younger than patients with non-HPV-related OPSCC and lack the traditional OPSCC-related risk factors of smoking and alcohol use. The objective of the present study is to assess whether knowledge of this demographic shift in the patient population affected by OPSCC has been disseminated to primary care practitioners.

Methods: A quantitative cross-sectional needs assessment was performed using an original questionnaire. The questionnaire assessed general knowledge regarding OPSCC and its recognition in at-risk patients and was distributed to family physicians, family medicine residents and advanced practice registered nurses in Ontario, Canada.

Results: Of 11,000 primary care practitioners contacted, fifty-four responded (0.5% response rate), the majority of whom were CCFPs (n=29; 59.18%) or FCFPs (n=9; 18.37%). The survey included two case scenarios of patients presenting with possible OPSCC and eleven true/false questions. In Case 1, the majority of respondents (98%; n=50) indicated that they would not refer the patient immediately. Of those who did not refer after first and second line management (n=33), the majority (n= 20; 60.6%) would wait 1-4 weeks before referring. In Case 2, a sexual history was elicited always (64.7%; n=33), sometimes (31.37%; n=16) and never (3.92%; n=2), while smoking and alcohol history was almost always elicited (90.2%; n=46 and 62.8%; n=32, respectively). Two out of eleven true/false questions regarding prevalence and prognosis were answered incorrectly by a majority of respondents: 69.4% (n=34) falsely believed that tonsillar cancer is not the most prevalent type of oropharyngeal cancer in Canada; 59.2% (n=29) falsely believed that there is a poorer overall survival rate associated with HPV-related tonsillar cancer as compared to non-HPV-related tonsillar cancer. Most participants (95.9%; n=47) expressed an interest in learning more about OPSCC.

Conclusions: The results of the questionnaire suggest that a knowledge gap exists among primary care practicioners regarding the demographic shift in OPSCC. Closing this knowledge gap may lead to earlier referral to head and neck specialists and lead to improved patient outcomes.

Background

Head and neck squamous cell carcinoma is the sixth most common cancer globally.[1] From 1992 to 2006, the incidence of oropharyngeal squamous cell carcinoma (OPSCC) in Canada increased by 27.1% in men and by 13.7% in women.[6] A growing body of research suggests that human papillomavirus (HPV) has played a major part in the emerging epidemic of OPSCC,[3-6] with studies demonstrating that 80% of OPSCC is attributable to HPV infection.[3-5]

Risk factors for HPV-related OPSCC differ from those for non-HPV-related OPSCC.[7-10] Risk factors for non-HPV OPSCC include smoking, alcohol consumption, and older age.[3] On the other hand, risk factors for HPV-related OPSCC include high lifetime number of sexual partners, oral sex, and earlier age at sexual debut.[7-10] The incidence of non-HPV OPSCC in North America has declined in recent years, consistent with a decrease in tobacco use.[3] Although there are likely additional contributing factors, the emerging epidemic of HPV-related OPSCC is likely at least in part due to changing sexual practices.[1-5,7,10,11]

Early detection of HPV-related OPSCC is important, as HPV-related-OPSCC has a better prognosis than non-HPV related-OPSCC and because treatment has a high potential for cure.[18-20] However, early detection can be challenging in this patient population, as patients often present with symptoms also associated with other prevalent diseases, such as chronic tonsillitis and lymphadenitis.[19]

The role of primary care practitioners in early detection and subsequent referral cannot be overemphasized. It is hypothesized that educating primary care practitioners about the etiologic shift in OPSCC might allow for otherwise-missed early disease detection in this emerging at-risk population. The objective of this pilot study is to assess the knowledge of primary care practitioners regarding the change in epidemiology and etiology of OPSCC. We predict that this new information about the epidemiologic shift of OPSCC has not been adequately disseminated to primary care practitioners.

Methods

Research participants were recruited through the Ontario College of Family Physicians (OCFP). After obtaining Research Ethics Board (REB) approval, the questionnaire was distributed by the OCFP. Included in this group were family physicians, family medicine residents, registered nurses and advanced practice nurses. Only respondents who perform office-based care were excluded from the study. Informed consent was obtained from all participants.

This study is a quantitative cross-sectional needs assessment. A thorough review of the relevant literature revealed no pre-existing studies that adequately addressed the research question. The questionnaire was devised by two otolaryngologists and revised by two family physicians. Questions were either multiple choice or true/false, and assessed five areas: (1) respondent demographics; (2) management; (3) detection; (4) general knowledge; and (5) continuing medical education.

The questionnaire was emailed to OCFP members as a SurveyMonkey® (SurveyMonkey Inc., Palo Alto, USA) link. Descriptive statistics were also performed using SurveyMonkey®.

Results

Of the 11,000 primary care practictioners who received the questionnaire-containing email, 54 eligible individuals responded (0.49% response rate. Respondent demographics are summarized in Table 1.)

The survey included two case scenarios and eleven true/false questions. Results of the two case scenarios are presented in Table 2 (Figures 1 and 2) and Table 3. Results are presented as the relative frequency of responses among participants. Of the 11 true/false questions, the majority of respondents selected the correct response in all questions, except for two. Most participants (69.4%, n=34) falsely believed that tonsillar cancer is not the most prevalent type of oropharyngeal cancer in Canada and that there is a poorer overall survival rate associated with HPV-related tonsillar cancer as compared to non-HPV-related tonsillar cancer.[1,15] In the first of two multiple choice question, respondents identified risk factors for tonsillar cancer, with the following response frequency: 100% (n=49) HPV; 98% (n=48) smoking; 89.8% (n=44) alcohol; 42.9% (n=21) environmental, and 28.6% (n=14) Epstein-Barr Virus (EBV). The second multiple choice question asked respondents to identify symptoms of tonsillar cancer at presentation, with results as follows: neck mass, throat pain, and odynophagia identified by 95.9% (n=47) of respondents; dysphagia and ear pain identified by 71.4% (n=35) of respondents.

Table 1. Respondent Demographics

	No. of Respondents	Percent of Respondents (%)
Clinical Practice Settings		
Family health team, organization or network	23	47.0
Family health group	6	12.2
Academic teaching unit	4	8.2
Community health centre	5	10.2
Solo	2	4.1
Other	9	18.4
Levels of Post-Graduate Training		
FCFP	9	18.4
CCFP	25	51.0
APRN	1	2.0
PGY1	4	8.2
PGY2	6	12.2
PGY3	3	6.1
Other	1	2.0
Length of Time in Practice		
Currently in residency	11	22.5
0-5 years	14	28.6
6-10 years	7	14.3
11-20 years	8	16.3
>20 years	9	18.4
Average Number of Patients per Week		
<50 patients	13	26.5
50-100 patients	30	61.2
100-150 patients	6	12.2
Predominant Age Group in Practice		
0-20 years old	2	4.1
21-40 years old	16	32.7
41-60 years old	24	49.0
61-80 years old	7	14.3

Table 2. Case 1
A 45-year-old presents with a sore throat and an enlarged left tonsil

	No. of Respondents	Percent of Respondents (%)
"What would be your first line of treatment?"		
Observation with follow-up	8	15.7
Complete the Sore Throat Score Card and follow its guidelines	23	45.1
Swab for culture & sensitivity	15	29.4
Antibiotics	4	7.8
Referral	1	2.0
"If this patient's symptoms do not improve with observation or antibiotics, what would be your second line treatment?"		
Continued observation with follow-up	4	7.8
Swab for culture & sensitivity if you empirically treated the patient	14	27.5
2nd line antibiotics	3	5.9
Referral	18	35.3
Further investigations (please specify)	12	23.5
Bloodwork	6	50
Head and neck ultrasound	5	41.7
Head and neck MRI	1	8.3
Those who had not yet referred this patient were asked, "If the patient has persistent symptoms, how long would you wait before referring?"		
<1 week	1	3.0
1-4 weeks	20	60.6
5-12 weeks	12	36.5
>12 weeks	0	0
"If the same patient presents with neck lymphadenopathy on the affected side, what would be your next step?"		
Observation	3	9.1
Swab	5	15.2
Antibiotics	3	9.1
Referral	12	36.4
Further investigations (please specify)	10	30.3
Ultrasound	6	60
Ultrasound with TSH	1	10
Bloodwork	1	10
Bloodwork with biopsy	1	10
CT neck and MRI	1	10
"Do you routinely palpate the tonsil or tongue base in a patient presenting with a unilateral tonsil mass with sore throat?"		
All the time	6	11.7
Sometimes	11	21.6
Never	34	66.6
"Do you routinely examine the neck for lymphadenopathy in patients presenting with a unilateral tonsil mass with sore throat?"		
All the time	49	96.1
Sometimes	2	3.92
Never	0	0

Table 3. Case 2
A 45-year-old non-drinker, non-smoker presents with a 5 week history of progressively worsening sore throat, an asymmetrically enlarged left tonsil, and an enlarged lymph node on the affected side

	No. of Respondents	Percent of Respondents (%)
"What is on your differential diagnosis?" (Select all that apply)		
Bacterial tonsillitis	30	58.8
Viral tonsillitis	19	37.3
Peritonsillar abscess	44	86.3
Tonsillar cancer	41	80.4
Lymphoma	31	60.8
"Would you take a sexual history?"		
All the time	2	3.92
Sometimes	33	64.7
Never	16	31.4
"If yes, would you include oral sex in your history of this patient?"		
All the time	12	24.5
Sometimes	20	40.8
Never	17	34.7
"If yes, would you include number of sexual partners in your history of this patient?"		
All the time	7	14.3
Sometimes	23	46.9
Never	19	38.8
"Would you take a smoking history?"		
All the time	46	90.2
Sometimes	3	5.9
Never	2	3.9
"Would you take an alcohol history?"		
All the time	32	62.8
Sometimes	15	29.4
Never	4	7.8

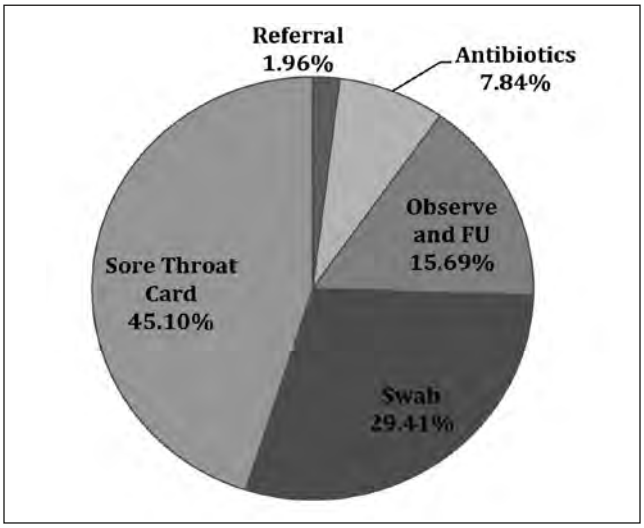

Figure 1. Case 1 – First Line of Management

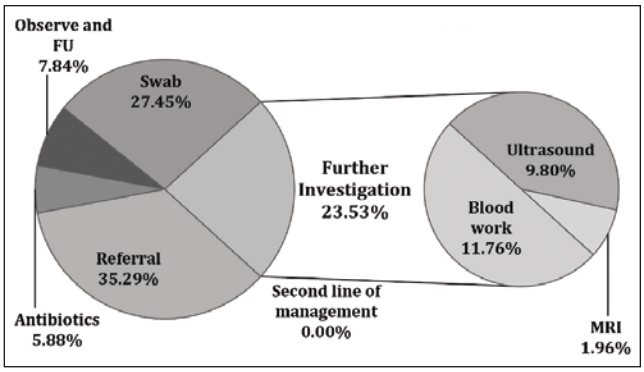

Figure 2. Case 1 – Second Line of Management

The majority of respondents answered that they were aware that HPV causes tonsillar cancer (69.4%; n= 34 versus 30.6%; n=15) and that they learned this through: medical training (52.9%; n=18); independent reading (35.3%; n=12), continued medical education (CME) (29.4%; 10); conferences (17.7%; n=6); the media (11.8%; n=4); other (14.7%; n=5). Of the five who responded "other," four had personal contact with a patient with HPV-related OPSCC. All but two participants (95.9%, n=47) expressed an interest in learning more about HPV and OPSCC, and identified their preferred educational modalities (respondents could select more than one answer): continuing medical education (CME) (77.6%; n=38); online CME (71.3%; n=35); an educational pamphlet (46.9%; n=23); a group lecture (34.7%; n=17); one-to-one teaching (10.2%; n=5).

Discussion

The results of the present study demonstrate a gap in the knowledge of primary care practitioners regarding the recent epidemiologic shift in OPSCC. While the results suggest that the majority of primary care practitioners are aware of the risk factors for non-HPV OPSCC, only some are aware of those associated with HPV-related OPSCC. Furthermore, while the majority of respondents considered tonsillar cancer in their differential diagnosis for Case 1, only one elected to refer a patient with persistent symptoms within a week. One third of respondents reported that they would wait between one and three months before making a referral. This time lapse between patient presentation and referral is a delay that could be reduced.

There are some key limitations to this study. Firstly, a poor response rate and resulting small sample size meant that only descriptive statistics could be utilized for analysis. In addition, the small sample size might confer a lack of generalizability to the broader community of primary care practitioners. The degree of generalizability might be further impaired by the fact that 65% of respondents had been in practice for less than 10 years. Secondly, while a variety of professionals were consulted in the making of the original questionnaire utilized, it is not a formally validated tool. There is also an inherent rigidity in the asking of closed-ended questions, limiting detail in answers that could have been available with an open-ended question format. Finally, by virtue of not having a control group in this study (i.e., a group that is aware of the etiologic shift in OPSCC), the baseline error rate in responses is unknown. As such, it cannot be concluded that the results indicate a true gap in knowledge among primary care practitioners.

The aim of this study was to assess knowledge of the epidemiologic shift in OPSCC in the primary care setting. Improving OPSCC-related knowledge in primary care practitioners may allow for earlier identification of HPV-related OPSCC and for more expedient referral to head and neck specialists, potentially improving patient outcomes.

When respondents were asked if they were interested in further education regarding HPV-related OPSCC, 95.9% answered positively. The knowledge gap demonstrated by this study, coupled with this interest in education, suggests that an educational strategy is not only needed, but would also be welcomed in this community of practitioners. According to the respondents of this survey, the preferred method would be via a modular online CME model.

This study represents an initial analysis of the knowledge gap among primary care practitioners regarding the etiology of OPSCC. A logical extension of this project might involve implementing an educational intervention relating to OPSCC and subsequently assessing its efficacy. Ideally, education of practitioners will result in expedited diagnosis and improved patient survival.

Conclusions

Our results indicate that knowledge of the etiologic shift in OPSCC has not adequately been disseminated among primary care practitioners. This likely contributes to the diagnostic delay related to OPSCC and subsequent referral to a head and neck specialist. More research is warranted to further understand the depth of this knowledge gap and how best to address it.

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Case Report

A Female with Severe Developmental Delay, Aggressive Behaviour, Hyperphagia, and Obesity: An Atypical Phenotype of a MECP2 Mutation

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Introduction

Rett syndrome (RTT; OMIM 312710) is a neurodevelopmental disorder characterized by language and motor regression, loss of purposeful hand movements, and the development of stereotypical hand movements.[1,2] RTT is known to be caused by mutations in the X-linked gene, *Methyl-CpG-Binding Protein 2 (MECP2)* (OMIM 300005). Interestingly, *MECP2* mutations have also been implicated in other neurodevelopmental conditions such as autism, non-specific intellectual disability, and neonatal encephalopathy.[3-5] Here we describe a female, with a previously reported *MECP2* mutation, who displayed none of the features of typical or atypical RTT. Rather, the patient presented with severe developmental delay, prominent aggressive behaviour, hyperphagia, and obesity. In this report, we aim to broaden the phenotypic spectrum of *MECP2* mutations. We suggest that these mutations should be considered more broadly in patients with severe behavioural disturbances with or without intellectual disability. Overall, a precise genetic diagnosis can have important ramifications for anticipatory guidance and a patient's ability to access adequate social support services.

Case Presentation

We report a female with severe developmental delay and behavioural issues whom we followed in our genetics clinic from the age of 4 until the age of 19. She was the first child born to healthy, non-consanguineous Filipino parents. The pregnancy, delivery, and neonatal course were uncomplicated. Her birth weight was 2800 g (15th to 50th percentile, WHO growth chart). Apart from mild episodes of wheezing, treated with fluticasone and salbutamol puffers as needed, the patient was healthy and was on no other medications.

At present, the patient remains severely delayed in all developmental domains. She was hypotonic as an infant and only began walking at 23 months. Her fine motor skills are impaired as well; she finger feeds but uses utensils poorly. She is able to use scissors and scribble. She is unable to dress independently and has never been toilet trained.

She uttered her first words at 18 months, but presently still only speaks a few words. As a result, she communicates via pointing, grunting, gestures, and picture exchange; she often leads a caregiver's hand towards a desired object. Overall, she can follow simple 1-2 step commands. Socially, she has always been very affectionate with her parents and workers, has always had good eye contact, and has never exhibited any autistic features. In particular, she has never developed perseverations, hand stereotypies, or loss of purposeful hand movements.

At present, most concerning for her parents is her extremely aggressive behaviour. She has exhibited this behaviour all her life, but it has worsened when she started menstruating at the age of 9. The aggression is directed against both her parents and other people, and consists of pinching, hitting, biting, and throwing objects. She underwent behaviour therapy and was tried on multiple psychiatric medications, eventually showing mild improvement on risperidone. Her behaviour becomes particularly difficult about one week prior to her menstrual period until about one week after it. Furthermore, several attempts at hormonal suppression did not improve her aggressive behaviour.

The patient has never experienced feeding difficulties, but by the age of 7 developed hyperphagia and gained a significant amount of weight. Her weight increased from the 75th percentile at 4 years, to the 90th percentile at 7 years. At 19 years, she weighs 75.8 kg (97th percentile, WHO growth chart). She does not wake up at night to eat but does take other people's food. She also becomes interested in eating anytime she sees someone else having a meal.

She has also had impaired growth velocity. Her height dropped from the 50th percentile at 4 years, to the 10th percentile at 7 years, and to below the 3rd percentile (145 cm) at 19 years. Her head circumference has remained steady at around the 50th percentile.

The patient has had generalized seizures between 4 and 6 years of age; several anti-epileptics were tried until they were

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controlled with carbamazepine. She remained on carbamazepine until the age of 12, and has not had seizures since.

On family history, the patient has a younger sister who is healthy. Her mother has a first cousin and a first cousin once-removed who both have developmental delay, and another first cousin once-removed with Down Syndrome. The family history is otherwise negative for any known childhood illnesses or genetic conditions.

On examination, the patient has facial features in keeping with her Filipino background and is not grossly dysmorphic. She has a central hair whorl, mild synophrys, epicanthal folds, a broad nose with a flat nasal bridge, a well-formed philtrum, full lips, a normal palate, and ears of normal shape and set. She has mild clinodactyly. Her feet are flat with calloused arches. The rest of her physical examination has been unremarkable except for a red reticular birthmark on her left leg. Generalized hypotonia was noted during infancy and childhood, but at 19 years her tone is grossly normal.

Investigations and Diagnosis

Initial investigations at the age of 4 revealed a normal female karyotype and were negative for a Fragile X mutation. Complete blood count, thyroid stimulating hormone, ferritin, plasma amino acids, urine organic acids, and urine oligosaccharide and mucopolysaccharide screen were normal. At the age of 7, her symptoms of aggression, hyperphagia, and weight gain prompted a suspicion of Smith Magenis Syndrome, Prader Willi Syndrome, or Angelman Syndrome; genetic testing for all three conditions was negative. A waking electroencephalogram at 7 years was abnormal, showing intermittent slow waves over the bilateral fontal and central head regions.

At the age of 19, a single nucleotide polymorphism microarray and a comprehensive intellectual disability (ID) genetic panel were performed. The microarray was normal, but the ID panel revealed a truncation mutation in *MECP2*: c.1164_1207del (p.389*). Information on RettBASE[6] showed that this is a known *MECP2* mutation, previously reported in 45 individuals in association with classic and atypical RTT as well as non-RTT phenotypes. Several variants of uncertain significance were found in other genes, but no other pathogenic mutation was identified.

Discussion

In addition to severe developmental delay, this female presented with prominent aggressive behaviour, hyperphagia, and obesity, which are features typically associated with other neurodevelopmental syndromes, most notably Smith-Magenis Syndrome and Prader-Willi Syndrome.[7-8] Aggression and obesity have emerged in a small number of reports, however, in association with *MECP2* mutations in individuals presenting with both RTT and non-RTT phenotypes.

Prominent aggression has been reported in two female patients with *MECP2* mutations and skewed peripheral X chromosome inactivation. One of these patients also exhibited typical features of RTT, including stereotypical hand movements and developmental regression.[9] The other, who carried the same *MECP2* deletion as our patient, had normal development but exhibited mild learning difficulty, occasional hand stereotypies, hyperventilation when under stress, and episodes of uncontrolled aggression.[10] Another recent report discusses a female with typical RTT, severe irritability and aggression, successfully treated with lithium.[11] On the other hand, a small study comparing behavioural characteristics in adults with typical RTT and autism identified elopement and mouthing/swallowing objects, but not aggression towards others, as prominent features of RTT.[12]

Obesity has been reported in various studies among both males and females with *MECP2* mutations and milder phenotypes.[13-14] In one report, a familial *MECP2* mutation was identified in four related males with moderate intellectual disability, resting tremors, and obesity, one of whom also displayed aggressive behaviour.[15] In another report, a novel *MECP2* missense mutation was found in a father and daughter both affected with obesity and various behavioural disturbances. The daughter exhibited aggressive outbursts and mild autistic traits, mild intellectual disability, and fine motor impairments. The father's difficulties included behavioural dysregulation, ADHD traits, a learning disability, low average intellectual functioning, and perceptual-motor difficulties.[16]

It has been proposed that much of the phenotypic variability of individuals with *MECP2* mutations can be attributed to variations in X chromosome inactivation patterns in different regions of the brain.[17] In fact, in an interesting mouse study, conditional knockout of *MECP2* from Sim1-expressing neurons in the hypothalamus resulted in behaviours similar to those manifested by our patient – namely, aggression, hyperphagia, and obesity – but not the typical RTT features of motor incoordination and learning and memory deficits.[18] Peripheral X chromosome inactivation patterns were not measured in our patient, as it is unclear to what extent peripheral patterns can predict X chromosome inactivation patterns in the brain.[19]

Conclusion

In summary, this case illustrates that the phenotypic spectrum of *MECP2* mutations is broader than often considered, and that *MECP2* mutations should be considered in the differential diagnosis even for patients presenting with predominantly behavioural disturbances.

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Cancer Predisposition Syndromes 101: A Case History and Review of the Challenges

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Case History

In April of your third year of medical school, you are starting an elective in Pediatric Oncology. You are asked to see a 10-year-old boy who just completed chemotherapy for a localized osteosarcoma of his distal femur. You take a few minutes to review his medical chart and discover that this child's mother is currently being treated for a second breast cancer lesion, and she is only 40 years old. You then notice a report of a genetic test done two weeks ago showing a mutation in the *TP53* gene. You search the meaning of a *TP53* mutation on the Internet and find out that it is associated with Li-Fraumeni syndrome (LFS). The resident working with you explains that LFS is a cancer predisposition syndrome (CPS), but then gets paged away. Many questions flow through your curious mind. What is a CPS? What should I worry about in LFS? How do I best manage this patient? Motivated, you decide to take a few more minutes to read and better plan out the upcoming medical encounter with the child.

What is a cancer predisposition syndrome (CPS)?

When a child or adult is diagnosed with a cancer, among the first questions that arise in the patient's or parents' mind are what caused this tumour and are their family members at increased risk of cancer? These concerns can rapidly become anxiety provoking for a patient who already has so much to worry about. Although a combination of genetic and environmental factors is the most likely explanation for tumorigenesis,[1,2] a precise etiology cannot be identified in the majority of cases. In adults, environmental factors including tobacco, excessive sun exposure, gamma-irradiation, and alcohol intake have been linked to the development of various maligancies.[1,3,4] Viruses, such as the human papilloma virus (HPV)[5] and the Epstein-Barr virus (EBV),[6] have also been linked to specific cancers. In contrast, most children have not had significant long-term exposures to such environmental factors yet they can still develop malignancies. In this age group, cancers may arise as a result of genetic and epigenetic alterations at a cellular level during the normal processes of growth and development.[7]

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A smaller proportion of cancers are hereditary in nature, implying that a genetic alteration has been passed on to a child from a parent or that a new mutation has occurred in the germinal cells prior to fertilization (*de novo* mutation). When these processes arise, all the child's cells carry this genetic change. This is the definition of a germline mutation, in contrast to a somatic mutation which is acquired during one's lifetime.[8,9] A CPS results from a germline genetic alteration leading to an increased risk of tumour development over one's lifetime. Genetic mutations can affect cellular function in a variety of ways that will lead to abnormal proliferation, survival, and apoptosis or DNA breakage and repair mechanisms.[8] Cancer susceptibility genes are usually categorized as one of two subtypes: a tumour suppressor gene or an oncogene. A tumour suppressor gene normally acts by inhibiting cell proliferation and tumour development. Examples include *RB1*, *TP53*, and *ATM*, associated with retinoblastoma predisposition, LFS, and ataxia-telangiectasia respectively. In contrast, an oncogene drives abnormal cell proliferation and protein expression. For example, mutations in the *RET* oncogene leads to multiple endocrine neoplasia syndrome type 2. Each CPS is thought to be driven by pathogenic variants in a tumour suppressor or oncogene; however, a complex array of germline and somatic alterations of other genes is likely responsible not only for the variable spectrum of tumours associated with each CPS, but also the age of onset, disease penetrance, and probably the biological aggressiveness of these tumours.

How common are inherited cancer syndromes?

An underlying CPS is thought to be present in at least 10% of patients diagnosed with a malignancy, with a higher prevalence in children.[10,11,12] This estimate is increasing as we continue to discover the genetic background of cancer. According to a recent publication by Rahman,[9] approximately 114 cancer predisposition genes have been discovered in the past 30 years.[8] Several recent studies using next generation sequencing platforms report a germline pathogenic variant in a known "cancer gene" in 8.5-10% of children whose tumours were sequenced for the purpose of identifying molecular targets for novel drug therapies.[13,14,15] A more complex genetic etiology is suspected in approximately 45% of other

Table 1. Cancer Predisposition Syndrome Types with Associated Cancers and Causal Genes[8,11,22,23,24]

Cancer Susceptibility Syndrome	Related Cancer Types	Affected Genes (chromosomal locations)
Ataxia-telangiectasia syndrome	Leukemia, lymphoma (majority T cell)	*ATM* (11q22)
Beckwith-Wiedemann syndrome	Wilms tumour, hepatoblastoma, adrenocortical carcinoma, rhabdomyosarcoma, neuroblastoma	*CDKN1*, 11p15 methylation defects/uniparental disomy, *IGF2*
Biallelic mismatch repair deficiency	High grade glioma, leukemia, lymphoma, colorectal cancer	*MSH2* (2p21), *MSH6* (2p16), *PMS2* (7p22), *MLH1* (3p21)
Birtt-Hogg-Dubé syndrome	Renal cell carcinoma	*FLCN* (17p11)
Bloom syndrome	Leukemia, myelodysplastic syndrome, lymphoma, epithelial cancers, hepatocellular carcinoma, sarcoma, brain tumours, Wilms tumour	*BLM* (15q26)
Breast/ovarian cancer syndrome	Breast cancer, ovarian cancer	*BRCA1* (17q21), *BRCA2* (13q12)
Costello syndrome	Rhabdomyosarcoma	*HRAS* (11p15)
Cowden syndrome (PTEN hamartoma syndrome)	Cerebellar dysplastic gangliogliomа, breast cancer, endometrial cancer, thyroid cancer, hamartomas of the central nervous system, eyes, gastro-intestinal/genito-urinary tracts and bone	*PTEN* (10q23)
DICER1 syndrome	Pleuropulmonary blastoma, cystic nephroma, pineoblastoma, pituitary blastoma, ovarian sex-cord stromal tumour, ovarian Sertoli-Leydig cell tumour, multinodular goiter, rhabdomyosarcoma	*DICER1* (14q32)
Familial Wilms Tumour syndrome (WAGR, Denys-Drash, Frasier syndromes)	Wilms tumour	*WT1* (11p13)
Familial adenomatous polyposis - Turcot syndrome - Gardner syndrome	Colorectal carcinoma, gastric carcinoma, hepatoblastoma, thyroid tumour, desmoid tumour, aggressive fibromatosis, medulloblastoma, astrocytoma	*APC* (5q21)
Familial neuroblastoma	Neuroblastoma	*ALK* (2p23), *PHOX2B* (4p12)
Fanconi anemia	Myeloid leukemia, myelodysplastic syndrome, medulloblastoma, primitive neuroectodermal tumour, Wilms tumour, squamous cell carcinoma, epithelial cancers, genitourinary tract tumours, breast cancer	*FANCA* (16q24), *FANCB* (Xp22), *FANCC* (9q22), *BRCA2* (13q12), *BRIP1* (17q22), *FANCD2* (3p26) *FANCE* (6p21), *FANCF* (11p15), *FANCG* (9p13) *FANCI* (15q26), *FANCL* (2p16), *FANCM* (14q21) *PALB2* (16p12), *RAD51C* (17q22), *SLX4* (16p13)
Gorlin syndrome (nevoid basal cell carcinoma syndrome)	Basal cell carcinoma, medulloblastoma, cardiac and ovarian fibroma	*PTCH1* (9q22), *SUFU* (10q24)
Hereditary leiomyomatosis and renal cell cancer syndrome	Leiomyoma, renal cell cancer	*FH* (1q42)
Hereditary retinoblastoma	Retinoblastoma, pineoblastoma	*RB1* (13q14)
Juvenile polyposis syndrome	Hamartomatous polyps of the gastro-intestinal tract, colorectal cancer, gastric cancer	*SMAD4* (18q21), *BMPR1A* (10q22)
Li-Fraumeni syndrome	Sarcoma, brain tumors, leukemia, breast cancer, choroid plexus carcinoma, adrenocortical carcinoma	*TP53* (17p13), *CHK2* (22q12)
Lynch syndrome (HNPCC)	Colorectal cancer, endometrial cancer, ovarian cancer, urinary tract carcinoma	*MSH2* (2p21), *MSH6* (2p16), *PMS2* (7p22), *MLH1* (3p21)
Multiple endocrine neoplasia type 1 (MEN 1)	Pituitary tumor, parathyroid tumor, entero-pancreatic tumours (pancreatic islet cell tumor, gastrinoma, insulinoma)	*MEN1* (11q13)
Multiple endocrine neoplasia type 2 (MEN 2)	Medullary thyroid carcinoma, pheochromocytoma, paraganglioma, parathyroid hyperplasia	*RET* (10q11)
Neurofibromatosis type 1 (NF1)	Optic pathway glioma, neurofibroma, malignant peripheral nerve sheath tumor, leukemia, high grade gliomas, neuroblastoma	*NF1* (17q11)
Neurofibromatosis type 2 (NF2)	Meningioma, vestibular schwannoma, ependymoma, neurofibroma	*NF2* (22q12)
Nigmegen Breakage syndrome	Leukemia, lymphoma, medulloblastoma, glioma, rhabdomyosarcoma	*NBS1* (8q21)
Peutz-jeghers syndrome	Intestinal tumours (gastric and colon), pancreatic cancers, gonadal tumors, breast cancers	*LKB1* or *STK11* (19p13)
Hereditary pheochromocytoma/paraganglioma	Pheochromocytoma, paraganglioma	*SDHA* (5p15), *SDHB* (1p36), *SDHC* (1q23), *SDHD* (11q23), *SDHAF2* (11q12), *TMEM127* (2q11), *MAX* (14q23)
Rhabdoid predisposition syndrome	Rhabdoid tumors, schwannomatosis	*SMARCB1* (22q11), *SMARCA4* (19p13)
Rothmund-Thomson syndrome	Osteosarcoma, skin tumors	*RECQL4* (8q24)
Rubinstein-Taybi syndrome	Medulloblastoma, peripheral nerve sheath tumor, leukemia, neuroblastoma, pilomatrixoma, rhabdomyosarcoma, osteosarcoma	*CREBBP* (16p13)
Simpson-Golabi-Behmel syndrome	Wilms tumor, hepatoblastoma	*GPC3* (Xq26)
Sotos syndrome	Sacrococcygeal teratoma, neuroblastoma, Wilms tumor, leukemia, lymphoma	*NSD1* (5q35)
Tuberous sclerosis	Subependymal giant cell astrocytoma, hamartomas, cortical tubers, renal and extrarenal angiomyolipoma, renal cell carcinoma, cardiac rhabdomyoma	*TSC1* (9q34), *TSC2* (16p13)
Von Hippel Lindau	Retinal and cerebellar hemangioblastoma, renal cell carcinoma, pheochromocytoma, endolymphatic sac tumor	*VHL* (3p25)
Werner syndrome	Bone and soft tissue sarcoma, melanoma, thyroid carcinoma, meningioma, leukemia	*WRN* (8p11)
Xeroderma pigmentosum	Skin cancers	*XPA* (9q22), *ERCC3* (2q21), *XPC* (3p25), *ERCC2* (19q13), *DDP2* (11p11), *ERCC4* (16p13)

patients in these cohorts based on their (or their families) clinical features. In addition to the ongoing identification of novel cancer predisposition genes, other heritable cancer syndromes such as DICER1 syndrome,[16,17] biallelic mismatch repair deficiency,[18,19] and the SDH-TCA cycle syndromes[20,21] continue to be more effectively recognized by the clinical oncology community. Many of the best described CPSs with their respective tumour spectrum and associated genes are presented in Table 1.

And specifically, what is Li-Fraumeni syndrome (LFS)?

LFS is caused by alterations in the *TP53* gene located on chromosome 17p13.1. Several thousand families have been reported worldwide and the population carrier rate is thought to be approximately 1 in 5,000 births (although some estimates place this rate as high as 1:2000 births), making LFS one of the most commonly known inherited cancer syndromes.[10] *TP53*, often called "the guardian of the genome," mediates cell cycle arrest, DNA repair and apoptosis, and several other biological processes through its influence on the expression of a variety of target genes.[25] In simplified terms, p53 detects and assesses the severity of DNA damage. If the damage is deemed repairable, p53 will initiate a complex DNA-repair activation pathway. If the damage is deemed irreparable, p53 will mediate cell cycle arrest and apoptosis. Mutant p53 is unable to exert these functions, making cells more likely to evade cell cycle arrest and apoptosis to eventually become transformed and tumorigenic. In LFS patients, *TP53* is mutated in the germline (either inherited or *de novo*). Missense mutations account for the majority of these mutations, leading to altered protein expression.[26] The classic tumour spectrum in LFS includes bone and soft-tissue sarcomas, brain tumours, pre-menopausal breast cancer, adrenocortical carcinoma, and leukemia.[27] A wide spectrum of other tumour types have also been reported in these patients.[28] LFS is a highly penetrant disease with the lifetime risk of developing cancer being 75% in men and 93% in women.[10] This higher prevalence in women is partially, though not entirely, due to the excess risk of breast cancers. Half of patients with LFS will develop their first tumour by age 30 and approximately one-third of these cancer survivors will develop multiple primary cancers over their lifetimes.[29]

How can I suspect LFS or any other CPS?

A variety of features in the patient's personal and family history can lead to a higher suspicion of a CPS. Associated dysmorphic features, congenital abnormalities, or an abnormal growth pattern are clues to an underlying germline genetic mutation.[11,22] However, in many situations, identifying inherited cancers is challenging due to the fact that mutations in cancer predisposing genes do not necessarily result in a recognizable clinical phenotype.[22] Occasionally, the tumour itself can be a clue. The presence of more than one primary cancer or bilateral and multifocal tumours in a patient can hint towards a causal germline mutation.[11] An adult-onset cancer occurring at a strikingly young age should also arouse suspicion.[30,31] An example of this might be a colorectal cancer occurring in a 15 year old with familial adenomatous polyposis or biallelic mismatch repair deficiency.

Additionally, the importance of taking a thorough family history cannot be stressed enough. Parental ethnicity and history of consanguinity can hint towards certain autosomal recessive inherited syndromes.[22] The findings of a close relative with multiple cancers, a cancer in the pediatric age range, or the finding of multiple relatives with the same tumour type can heighten the likelihood for a cancer susceptibility syndrome.[11,31,32] Family history is not static; therefore, regularly updating the family history is essential. On the other hand, a common challenge is that patients often lack a positive family history, often because of a small family size, the malignancy has arisen due to a recessive or de novo germline mutation, or because family members are not aware of their relatives' health history.[22,33]

Independent of the personal or family history, certain tumour types such as a malignant rhabdoid tumour, pheochromocytoma, or adrenocortical carcinoma are highly associated with inherited cancer syndromes.[12,34] Occasionally, specific characteristics of the tumour histology can also suggest a diagnosis of a CPS. For example, anaplastic features in rhabdomyosarcoma and desmoplastic histology in medulloblastoma are associated with LFS and Gorlin syndrome respectively.[35,36] For all the reasons noted above, a geneticist and genetic counsellor are essential allies in the diagnostic process of CPSs.

Diagnostic criteria exist for a variety of inherited cancer syndromes including LFS, neurofibromatosis types 1 and 2, PTEN-hamartoma syndrome, von Hippel Lindau syndrome (VHL), and many others. Specific to LFS, three sets of diagnostic criteria exist: the Classic LFS-, the Chompret- and the *LF*-like syndrome criteria. The sensitivity and specificity of the Chompret criteria are 82% and 58% respectively, making it perhaps the most rigorous definition to justify *TP53* mutation testing.[10] The Chompret and Classic Li-Fraumeni criteria are presented in Table 2.

Table 2. Chompret and Classic LFS criteria

Classic LFS syndrome criteria[37]	A proband with: • A sarcoma diagnosed before age 45 years and • A first-degree relative with any cancer before age 45 years and • A first- or second-degree relative with any cancer before age 45 years or a sarcoma at any age
Chompret Criteria[26, 38, 39, 40]	A proband with one of 4 scenarios: 1) A tumour belonging to the LFS tumour spectrum (soft tissue sarcoma, osteosarcoma, pre-menopausal breast cancer, brain tumour, adrenocortical carcinoma, leukemia or broncho-alveolar lung cancer) before age 46 years and ≥ 1 first- or second-degree relative with an LFS tumour (except breast cancer if the proband has breast cancer) before age 56 years or with multiple tumours or 2) Multiple tumours (except multiple breast tumours), two of which belong to the LFS tumour spectrum and the first of which occurred before 46 years or 3) Diagnosed with adrenocortical carcinoma, choroid plexus tumour or embryonal rhabdomyosarcoma of anaplastic subtype, irrespective of family history or 4) Diagnosed with breast cancer before 31 years

How is a CPS diagnosed?

In most cases, molecular testing will confirm the diagnosis. Targeted gene analysis versus whole genome approaches will depend on the specific clinical scenario. Occasionally, a combination of clinical features will suffice to make the diagnosis, even without genetic confirmation. However, identifying the exact genetic alteration can be useful to establish a genotype-phenotype correlation. In other words, certain genetic mutations are known to predict the occurrence or severity of specific cancer types within a given syndrome. Such genotype-phenotype correlations are known for many, but not all, CPSs. For example in VHL, truncating and missense mutations confer a higher risk of renal cell carcinoma (RCC), whereas deletions in the gene are associated with a decreased risk of RCCs. Prenatal diagnosis can also be performed in situations in which the genetic alteration is known.

What are the benefits and risks related to the diagnosis of a CPS?

Many studies have described the risks related to the diagnosis of a CPS, including physical and psychosocial factors. During the diagnostic phase, genetic testing results are not always straightforward as they can often be of uncertain meaning (variants of uncertain significance (VUS) or noninformative).[29,30] Whole exome or cancer gene panel sequencing, increasingly used methods for molecular testing, may lead to the discovery of other genetic mutations in the patient which are not related to the actual condition but have a significant impact on the person's health. When a person is identified with a CPS, they are forever "labeled" as such. Social boundaries, including employment and insurance discrimination, are critical concerns for this population, notwithstanding the introduction of genetic non-discrimination legislation in many countries (currently under review in Canada's House of Commons).[41] In children, appropriate timing of genetic testing should be carefully evaluated according to the age at which cancers arise in a given syndrome and the possibility of using surveillance measures.[30,42] On a psychological and emotional level, living under the shadow of a "Damocles' sword" is extremely challenging. The constant and lifelong threat of a cancer diagnosis in a person or their loved ones can have a profound impact on their daily life and choices. Physicians need to be aware of these factors and address them in a serious manner. Allied health professionals, such as psychologists and social workers, are an essential part of the multidisciplinary management of this population.

Although, knowledge of a CPS may lead to significant anxiety and major life changes, knowledge is also power. Identifying a CPS is the key to proper medical management, surveillance, counselling, and education, which are all important factors affecting the overall outcome.

What can I do to prevent a cancer from arising in a patient with an inherited cancer syndrome?

Due to the inherent cancer risk conferred by the patient's mutated gene(s), the prevention of tumours is a complex measure that is most often impossible. In certain CPSs, risk-reducing surgery is an option because of the extremely high risk of developing a specific cancer type. For example, in familial adenomatous polyposis, a colectomy may be a suitable option to prevent a colorectal cancer. Likewise, bilateral mastectomy may be an option for a patient with a germline mutation in a BRCA gene. The balance between the risks and benefits needs to be carefully assessed in each clinical scenario. Minimizing potential toxic exposures, such as excessive sunlight, tobacco, or unnecessary radiation, is another important preventative measure.[43]

If I cannot prevent a cancer from occurring, how can I help my patients?

Cancer surveillance and education are the two key elements in the management of patients with CPSs. Specific tumour surveillance protocols have been created for various CPSs. These are designed for early detection of the malignancies known to be associated with a given inherited cancer syndrome, with the ultimate goal of reducing mortality and treatment-related morbidity.[44] The age at tumour presentation and the cancer prevalence are usually taken into account in the development of these guidelines. The surveil-

Table 3. Li-Fraumeni syndrome tumour surveillance protocol ("Toronto protocol"), adapted from Villani et al, 2016[44]

CHILDREN (0-18 YEARS)		
Adrenocortical carcinoma	Ultrasound abdomen and pelvis Blood tests: 17-OH-progesterone, total testosterone, dehydroepiandrosterone sulfate, androstenedione 24 hour urine cortisol level, if feasible	q 3-4 months
Brain tumour	Brain magnetic resonance imaging (MRI)	q 1 year
Soft tissue and bone sarcoma	Rapid whole body MRI	q 1 year
Leukemia/lymphoma	Blood tests: complete blood count, sedimentation rate, lactate dehydrogenase	q 3-4 months
General assessment	Complete physical examination with anthropometric measurements plotted on a growth curve, signs of virilisation and full neurological assessment	q 3-4 months
Prompt assessment with primary care physician for any medical concerns		
ADULTS (18 YEARS +)		
Adrenocortical carcinoma	Ultrasound abdomen and pelvis Blood tests: 17-OH-progesterone, total testosterone, dehydroepiandrosterone sulfate, androstenedione 24 hour urine cortisol level, if feasible	q 3-4 months (18-40 years)
Brain tumour	Brain MRI	q 1 year (18 years +)
Soft tissue and bone sarcoma	Rapid whole body MRI	q 1 year (18 years +)
	Ultrasound abdomen and pelvis	q 3-4 months
Colorectal cancer	Colonoscopy	q 2 years (25 years or 10 years before the earliest known colon cancer in family, whichever comes first)
Breast Cancer	Self breast examination	q 1 month
	Clinical breast examination	Bi-annually (20–25 years, or 5–10 years before earliest known breast cancer in family, whichever comes first)
	Mammography[1] and breast MRI screening[2]	q 1 year (20–75 years, or 5–10 years before earliest known breast cancer in family, whichever comes first)
Melanoma	Dermatologic examination	q 1 year
Leukemia/Lymphoma	Blood tests: complete blood count, sedimentation rate, lactate dehydrogenase	q 3-4 months
General assessment	Complete physical examination	q 3-4 months
Prompt assessment with primary care physician for any medical concerns		

[1]Breast ultrasound with mammography as indicated by breast density, but not instead of breast MRI or mammography.
[2]Breast MRI to alternate with annual rapid whole-body MRI (one scan every 6 months).
#Consider risk-reducing bilateral mastectomy

lance modalities used are also carefully chosen and should comply with certain criteria including accessibility, minimal radiation exposure and risk for the patient, adequate test sensitivity/specificity, and cost-benefit. These features are applicable to any screening procedure in the population. The tumour surveillance protocol for LFS is outlined in Table 3. This surveillance protocol, developed in Toronto in the early 2000's, was recently demonstrated, after an observation period of 11 years, to significantly increase long-term survival and decrease morbidity in patients with LFS. The protocol has been adopted in multiple centres around the world with similar beneficial results.

Published tumour surveillance guidelines exist for many CPSs including familial adenomatous polyposis, overgrowth syndromes, Lynch syndrome, hereditary pheochromocytoma/paraganglioma syndrome, tuberous sclerosis, and VHL. Because this is a rapidly evolving field and because each CPS is a rare entity in itself, most of the surveillance protocols are based on literature review and expert opinion. Proper validation studies have been undertaken for various protocols, but this is a work in progress.

Family and patient education cannot be underestimated in the management of CPSs. Educating and offering support to these families is the key to empowerment. The inheritance

pattern, the cancer risks, the tumour surveillance procedures, and the optimal lifestyle changes are important discussion points to have with the family. A genetic counsellor is again essential for the education of these families. Furthermore, ensuring that these patients undergo regular medical visits and are prompted to seek medical services in the case of a change in their health status is important and may even diminish the disease-related anxiety.

Finally, ongoing research aimed at better describing and gaining insight into the molecular defects related to tumorigenesis is essential. Animal models have been instrumental in understanding the links between a genetic defect and cancer phenotypes. They are also extremely helpful for the evaluation of toxic effects and efficacy of possible novel therapeutic agents.

When a cancer arises in a patient with a CPS, how do I manage it?

In most cases, tumours are managed in the same way as their sporadic counterparts. Certain inherited syndromes, especially those in which there is a defect in DNA repair, warrant the limitation of therapeutic modalities such as radiation. Unfortunately, many chemotherapeutic agents are associated with severe toxicity and increased tumour risk in this context, making treatment decisions for these patients particularly challenging. Staging, evaluation of tumour response, and surveillance during and after the diagnosis of a cancer requires the use of imaging techniques, some associated with radiation exposure. These should be used judiciously in order to minimize further tissue damage and risk of secondary malignancies. This concept is essential in LFS, where radiation is believed, though not as yet definitely proven, to increase the risk of new tumour development.

In certain circumstances, having a CPS opens the door to targeted therapy, thereby broadening the therapeutic arsenal. Targeted agents include medications that act on specific components of the altered molecular pathways related to tumorigenesis. For example, Sunitinib, a tyrosine kinase inhibitor known to inhibit the action of growth factor receptors, is used for patients with VHL diagnosed with clear cell renal carcinoma.[45] At this point in time there are no targeted agents used in patients with LFS as drugs do not readily target p53 itself, although much research is still ongoing. Likewise, there is active and exciting research evaluating the implicated molecular pathways and possible therapeutic agents for many other inherited cancer syndromes.

After going through the who, what, why, and how of the CPSs and LFS, you are now ready to evaluate and discuss the management and surveillance options for your patients. Realizing the importance of research in this growing and exciting field, you have also found the answer to how to spend your upcoming summer months: a research elective in cancer genetics!

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Gender Dynamics and Socio-Cultural Determinants of Middle East Respiratory Syndrome Coronavirus (MERS-CoV) in Saudi Arabia

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Abstract

Middle East Respiratory Syndrome (MERS) is a potentially severe viral respiratory illness that is caused by a new strain from the beta group of coronavirus (CoV). Almost all cases arise from Saudi Arabia, and men are at a greater risk of contracting the virus (68%) in comparison to women. This disparity presents an interesting question: What accounts for these observed sex differences in MERS infection rates? Using an analytic lens that considers the unique dynamics of socially constructed and specific gender roles, this review challenges the common assumption that biological differences in vulnerability (genetic disposition) are the primary drivers for the disparate male infection rates. Specifically, the author uses a gender-based analysis (GBA) to explore gender-based risk factors within Saudi Arabia that may contribute to this disparity. The findings of this review suggest that particular gendered risk factors including religious (Hajj) and cultural practices (shisha smoking) as well as social roles pertaining to livestock management (dromedary camels) may create different exposures to MERS-CoV. Ultimately, this research illustrates a significant gap in the current knowledge and understanding of how gender dynamics affect infectious diseases, especially concerning the issue of containment of and protection from MERS.

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Introduction

Middle East Respiratory Syndrome (MERS) is a potentially severe viral respiratory illness that is caused by a new strain from the beta group of coronavirus (CoV).[1] MERS-CoV may cause acute respiratory disease, affecting both the upper and lower respiratory tracts, especially among individuals with underlying health conditions such as diabetes, renal disease, chronic lung disease, and immunodeficiency.[1,2] Symptoms of MERS include pneumonia, high fever, coughing, and severe shortness of breath.[3] Currently, there are no effective anti-viral treatments or preventative interventions, namely vaccines, for patients with MERS.[4]

Since the first confirmed case of MERS in 2012, the World Health Organization (WHO) has reported 1806 laboratory-confirmed cases with 643 deaths globally.[5] Saudi Arabia demonstrates a similar case-specific mortality rate (1,437 and 615 respectively), making it the country with both the highest incidence and mortality rates across the Arabian Peninsula.[6-8] Both globally and in Saudi Arabia, men are at a greater risk of contracting the virus (68%) when compared to women.[9] This disparity presents research and clinical communities with an interesting question: What accounts for the observed sex differences in MERS infection rates?

Using an analytic lens that considers the unique dynamics of socially constructed and specific gender roles, this paper seeks to challenge the assumption that biological differences in vulnerability (genetic disposition) are the primary drivers for the disparate male infection rates. It calls on researchers to use gender-based analysis (GBA) to better account for the impact that culturally specific gender roles play in MERS infection rates. GBA is a particularly powerful analytic tool, because it integrates both the complexity of social location and its influence on infectious diseases. In doing so, it challenges the traditional approaches to infectious disease and offers the promise of new insights into the nature of MERS risk patterns. To demonstrate this analytical framework, this paper begins by considering several gendered risk factors, including gender segregation, gendered religious and cultural practices, and gendered social roles concerning livestock management within Saudi Arabia. This paper considers issues beyond traditional epidemiological approaches by illustrating the link

between socio-cultural norms and practices and the risk patterns affecting MERS health outcomes. Applying a GBA to existing and future MERS scholarship can yield valuable information that can be used to develop culturally appropriate and thus effective public health programmes to counteract this serious emerging infectious disease.

Gender and (Emerging) Infectious Disease

The WHO defines gender as being "socially constructed roles, behaviours, activities, and attributes that a given society considers appropriate for men and women".[10] Men and women illustrate diverse characteristics including social and economic behaviour, roles, expectations, and responsibilities. Gender-based health differences emphasize social, political, and economic inequalities and intersect with other important forms of social stratification including class, race, ethnicity, and disability. Importantly, gender differences can be developed, sustained, and reproduced within core institutions and manifest into social relations based on those differences.[11] Assessing the parameters of gender roles, which include socio-cultural dynamics as well as male-female differences, is therefore crucial in examining both the patterns of exposure to infectious agents (frequency and intensity) and the treatment of infectious diseases.[12] Historically, and even presently, the relationship between gender and infectious disease has been under-researched, particularly when assessing approaches to disease management and control.

Applying Gender-Based Analysis to the Study of (Emerging) Infectious Diseases

The WHO advocates the use of a gender framework to advance our understanding of communicable diseases among men and women.[13] Disease experience differs greatly for men and women – a disparity that should be examined in relation to social, cultural, economic, and individual contexts and consequences.[13] GBAs, like the one advocated by the WHO, are aligned with approaches to infectious diseases that underscore the social determinants of health. Specifically, GBA is a powerful tool for exposing and exploring the relationship between gendered, socio-cultural norms in Saudi Arabia and the emergence of MERS-CoV, including gendered and culturally-specific social roles that affect exposure, available support networks, social stigmas, the use and quality of health services, and decision-making power at the household and community levels.[13]

Gender Dynamics within Saudi Culture

Saudi Arabian culture and the status of Saudi Arabian women within the public domain constitute a complex, culturally-specific social phenomenon. The religion of Islam and the existing ruling-family Sunni Wahhabism have taken precedence in shaping Saudi Arabian culture, from the legal system to the day-to-day living of Saudi Arabian citizens.[14] Indeed, gender-based segregation is permitted and enforced by the state. Although women are segregated to varying degrees across the Middle East, this segregation is strictly practiced in Saudi Arabia. Deep historical forces, notably religion and cultural customs/norms, have shaped social and governmental sanctions for gender segregation to the extent that the day-to-day life of Saudi Arabian women is largely controlled by defined gender roles within predominantly domestic settings.[14] Women's roles are largely defined within familial spaces: they tend to stay at home and act as both the reproducers and educators of traditional values for their children.[14]

Another key feature of Saudi Arabian culture is the concept of modesty. Modesty is expressed by both genders but more evidently by Muslim women and girls.[15] Traditional clothing for Saudi Arabian women consists mainly of the abayah (black cloak) and tarha (black head scarf). This cultural practice is of potential significance when considering disease risk, because it incorporates the veil.[15,16]

Focusing exclusively on gendered religious customs is inadequate, because doing so ignores other social, political, and economic factors that intersect and shape cultural and religious practices as well as behaviours that may be associated with disease risk. Moreover, the complexity of Saudi Arabian culture, which includes high cultural homogeneity based on tribal and Islamic affiliation, makes it difficult to distinguish between Islamic principles and cultural traditions/customs of Arabs.[17] It is precisely this unique intersection of religion, culture, and corresponding social positioning of Saudi Arabian women, and gender inequality more broadly, that makes it more difficult for them to navigate through society. Although the Qur'an advocates for the rights of Muslim women, Saudi society is deeply patriarchal; men dominate social institutions and systems, holding legal power and authority across the region.[17,18] In addition, Saudi Arabian families are generally patrilineal, with the inheritances of property, rights, names, or titles traced to a person's male kin.[17,19]

All of these culturally-specific gendered roles and relationships, including deeply-gendered norms that restrict women's social mobility, influence MERS outbreaks in the region. Applying GBA in infectious disease research allows us to expose these conditions in order to develop a more nuanced understanding of the ways in which the MERS virus manifests itself in this context. Specifically, GBA can expose gendered, socio-cultural practices that may be detrimental or advantageous to the affected community. Moreover, understanding different gendered, socio-cultural norms and practices in Saudi Arabia can help us to identify those gendered practices that contribute to the significant sex differences in MERS-CoV risk between women and men.

MERS - Socio-Cultural Norms within Saudi Arabia

Gender Segregation, Modesty and the Practice of the Veil

Saudi Arabia's laws and moral standards, particularly those surrounding dress, drink, behaviour, and the association of unrelated members of the opposite sex, place the country in a unique position compared to other Muslim countries.[14] The association between socio-cultural practices could have a profound effect, especially in relation to how the MERS virus behaves among these particular practices and norms. For instance, there may be an association between Saudi Arabia's unique cultural customs (e.g. Saudi women wearing both the purdah and veil) and reduced risk of air-borne transmission of respiratory-borne diseases like MERS. Specifically, the practice of modesty and other cultural and religious customs such as wearing of the veil/niqab, which guards the mouth and nose, may act as a protective mechanism[20] that prevents women from coming into contact with contaminated fingers, mucosal membranes, and respiratory droplets. As a result, the use of face cover may unintentionally serve to reduce the risk of women contracting the virus.

The small body of research on these kinds of potentially protective effects is conflicting. Indeed, a recent clinical study did not find a significantly lower incidence of upper respiratory tract illnesses among women wearing a face mask or cover.[20] Furthermore, other studies present the veil as an imperfect substitution for the medical face mask, as Muslim women take off their veil within their homes or in the presence of other women, thus "having the same high risk of disease transmission in a closed environment with exposure to droplet infection".[21] Other potentially relevant distinctions include the absence of a filter and the loose application of the veil to the face in comparison to a face mask, which is elasticized and therefore closely covering the face – a mandatory aspect of clinical practice to prohibit the transmission of viral strains, bacteria, dust, etc.[20] Additionally, Ahmad et al. (2001) found that long-term effects of niqab use include reduced ventilation function and forced vital capacity.[22] This is important, as the combination of airway resistance, increased microclimate temperature, humidity, and skin temperature created inside the niqab could produce an ideal environment for organisms to grow and infect the host.[22] Other possible reasons why the veil is an imperfect substitute for a clinical face mask is the sharing of veils among family members and the fact that Saudi women do not usually cover their face when alone in their homes, thus resulting in a high risk of contracting infections in closed environments.[22]

Gendered Cultural Practices and MERS: Shisha Smoking

Another gendered, cultural practice that may influence the transmission of MERS in Saudi Arabia is shisha smoking. Sultan Ayoub Meo, a senior physiology professor at King Saud University, recently suggested a shisha-MERS linkage. Specifically, he argued that shisha café culture, which is common in Saudi Arabia and is predominantly practiced by men in public, may further exacerbate the spread of the MERS virus in Saudi Arabia. Other studies suggest shisha smoking, also known as "hookah" smoking, may be a mechanism that increases the risk of MERS virus among family and friends. Notably, shisha uses tobacco that is sweetened with fruit or molasses sugar, which makes the smoke more aromatic than a cigarette.[23] Wood, coal, or even charcoal is used to burn the tobacco in order to create the smoke while the fruit syrup or sugar dampens the tobacco and the water acts as a cooling mechanism to decrease the harshness of the smoke,[23] thus making the shisha smoker inhale more deeply.

A 2012 study conducted by the Centers for Disease Control reported that many shisha smokers believe that smoking shisha carries less of a risk of contracting tobacco-related illnesses than does cigarette smoking. As a result, the act of shisha smoking as a social and entertainment-related activity has increased in recent years, with the majority of shisha-users being male amongst Middle Eastern countries.[24] Contrary to public opinion, a study by the WHO concluded that shisha sessions expose individuals to harmful smoke over a long period of time as opposed to cigarettes.[25] This is because cigarette smokers typically inhale 0.5 L to 0.6 L of smoke per cigarette, whereas a shisha session can involve the inhalation of anywhere between 7.5 L and 200 L of smoke.[25,26] Importantly, these findings demonstrate how shisha use creates an ideal environment – the higher amount and duration of shisha smoking, indoor pollutants, and the possibility of exchanging saliva through sharing and second-hand smoke – for shisha smokers (in Saudi Arabia, mainly older males) to be more likely to come in contact with communicable diseases, such as MERS-CoV, when compared to non-shisha smokers.[24,26,27] More importantly, hookah smoking – especially in regard to sharing of the mouth piece during session and coupled with the use of charcoal and tobacco – was associated with health effects, particularly for infectious diseases like influenza and tuberculosis[28] as well as respiratory viruses.[29] This gendered, cultural practice may then contribute to the disproportionately high rates of MERS infection in Saudi men compared to Saudi women (the perception that smoking is 'unladylike', which may decrease participation among Muslim women).[30]

Gendered Dynamics of Religious Practices - Hajj

Hajj (the fifth pillar of Islam) is a religious practice enacted among Muslims, and is one of the most significant manifestations of Islamic faith and unity. Performing the Hajj is a duty that all Muslims (with physical and financial capabilities) must do at least once during their lifetime. Every year, millions of pilgrims across 184 countries arrive at Makkah and Madinah for Hajj.[31]

In recent years, the emergence of MERS has impacted the number of pilgrims participating in the Hajj. For example, in 2013, the number of pilgrims decreased due to the emergence of MERS, during which time the Saudi Arabian Ministry of Health announced that pilgrims were at a high risk of contracting the strain, especially pregnant women, children under the age of 12, the elderly, and those with acute or chronic diseases.[31] During the event of Hajj, there is an overwhelming attendance of Muslims, with limited geographical space to accommodate everyone. These conditions – crowding, shared accommodations, and exposure to environmental dust and pollutants – collectively create an ideal ecology for transmission of respiratory infections, including MERS.[32]

Research exploring communicable and non-communicable diseases during Hajj found that of the pilgrims who were afflicted with common health problems (CPH), the majority (65%) were elderly males.[33] Additionally, current literature examining Hajj have highlighted respiratory diseases (76.2%) as the main health problem facing Hajj pilgrims,[33] with viral respiratory infections such as influenza and rhinovirus being the second leading pattern of CPH facing hajj pilgrims. Specifically, 57% of patients admitted into Saudi hospitals were reported to have respiratory tract infections, making it the leading cause of hospitalization during Hajj.[33] Importantly, elderly hajjis were identified as being a high-risk group during hajj,[33] which is significant, as the majority of cases involving MERS were found to be male, and even higher rates were found amongst elderly males with underling medical conditions.[34]

This is particularly interesting since the practice of gender-segregation and wearing of the veil by Muslim women does not occur during the majority of the Hajj event. Notably, while the event is not explicitly separated by gender, the notion of modesty still applies to female pilgrims. Accordingly, it is obligatory for female pilgrims to travel to Hajj with their husband or mahram, a male relative whom they are permanently forbidden to marry because of blood ties. In light of these conditions, further research is needed to determine whether female pilgrims' exposure to and risk of MERS infection increases during the Hajj.

It is equally important to consider the impact of the gendered customary practices during the Hajj on men's exposure and risk of MERS infection. During the Hajj, it is obligatory for all pilgrims to wear ihram. For men, this consists of white garment that covers them from the waist down and includes a white garment over the shoulder. For women, ihram typically consists of a white dress and headscarf or their native dress. Because male pilgrims' customary clothing does not necessarily cover the entire body (exposing their upper body, hands, and legs), their risk of being exposed to the MERS virus presumably increases as they come into direct close contact with contaminated fingers and mucosal membranes of others.

Although there have been no Hajj-related MERS cases reported to date, MERS-CoV remains at the top of the WHO's list of emerging diseases that have the potential to cause major epidemics.[35] Mass gatherings and religious events create an ideal high-risk condition for the rapid spread of infections by attracting large crowds, thus posing a significant public health threat.[35] Conversely, a number of unanswered questions still remain, especially in regard to epidemiology, pathogenesis, management, and control.[35] As such, continuous monitoring of the virus is crucial for maintaining a safe environment for pilgrims to perform their religious duties, and for preventing it from spreading and becoming pandemic.

Gendered Social Roles and Livestock Management

Epidemiological reports suggest that the MERS virus is zoonotic by nature,[36-38] with the potential to infect various mammalian cell lines, including primates, pigs, bats, and rabbits.[39] Although bats were initially presumed to be the primary host, most patients did not directly contract the virus from bats.[38-41] Therefore, a potential trajectory of the MERS virus could be traced as follows: a single variant related beta-coronavirus in bats → intermediate animal → host → human population.[42] This trajectory appears likely in light of emerging evidence that suggests camels may play intermediate roles, both as disease victims and as reservoirs to exacerbate transmission.[43] This, in turn, suggests that the MERS virus travelled from the primary host (bats) to this potential intermediate animal before infecting humans, as both the geographical and cultural context favour this mechanism.

A number of sero-epidemiological studies suggest that dromedary (single-humped) camels residing in regions within the Arabian Peninsula and the Middle East were the only domestic livestock reported to have specific antibodies to the MERS-CoV virus.[44-46] Furthermore, there are several studies that highlight the link between MERS-CoV and dromedary camels. For instance, two human cases of MERS-CoV infection diagnosed in 2013 were linked to a camel farm in Qatar.[47] Moreover, MERS-CoV and dromedary camels were found to have cross infection potential, wherein the virus can be transmitted from camel to human via close contact.[47] Serum samples obtained from dromedary camels in Saudi Arabia were found to exhibit a high sero-positivity (72%) to the MERS virus.[47] Specifically, sero-positivity was greatly significant amongst those who were exposed to dromedary camels; indeed, it was found to be 15 and 23 times higher amongst shepherds and slaughterhouse workers, respectively.[47] Additionally, transmission of MERS virus via droplets was emphasized both in hospital settings and especially in dromedary camels, which were found to have very high concentrations in their nasal secretions, making this transmission avenue a likely route.[48] Additionally, transmission routes via dust particles should not be excluded, as these particles can be contaminated by camel urine and droppings.[48]

In addition, some studies have revealed that MERS-CoV has been prevalent among dromedary camels for approximately

20 years,[35] with some documenting an association as early as 1992 in Saudi Arabia,[49] suggesting that it is not a newly-emerging zoonotic pathogen from camels.[44] The Arabian Peninsula is home to only 1.2 of the 30 million camels worldwide, of which 95% are dromedary camels.[48] Despite this relatively low number, dromedary camels in Saudi Arabia carry the MERS virus at significantly greater rates than those imported across the African region.[49] The study of dromedary camels not only supports their role in human infection theory but has also found them to be an important source of income and social prestige, as they are "indispensable to the traditional nomadic lifestyle, provide milk, meat, wool, leather, medicinal purposes as well as for transport, trade and racing".[44]

Camel husbandry is a gendered practice; occupations that incorporate huge commercial farms and those that manage and herd large animals are male-dominated.[50] A gendered division of labour characterizes pastoralist societies.[51] Specifically, while pastoral societies are male-dominated, women living in these communities are typically responsible for subsistence, which includes the care of animals near the household.[51] Moreover, existing literature has reported a drastic change in dromedary camel farming practices in Saudi Arabia, where the number has changed from 80,000 to as high as approximately 800,000, with 20% of the dromedary camel owners to be retired.[48] This could explain the responsibility of herding and managing large animals (including dromedary camels) to be male-dominated, as studies have highlighted camel rearing to be both an exclusively male activity and popular among middle-aged and retired men.[48] Furthermore, these data could potentially underline an important gendered channel of transmission and may also help to explain the high rates of male infection given that these men are in continuous contact with this important intermediary host.[52] Unfortunately, there is limited research on the care of specific species of farm animals, which makes the empirical investigation of those possible gendered relationships exceedingly difficult. The situation is complicated further, because "[labour] force surveys do not often separately list activity rates by sex for the care of different types of animals".[53]

Notably, camel herds normally move across the Arabian Peninsula (by grazing, participating in camel races and camel shows) in Saudi Arabia and many other Gulf countries such as Kuwait, Oman, Qatar and United Arab Emirates (UAE).[44] These movements are important, because they can explain the link between epidemiology and viral evolution. In addition, by incorporating the concept of gender roles, it is possible that the movement of camels between locations provides an understanding of how the virus may spread and predicts particular gender roles that may be at risk of the MERS infection. For instance, camel shows (also called Mazayin al-Ibl – meaning "best of camels") are an annual tradition among many Gulf countries, especially in the eastern region of Saudi Arabia where one of the largest camel shows has more than 100 camel herds representing over 160,000 camels from various regions in the Arabian Peninsula and 160,000 people attending every year. Moreover, there are major annual racing competitions held around February called Janadriyah.[44] Similar festivals are held among other Gulf countries such as the UAE, Oman, Qatar, and Kuwait.[39]

This important consideration could explain how the continuous movement of camels across borders might influence the amplification and evolution of MERS-CoV.[44] For example, previous reports have suggested a high degree of similarity amongst MERS-CoV sequences obtained from Al-Ahsa and MERS-CoV from humans in the UAE and Burydah.[44] The pre-existing social norms that exist in the majority of the Middle East and more specifically in Saudi Arabia – the majority of participants are middle-aged and retired men, and women are generally not involved in sports and other leisure activities – may potentially impart a gender-based discrepancy in the risk of acquiring the virus.[48] Therefore, the increased occurrence of male-dominated sports, such as camel racing, and higher male participation within these activities could potentially increase the risk of males acquiring the virus.

While researchers have yet to conclusively determine if this animal does, in fact, function as an intermediary linking the virus from an unknown animal reservoir to human beings or even as the reservoir for MERS-CoV,[44] there is considerable evidence pointing to dromedary camels being the primary host animal for the MERS-CoV virus as well as an important vehicle in transmitting the virus to humans, which by nature of husbandry practices in the region is deeply gendered.

Conclusion

The present review has explored gendered socio-cultural norms and practices that may influence observed sex-differences in MERS infection. Research suggests that, in some contexts, the veil may service to reduce exposure and risk of infection, while in others, the practice of the veil may actually increase women's risk of infection. Other kinds of gendered, culturally-specific practices including shisha smoking, participating in the Hajj, and livestock management of dromedary camels may exacerbate transmission of the MERS-CoV virus and, in part, account for the observed sex differences in MERS infection.

To better understand potential models of transmission and infection, it is vital that we develop a more nuanced understanding of religious and cultural practices in Saudi Arabia that takes gender norms into consideration. Indeed, applying a gender-based analysis to the review of emerging infectious disease can help us to understand how behaviour, activities, and differential access to resources and decision-making affect disease transmission and outcomes. This review of the literature demonstrates the utility of this type of analysis in generating areas for future research and public health policy, particularly in regard to the MERS coronavirus.

Acknowledgments

The author would like to thank Dr. Suzanne Sicchia and Ms. Sandra Romain for providing feedback on early drafts of this paper, including extensive editing. Special thanks are also owed to University of Toronto librarians, Ms. Angela Hamilton and Ms. Sarah Guay, and Dr. Sheryl Stevenson for providing me with research assistance.

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Newfound Aboriginal Right to Pursue Traditional Medicine

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Abstract

This article discusses the newfound aboriginal right to pursue traditional medicine. A 2014 Ontario court decision relating to J.J., an 11-year-old First Nations girl with leukemia, is analyzed. The events leading up to the court case are followed by a description and analysis of the court's decision. The court found, for the first time in Canada, that there is an aboriginal right to pursue traditional medicine on behalf of a child, despite the medical evidence that chemotherapy would almost certainly result in remission while the absence of chemotherapy would almost certainly result in death. This article concludes that the case provides limited guidance for those that find themselves in similar situations in the future, and demonstrates the need for collaborative problem solving when making treatment decisions for children, perhaps through the use of mediators or ethicists.

Consent Sought for Chemotherapy to Treat Acute Lymphoblastic Leukemia

In 2014, two First Nations children were diagnosed with acute lymphoblastic leukemia. The children were aged 11 and lived near Brantford, Ontario. Regarding one of these children, known as J.J., the healthcare team at McMaster Children's Hospital sought consent to treat her cancer with chemotherapy. J.J.'s mother refused.

While cases where parents withhold consent for medical treatment on behalf of their children are not new, unique to this situation was that the refusal was on behalf of a First Nations child. This article describes how that fact played a significant role and saw an Ontario court identify, for the first time in Canada, an aboriginal right to pursue traditional medicine. The discussion is broken down into the following sections:

1. The events leadings up to the court case,
2. The Court's reasons for decision,
3. The potential impact this decision has on similar situations.

The Disagreement Between the Mother, Healthcare Team, and the Children's Aid Society

Having diagnosed J.J. with acute lymphoblastic leukemia in August of 2014, the healthcare team sought consent from J.J.'s mother to treat using chemotherapy. J.J.'s treating physician, oncologist Vicky Breakey, wrote that with timely medical intervention and considering J.J.'s clinical assessment and genetic test results, there was a 90-95% "cure rate".[1] Others were less confident, saying the five-year survival rate might be only 70% in a similar but not identical situation.[2] All of the physicians agreed that they had not heard of a patient surviving this condition without the use of chemotherapy.

Dr. Philip Hébert wrote the following regarding Makayla Sault, the other First Nations 11-year-old diagnosed with acute lymphoblastic leukemia referred to in the beginning of this article:

> *In 1960, children with the disease were given no chance of survival. Now, with chemotherapy and bone marrow transplantation the five-year survival has reached 90 per cent. On the other hand, 80 per cent of children will experience a serious or even life-threatening complication from the intensified treatments now used. Makayla's leukemia was Philadelphia chromosome-positive, a factor that reduced her five-year survival rate to 70 percent.[2](p126)*

Sadly, Makalya died after being withdrawn from chemotherapy.[3] A court challenge was not initiated in her case.

Initially, J.J.'s mother agreed to treatment with chemotherapy, but 10 days into the 32-day treatment plan she withdrew her consent. It is unclear why J.J.'s mother withdrew her consent, but her position later on stated that she wished to pursue traditional medicine, possibly in combination with chemotherapy.

There is no clear definition of traditional medicine. After withdrawing J.J. from the care of the physicians at McMaster Children's Hospital, J.J.'s mother planned to take her to Florida to undergo a form of alternative medicine. Despite an interim order by the Court that J.J. not be removed from Ontario, J.J.'s mother took her to the clinic in Florida. The Children's Aid Society said that by the time they were aware of the mother's actions, the two were already on their way.

J.J.'s physicians sought the help of Brant Family and Children's Services. Under the *Child and Family Services Act*, the child welfare agency had the power to declare J.J. "a child in need of protection".[4] Brant Family and Children's Services contacted the Six Nations of the Grand River Band Council (Six Nations Band) regarding J.J., but ultimately declined to intervene. The hospital, on behalf of its physicians, brought a court application to have J.J. declared a child in need of protection, in order to treat her cancer with allopathic medicine. Initially, the only parties to the application were the hospital, Children's Aid Society, and the Office of the Children's Lawyer. The Court added J.J.'s parents and the Six Nations Band as parties.

The Court's Reasoning and The Newfound Aboriginal Right to Traditional Healing

The Court determined that given the evidence of J.J.'s maturity, life experience at age 11, and lack of independence from her mother, as well as the circumstances surrounding the treatment of her specific condition, she was not capable of making this decision herself.[1] As a result, J.J.'s mother was found to be her substitute decision maker.

The Children's Aid Society urged the court to find that the appropriate forum for this dispute was the Ontario Consent and Capacity Board. That Board is an administrative tribunal that sits as a three-person panel comprised of a lawyer, physician, and member of the public. It adjudicates treatment decisions made on behalf of others. The Court, citing earlier cases involving children whose parents were Jehovah's Witnesses refusing blood transfusions for their child, found that when the issue is a matter of child protection, the Court has jurisdiction to decide the matter.[1] As a result, the case was not referred to the Consent and Capacity Board.

The Court then identified the main issue as being whether there were reasonable and probable grounds to believe that J.J. was a child in need of protection, as defined by the legislation. All parties agreed that the only applicable part of the legislation defining a child in need of protection was section 37(2)(e), which reads:

> *(e) the child requires medical treatment to cure, prevent or alleviate physical harm or suffering and the child's parent or the person having charge of the child does not provide, or refuses or is unavailable or unable to consent to, the treatment;*[4]

The hospital asserted that J.J.'s mother's decision to discontinue chemotherapy made J.J. a child in need of protection. The Band asserted that s. 35 of the *Constitution Act, 1982* protected J.J.'s mother's right to pursue traditional aboriginal medicine. Section 35 reads:

> *35.(1) The existing aboriginal and treaty rights of the aboriginal peoples of Canada are hereby reorganized and affirmed.*[5]

In the *Canadian Charter of Rights and Freedoms* ("the *Charter*"), the very first section (s.1) operates to limit the rights contained within the *Charter*. Section 1 reads:

> *1. The Canadian Charter of Rights and Freedoms guarantees the rights and freedoms set out in it subject only to such reasonable limits prescribed by law as can be demonstrated in a free and democratic society.*[6]

The Court then correctly noted that section 35, which affirms existing aboriginal rights, is not part of the *Charter* and therefore is not subject to the limitation contained in s. 1.[1] Justice Edward went on to find that, in accordance with the legal test for identifying an aboriginal right, there was an aboriginal custom of traditional healing that existed before Europeans made contact with the First Nations.[1] Evidence for this was provided by testimony from Professor Dawn Martin-Hill who holds the McPherson Indigenous Studies Research Chair in the Anthropology Department at McMaster University. She was found to be an expert witness in the area of First Nations traditional medicine.

Further evidence from Dr. Karen Hill, a medical doctor practicing family medicine in the Six Nations Band, was that traditional medicine was still practiced at the Six Nations as it was prior to European contact, and that it formed an integral part of the customs of the Band. After finding that traditional medicine preceded European contact, was maintained to the present day, and that the right had not been extinguished, Justice Edward found that an aboriginal right to pursue traditional medicine existed.

Having affirmed an aboriginal right to pursue traditional medicine, and that J.J.'s mother was deeply committed to those beliefs (as opposed to simply attempting to adopt them at the last minute in order to withdraw her child from allopathic medical care), the Court found that J.J.'s mother's decision to withdraw J.J. from chemotherapy was her aboriginal right.[1] Interestingly, Justice Edward then found:

> *Further, such a right cannot be qualified as a right only if it is proven to work by employing the western medical paradigm. To do so would be to leave open the opportunity to perpetually erode aboriginal rights.*[1](para81)

In an unusual step, lawyers for the Ontario Ministry of the Attorney General, along with the parties to the hearing, asked Justice Edward to "clarify" his decision.[7] This, ostensibly, was to spare the family from the appeal process, which may have reversed the Court's decision, and in any event would have prolonged the matter. In its clarification, the Court found the paramount concern in cases such as this is the best interests of the child, despite the fact that no such wording or analysis was present in its original ruling.[7]

A couple of weeks after the initial court decision was released, J.J.'s mother agreed to consult another pediatric oncologist, at a separate hospital, regarding treating J.J.'s leukemia.[8] She said, "This time, I will be respected. The Court decision gave that to me."[8] News reports indicate that as of April 2015, J.J. was receiving a mix of traditional and conventional medical care, which included chemotherapy.[9] These reports also indicate that in early 2015, J.J. was doing well, though it is unclear how her health is today, as neither J.J. nor her mother have appeared in the media since that time.[10]

J.J.'s Case Provides Limited Guidance for Future Cases and Demonstrates the Need for Collaborative Problem-Solving

This case is notable for its divergence from similar cases where parents refused potentially life-saving treatment for their children. The primary reason for that divergence is the parent's reliance on s. 35 (aboriginal rights) of the *Constitu-*

tion Act, 1982, as opposed to on the right of freedom of religion contained in the *Charter*.

Another striking feature of this decision is the complete absence of analysis of J.J.'s rights, the legal presumption in favour of life, or even "the bests interests of the child" in the original decision. The after-the-fact addendum which provides that of course, the paramount concern must be the best interests of the child makes this case of extremely limited value in terms of providing guidance for those that find themselves in similar situations in the future.

Resting the entire decision on the aboriginal rights section of the constitution also has the putative effect of providing aboriginal parents the absolute right to pursue traditional medicine and forsake allopathic treatment for their children. In Jehovah's Witness and other similar cases involving freedom of religion, Canadian courts found that parents' freedom of religion was not absolute and the state's interest in preserving life prevailed, in certain circumstances. (See, for example, the Supreme Court of Canada's decision of B. (R.) v *Children's Aid Society of Metropolitan Toronto* for how this balancing was accomplished in the context of parents of the Jehovah's Witness faith refusing blood products for their infant daughter.[11]) No such balancing can be done under the aboriginal rights provision because it is not governed by s. 1 of the *Charter*. As a result, in future cases involving an aboriginal right to pursue traditional medicine, courts may need to balance that right with the child's *Charter* right to life and security of the person.

Additionally, commentators have pointed to the fact that the clinic in Florida was not in fact providing traditional aboriginal healing, and so the basis for the refusal of treatment could not properly be said to be in pursuit of an aboriginal right.

Finally, the Court's analysis of the aboriginal right to pursue traditional medicine is questionable. This was the first time such a right was found. Previously, this section was used for hunting and fishing rights, and for enforcement of treaties.[12] The Court's analysis was exceptionally brief considering what was at stake and the lack of prior jurisprudence. With that said, such cases are often conducted under exigent circumstances.

For these reasons, this case would have benefited from appellate review. Unfortunately, that opportunity was denied when the parties agreed that rather than appeal the decision, the addendum affirming that the best interests of the child test applied would suffice.

It must be remembered that this decision occurred against the backdrop of the ongoing recovery from the residential school system. This was a policy by the Canadian government where aboriginal children were removed from their families, band, and culture, and placed into residential schools where they experienced horrific abuse.[12] While not made explicit in this decision, it is clear that Canadian courts should be slow in removing children, especially First Nations children, from the care of their parents and band, and force Western treatment on them.

While caution is needed, blindness to the realities of the proven benefits of evidence-based medicine can also harm the child. Perhaps what this case best illustrates is the importance of Alternative Dispute Resolution as an alternative to litigation. It is a maxim of law that one can never truly predict what the outcome will be of any dispute that is adjudicated. As a result, the best outcomes are often those crafted by the disputants themselves. To that end, bioethicists and mediators can assist parents and healthcare teams in finding a solution that works for everyone involved.

Accreditation Canada requires a bioethicist be available at all accredited hospitals in Canada. Ethicists do not advise or suggest a particular course of action. Rather, they inform the people involved as to the ethical principles at play, and suggest factors to consider in making a decision. Ethicists are often consulted by families making decisions on behalf of others, or by healthcare teams when there is disagreement or apprehension involved in making difficult decisions. Either the family or the healthcare team can approach a bioethicist to initiate a consultation.

Mediators are neutral third parties who assist two or more parties who are in conflict. The methods that mediators use to resolve disputes vary. It is important to note that mediators cannot make binding decisions or force any party to make a decision. Often, however, their presence, impartiality, and skillful communication result in lasting decisions for all involved that are far more satisfying than an imposed decision made by a tribunal or judge. Mediated decisions are typically more creative and far less costly than ones that result from adjudication.

Given J.J.'s mother's comments and her ultimate decision to pursue both traditional aboriginal medicine and chemotherapy, it seems that she was primarily concerned about being forced into a particular mode of treatment and the impact this would have had on her dignity as a mother and First Nations person. When this is considered in the context of survivors of the residential school system, it seems clear in retrospect that some form of Alternative Dispute Resolution would have been useful in this situation.

Considering the following excerpt from Justice Edward's addendum, one wonders if some form of Alternative Dispute Resolution is in fact the approach that eventually prevailed in this case:

> *Written reasons given in a case seek to explain how a court has resolved an issue between parties who appear before it. Sometimes such reasons attract a wider audience. The Attorney General of Ontario was in that audience in this case. There were many calls for the Attorney General of Ontario to pursue litigation; however, the Attorney General chose to engage in a dialogue with the parties that ultimately led to an*

approach that spoke more to what joins us as opposed to what separates us. The joint submission, that has been read into the record, notes how the province and the family collaboratively worked to form a health care team to bring the best both had to offer to address J.J.'s ongoing treatment. This approach recognizes the province's acceptance of the family's right to practice traditional medicine and the family's acceptance western medicine will most certainly help their daughter. It is simply a recognition of what is in J.J.'s best interest.[7](para5)

This case should serve as a cautionary tale. Practitioners who find themselves in similar situations should strongly consider seeking early consultation with an ethicist and the use of a mediator with a background in health law. As perhaps occurred in this case, it should be noted that it is never too late to use these services.

Acknowledgements

I would like to thank my wife, Christina Shehata, for her continued support throughout my legal and medical career.

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Rising Up to the Challenge: Strategies to Improve Health Care Delivery for Resettled Syrian Refugees in Canada

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The haunting image of three-year-old Alan Kurdi lying dead on a Turkish beach struck a chord across the world and brought the urgency of the Syrian refugee crisis to light. Notably, it ignited fervor in the Canadian political landscape following the revelation that the boy's family was trying to eventually reach Canada. In response, the newly elected Liberal government pledged to welcome 25,000 government-assisted Syrian refugees into Canada by the end of 2015.[1] Following the Paris terror attacks of November 2015, however, the government revised their target by committing to resettle 25,000 government-assisted refugees by the end of 2016, citing an intensified screening process as the cause for delay.[2] By the end of March 2016, over twenty-six thousand Syrian refugees had arrived in Canada, with approximately 15,000 classified as government-assisted.[3] As Canada continues to strive towards its commitment to resettle Syrian refugees, profound implications exist for the health care system with respect to its ability to meet refugees' specific health necessities. Health needs for refugees often differ as a result of their distinct environmental exposures, living conditions, and family histories of disease.[4] To fulfill these necessities, the quality of primary health care delivered to refugees needs to be significantly improved by promoting access to health services, mitigating language barriers, and stimulating health literacy.

Newly arrived immigrants and refugees frequently report having limited access to health care due to factors such as a lack of understanding of the health care system, language and cultural barriers, or discrimination.[5] These problems persist despite the implementation of policies to promote access to health services among refugees. The Interim Federal Health Program (IFHP) was introduced by the federal government to provide refugee newcomers with temporary coverage of health-care benefits as they await acceptance into a provincial health insurance plan.[6] At present, the IFHP provides resettled refugees with full health-care coverage that includes basic health-care services (i.e. physician and hospital care), supplemental services (i.e. limited vision and dental care, allied health services, and assistive devices), and prescription drug coverage.[6] Under the IFHP, refugees moving to Canada should have immediate access to both basic and supplemental health coverage. However, they still face difficulties in accessing these services. Statements from Resettlement Assistant Program workers, who assist government-sponsored refugees, indicate that primary care physicians frequently do not acknowledge the IFHP certificate.[7] This reluctance to treat refugees is usually due to unfamiliarity with the IFHP or an unwillingness to engage in the long administrative process required to be reimbursed for services provided.[7] In some cases, when the reimbursement process is slow, refugee patients have been approached by their primary care provider for payment for services.[7] These patients ultimately visit emergency rooms for non-urgent conditions.[7] Since hospitals have distinct departments to address billing issues, they accept IFHP certificates more readily, but this increases waiting times in the emergency room.[7] Moreover, reports indicate that refugee mothers with IFHP coverage who are refused care are often unable to locate an alternative provider, potentially resulting in adverse implications for their child's health.[8] Another barrier that limits refugee patients' access to health services is discrimination in health-care settings. Although overt forms of discrimination, such as racial slurs or stereotyping, have been documented, most discrimination in Canada today is subtle.[9] This may include rude or unfair treatment, exclusion, or being dismissed.[9] Documented incidences include health service providers becoming frustrated when asked to respect religious or cultural beliefs or pretending to not understand the patient.[8,9] The occurrence of these incidents is concerning due to the adverse effects associated with discrimination in health-care settings, which include poor physical health, mental health, and risky lifestyle behaviours.[9]

In order to tackle these issues, better training and mentorship services should be administered to medical students and primary care providers. As medical students graduate,

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they will be faced with a rapidly changing population with a diverse set of values and beliefs, and they will need to be culturally competent to deliver effective, patient-centered care. Students and physicians can gain vital exposure to these populations by working in specialty clinics that serve refugees. Studies indicate that medical students who have had the opportunity to care for refugee patients developed an increased awareness of their cultural background, which included an acknowledgement of the role of religion and spirituality in health care, identification of family structure and relations, and understanding of gender roles and relations.[10] Additionally, students also learned key lessons about cultural humility, enabling them to appreciate their own privileged background, meet the emotional needs of refugees through empathy, and demonstrate a willingness to integrate refugees into their community.[10] In Canada, medical students at the Memorial University of Newfoundland initiated a program that successfully connected resettled refugees with the health care system and offered medical students the opportunity to engage in clinical training with refugee populations and to practice cross-cultural care.[11] For primary care physicians, these types of services can be supplemented within the curriculum of professional development workshops.[12] Providing medical students and primary care providers with specific training will familiarize them with policies regarding the delivery of health services to refugees and enable the development of cultural competence when approaching refugee patients. Ultimately, this will enhance refugees' experience and improve their access when seeking healthcare.

There are several facets of health services that determine the quality of care being delivered to patients. For recently resettled refugees, proper communication of health information is paramount. Language barriers represent a serious obstacle to receiving a satisfactory level of health care and contribute to deficiencies in health literacy.[13] Not only do language barriers affect patients' ability to communicate with their primary care providers, but they also impact subsequent appointments with specialists and understanding of instructions associated with follow-up or prescriptions.[14] Canadian health care practitioners (HCPs) prioritized language interpretative services and communication support as the most important practice strategy needed to enhance the quality of primary health care for vulnerable populations.[12] Approaches to implement this recommendation include matching patients with primary HCPs who speak the same language or administering interpretive services using staff interpreters or contracting qualified interpreters.[12] Furthermore, the recent emergence of mobile technologies has led to the development of applications that can be used by physicians to surpass language barriers and effectively communicate with patients. *MediBabble Translator* is an excellent tool that allows physicians to take patient histories and make diagnoses. The program performs these functions in a number of widely spoken languages.[15] A less specialized mobile application that can be used is *Google Translate*, which can allow HCPs to easily translate English phrases into a language of their choice.[16] Along with traditional interpretive services, modern technologies can be effective in facilitating transparent communication between Syrian refugees and their health care providers.

Community-level interventions have also been identified as a strategy to improve health service delivery to vulnerable migrants.[12] Community health workers (CHWs), which possess advanced knowledge of social determinants of health, play an integral role in implementing these strategies.[17] CHWs understand the difficulties faced by marginalized communities in accessing health and social services, and help members of these communities achieve better states of health through health education, community development, and advocacy.[17] Specifically in Syrian refugees, mental health conditions such as depression, posttraumatic stress disorder, and anxiety disorders are prevalent, owing to the effects of violence, displacement, travel, or family separation.[18] CHWs can act as facilitators to help refugees navigate the health care system and can link them with the necessary services through linguistically and culturally-appropriate support.[17] However, Canada currently lacks an organizing body to regulate the quality of community outreach programs.[17] Collaboration between community and governmental organizations in the development and evaluation of outreach programs is essential to encourage their growth. Proficient community outreach programs have strong potential to promote the adaptation, settlement, and integration of Syrian refugees into Canadian society.

The aforementioned strategies provide guidance to enhance the quality of primary health care services to meet the oncoming challenges posed by Canada's laudable initiative to resettle Syrian refugees. The health care system needs to adapt by providing specific training and mentorship of medical students and primary HCPs on current health policies related to refugees, implementing adequate language translation services, and fostering collaboration between governmental and community organizations to develop strong outreach programs.

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The Role of Food Education in Childhood Obesity [Book Review of French Kids Eat Everything]

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Karen Le Billon's *French Kids Eat Everything* is more than an amusing account of her family's move from Vancouver, British Columbia to her husband's hometown in northern France for a year. Le Billon describes the culture shock she experienced upon realizing that her two young daughters' eating habits were entirely incompatible with those of French children. For example, she shares her experience of being forbidden from packing her daughters' school lunches in lieu of the elaborate meal served at school. She was stunned by French school-age children's willingness to consume a diverse array of foods, from asparagus to aïoli, shrimp to soufflé, and nearly everything in between. To her dismay, she was even reprimanded for trying to slip her youngest a harmless snack: "It's a recipe for obesity!", she was lectured. How could she keep her daughters, who flee from the table when a food they do not like appears, from starving to death in this diverse food culture? Le Billon takes her readers on a journey of discovery as she articulates ten food rules by which the French appear to successfully abide. The first rule, exploring food education, provides a foundation upon which the other nine rules are built.

Le Billon describes how, in French, "education" includes knowledge acquired through formal schooling as well as the habits, tastes, manners and behaviours developed through discipline in the home. She rationalizes the wisdom inherent in French education as it relates to food: eating is one of the first acts an infant performs consciously and independently, even prior to walking and talking. Firm, but gentle guidance provided at this critical time and throughout childhood is essential to establish the foundation for healthy eating for the rest of a child's life. Le Billon provides her readers with a sobering reminder:

Chances are, my children are not going to grow up to go to Harvard or to be major league sports stars, concert musicians, or NASA astronauts. But no matter who they grow up to be, how and what my children eat will be of great importance to their health, happiness, success, and longevity.[1]

Le Billon provides a plethora of anecdotes, statistics, and personal observations to demonstrate to readers how the conceptual framework of food education manifests itself. For instance, readers might be surprised to learn that the French spend about twice as much time eating as do Americans. In her book, Le Billon argues that this time is well spent. Children are taught from a young age that meals embody a time for people to come together and take part in a special occasion. Food is always eaten around a table, never on the run, and tables are never barren, always adorned. In short, the French have a respectful and meaningful approach to food.

An important subject discussed at length by Le Billon is *from whom* the French children learn this approach to meals. Food education is incorporated in the curriculum of the French school system. In the classroom, teachers play an active role in opening the minds of children to food as a culture, art, and national heritage. It is here that basic principles of food habits, hygiene, and nutrition are introduced to children. In the cafeteria, these rules are put into practice. Tables are adorned with cloth and cutlery, students collectively gather, and the same three-course meal prepared by an in-house chef is served to all. Subsidization for low-income families is provided, so that no child brings lunch from home.

Furthermore, the French government plays an active role in supporting food education. Selective regulations in the production, marketing, and sale of food to children are strictly enforced. Le Billon notes the resemblance between warnings found on North American cigarette packs and those which appear on a white banner accompanying snack ads on television: "for your health, avoid snacking between meals."

What becomes clear from Le Billon's identification of those who educate the children is that no one party is solely responsible for this task. Importantly, lessons taught by parents are reinforced by teachers, and supported by the school system and the French government. Despite her thorough analysis of the French system of food education, Le Billon only skims the surface when it comes to exploring how food education is carried out in North America, and for good reason. North America, and particularly the United States, lacks a framework that fosters collaboration amongst different parties involved in the health of children.

Le Billon's book might have benefited from a chapter devoted to a focused discussion of the issue of obesity as a public health problem. The inclusion of such a chapter would not have significantly altered the tone of her memoir, but would have provided her readers with the opportunity

to think critically about the issues at hand and might have assisted them in placing her experiences within the broader context of public health. To achieve this, Le Billon might have drawn parallels between the French and North American school systems, concepts of parenting, and legislation regulating marketing and advertisement. Addressing discrepancies between the two systems and highlighting the consequences of these disparities would have allowed Le Billon to begin a conversation exploring why obesity is a problem that matters.

Host of *French Food at Home*, Laura Calder, considers Le Billon's memoir "*a book about how to help build and maintain the foundations of any civilized society.*" What we lack is that foundation. Attempts to foster healthy eating habits by parents in the home are foiled by television advertisements that push kids to consume fat-laden and sugar-infused snacks. Pressured from school boards to improve math and science scores on standardized tests, schools (particularly in the United States) have drastically reduced time for physical education[2] and have all but eliminated courses on home economics.[3]

In 2012, the Centers for Disease Control and Prevention (CDC) reported the incidence of childhood obesity in the United States to be roughly 20%.[4] A systematic analysis conducted in 2013 revealed that the incidence of childhood obesity in France was amongst the lowest of all industrialized countries: a mere 5%.[5] It is now predicted that this generation's children will be the first to live shorter lives than their parents.[6] At no other time have we needed more the cooperation of governments, schools, and parents to ensure the health of the youngest members of our society. Le Billon's memoir brings to light what can be accomplished if all levels of society identify a common goal and make a whole-hearted and collaborative effort to achieve it. The first step toward teaching our children the vital life skill of healthy eating is realizing that this is a collective responsibility. Most nations facing an obesity epidemic have yet to take this first step.

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Abraham Jacobi and the Evolution of Paediatric Advocacy

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Considered by many medical historians to be the "founder of paediatrics", Abraham Jacobi is a prolific paediatrician whose philosophies and innovations have immensely impacted our current paediatric practice.[1] Jacobi was the first paediatrics professor to teach at an American university, the first paediatric president of the American Medical Association (AMA) and the first president of the American Pediatric Association (APA).[2]

Jacobi used his influence in these organizations to bring about meaningful change in the way his peers approached and practiced medicine. As an advocate for institutionalized children, educational reform, breastfeeding and many other health issues affecting children, Jacobi revolutionized the practice of Paediatrics. In one of his most famous quotes, Jacobi argued "it is not enough... to work at the individual bedside in the hospital. In the near or dim future, the pediatrician is to sit and control school boards, health departments, and legislatures." This powerful shift in thinking enabled the role of a physician to expand beyond that of an exclusive medical expert. Almost a century has gone by since Dr. Jacobi passed away, yet the evolution of the specialty he helped define would likely have surpassed his expectations.[1] Today the CanMeds guidelines recognize advocacy as one of the fundamental roles of all physicians. A physician with a holistic approach to their patients has become a central dogma of our modern day medical culture, yet was once an innovative aspect of Dr. Jacobi's approach to medicine.

The field of paediatrics has come a long way in advocating for crucial changes in child health. For instance, the measles vaccine has single-handedly saved an estimated 17.1 million lives worldwide since 2000.[3] During Jacobi's practice in New York, 62.5% of all deaths occurred in children less than 5 years of age.[1] The majority of these cases were caused by infectious disease such as diphtheria; a disease which sadly claimed the life of Jacobi's son. Today, infectious disease has gone from being the leading cause of death in Canadian children to accounting for less than 5% of childhood deaths, largely due to stronger vaccination compliance.[5] Jacobi's work in this field is proof that a single physician's advocacy work can make a tremendous difference. Interestingly however, we are still working on this very topic one century later. The 2013 Canadian Childhood National Immunization Coverage Survey revealed that the current rate of childhood vaccinations is as low as 72%, which falls short of our goal of 95-99%.[4] With a backdrop of misinformed parents in opposition of vaccinations and an increased use of homeopathic alternatives such as nosodes, it remains crucial for paediatricians to be equipped as medical experts, advocates and educators. For example, a statement from the Canadian Pediatric Society recently released in February 2016 draws attention to the use of nosodes and leaves opportunity for physician advocacy in this area.[6] This statement explains the homeopathic process of using serial dilutions from a pathogenic source to create nosodes, and more importantly highlights the lack of evidence for their efficacy and safety.

It is important to reflect on the history and evolution of Paediatrics to truly appreciate it as an independent medical specialty. Furthermore, important figures such as Jacobi who portrayed advocacy and brought about meaningful changes in child health, should motivate us to continue these efforts in our modern day world. Continuous reflection on our mindset and methods while working towards helping our patients is key to ensuring our practice remains ethical and genuine.

Acknowledgements

We would like to thank all the physicians who have mentored us throughout our training, and all the physicians who continue to advocate for child health on a daily basis.

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Scrutineers Par Excellence: The Observational Prowess of Jean-Martin Charcot and Charles Miller Fisher

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"[…] there is no more difficult art to acquire than the art of observation, and for some men it is quite as difficult to record an observation in brief and plain language." - Sir William Osler[1]

Clarity of observation was the crowning virtue for clinician Jean-Martin Charcot, just as precise visualization was the key to unlocking each one of Charles Miller Fisher's discoveries. This essay compares and contrasts the observational techniques and the advice of these two great neurologists. Both Charcot and Fisher exhibited a remarkable aptitude for clinical-anatomic observations and made pioneering neurologic discoveries into transient ischemic attack, amyotrophic lateral sclerosis, and many more. For their pupils and biographers, these men leave a rich record of their learning and clues to their approach. This essay addresses the following three questions: How did Charcot and Fisher observe patients and visualize difficult cases? How did they generate new hypotheses? How and where did they record their observations?

Jean-Martin Charcot (1825-1893) was the second eldest of four sons born to a Parisian carriage designer. He exhibited an early interest in painting and a love for animals. After secondary school, he was torn between an artistic or medical career, and he eventually opted for the latter. At age 17, he entered the Paris Medical School as a black-haired, thinly mustachioed introvert who enjoyed sketching scenes from the Quartier Latin in his free time. He graduated with the highest grade for his thesis on gout and rheumatoid arthritis. On New Years' Day of 1852, he entered the Salpêtrière Hospital, whose 4000 residents included the crippled, elderly, and mentally ill. He would remain at this repurposed gunpowder storehouse for the rest of his career. He gathered around him a formidable group of students, investigators, artists, photographers, and a curious public, as he set about to describe the phenomenology he encountered there.[1] (Photograph: Wikimedia Commons)

Charles Miller Fisher (1913-2012) was born the son of an insurance businessman in Waterloo, Ontario, Canada to a family of nine children. He received his M.D. degree in 1938 from the University of Toronto. Soon afterward, he left his newlywed high school sweetheart to volunteer in the Canadian Navy. In 1941, the day his wife was expecting their first child, a German raider sank his ship, the HMS *Voltaire*, in South Atlantic waters. He spent the next three and a half years as a prisoner of war in the German camp Stalag XB Sandbostel, and later in Westertimke. After his release, he undertook a refresher course at the Montreal Neurological Institute. There, Wilder Penfield noticed his inquiring mind, mentored him, and arranged a neuropathology fellowship for him with Raymond Adams at Boston City Hospital. This gave him the expertise he needed for when he returned to Montreal. In 1954, he rejoined Adams at Massachusetts General Hospital where he created the world's first stroke service. Throughout his career, he touched the lives of numerous patients and students by his thoroughness and humility.[2] (Photograph: Graduation photo, Charles Miller Fisher, 1938, by Jeremy Zung at the Medical Sciences Building, University of Toronto, October 13, 2015.)

Precise Visualization and Juxtaposition

To see without bias was paramount for both of these masters because they knew that preconceptions could frequently obscure interpretation. Detractors disputing Charcot's description of hysteroepilepsy once received a curt reply during his weekly phenomenology rounds known as the Leçons du Mardi (Tuesday lessons): "I am not in the habit of advancing things not demonstrated experimentally. You know that I hold as a principle to disregard theory and to set aside all preconceptions; if you want to see clearly, you must take things as they are."[3] During another lesson on amyotrophic lateral sclerosis, Charcot cautioned against a premature diagnosis of aphasia, stating "I am doing everything I can to get you used to looking at patients carefully and observing every possible detail. Sometimes even those [details] that might seem incon-

sequential turn out to be significant. Here we have a man who cannot speak but who can write, and so, unless he is a congenital deaf mute, and we can dismiss that possibility, we are dealing with a distinctly uncommon phenomenon."[4] Charcot was always wary of deeming any familiar appearing syndrome *ipso facto* to be the correct diagnosis.

Fisher echoed Charcot's caveat, noting that physicians "are liable to find what we expect rather than what exists" and "accurate visualization is the foundation of all new concepts."[5] Fisher believed that elicitation of a case's relevant details distinguished the expert from the novice. His discovery of pure motor or pure sensory strokes required his personal attention for what was typically misreported as mixed sensorimotor findings. Careful observations uncoloured by pre-existing assumptions are crucial for accurate recognition and diagnosis.

Ironically, however, Charcot's own preconceptions sometimes hardened him to a patient's report. He developed a patronizing attitude toward patients or students who dissented with his views. For example, he quickly ignored a patient's "lightning pains" when it did not fit with a classical description and he was quick to call a patient a liar in the case of family history. He even stated that family can "sometimes even try to be obstructive and lead you down a false path."[5] In contrast, Fisher routinely insisted that the "patient and his family are always right" and that "the patient is doing the best he can". As well, Fisher often cautioned others never to become angry with a patient or their family, and he himself demonstrated a remarkable courtesy and patience. In one instance, Fisher waited twenty-six minutes for a patient, whom he suspected was abulic from a ruptured anterior cerebral artery, to return his greeting of "good morning".[7]

Charcot was well aware that the practising clinician faces a thorny, undifferentiated jungle of disease which is far removed from the artificial clarity of a previously solved tutorial case or archetypical example. Thus Charcot's Leçons du Mardi, unlike his polished Friday lectures, demonstrated his raw thought process with all of the nuanced surprises and complexities that confronted a practising neurologist. Charcot recognized that visualization requires contrast. Accordingly, his Leçons du Mardi favoured side-by-side comparisons of similar patients. For example, he contrasted Sydenham's chorea with Huntington's chorea, and compared multiple cases of tremors including Parkinson's, multiple sclerosis, or mercury poisoning. Allan Starr, a visitor from America, commented that Charcot's lessons were "theatrical" and left a "series of mental pictures of patients and of lessons which no amount of private study could possibly produce" on the mind of the student. Charcot firmly expressed his opinion of the physician's most prized attribute:

> *Let someone say of a doctor that he really knows his physiology or anatomy, that he is dynamic – these are not real compliments; but if you say he is an observer, a man who knows how to see, this is perhaps the greatest compliment one can make.*[5]

Fisher, who typically rounded postprandially with his fellows from 5 pm to 11 pm, must also have had ample clinical examples for cross-comparison. His dictum for success was that "it is all a matter of being in the right place, at the right time, with the right mentor". But it was in the neuropathology laboratory where serendipitous juxtaposition would most aptly describe his work. An abundance of pathologic material and the dissection of 1100 pairs of carotid arteries showed an association between carotid disease and stroke. His keen pattern recognition skills allowed for the description of the eponymous Miller Fisher syndrome and the discovery of transient ischemic attacks, one-and-a-half syndrome, and lacunar syndromes.[9]

Interpretation and the Working Hypothesis

While both Charcot and Fisher were not involved in direct laboratory experimentation, their observational methodology involved the testing of continually evolving hypotheses.[10] Charcot stated that even the most stoic of minds linked facts into unifying theories, which was a technique he often used to argue his own cases.[11] Fisher also vigorously opposed the categorization of patients into any ill-fitting diagnostic "cubbyhole". He often asked his students, "does this patient's findings fit the usual rules for a lesion in this anatomical region?" and advised them to "examine thoroughly and if something doesn't fit, re-examine and read what others have written."[12] True to his word, Fisher tried to disprove his own theories by continually retesting his hypotheses, and he accepted traditional medical dogma only after personally reading or verifying his own data. This method of acquiring data also influenced the way he taught. Instead of lecturing passively, he invited his students actively to explore and reason through their cases.[13]

Fisher's active generation of hypotheses began with even a single unique observation. One afternoon, while his senior physician Dr David McDougall had not yet arrived to the pathology laboratory, Fisher noted the patency of the middle cerebral arteries (MCA) in several specimens with supposed MCA thrombosis. Observing the disseminated hemorrhagic infarcts in brain, kidney, and spleen without any visible arterial occlusions, Fisher inferred a theory in which cardiac emboli circulated and subsequently dissolved. This merely required an "abundance of pathological material and the examination of nine brains at one sitting".[6] On another occasion, careful histories were taken from stroke patients within the course of one week to reveal the passing mention of a transient monocular blindness contralateral to the hemiplegic side. Fisher avoided the possible pitfall of misinterpreting this symptom as a hemianopic phenomenon, and it was this careful detail that contributed to the discovery of the transient ischemic attack as a warning sign of stroke. In another happenchance discovery, Fisher was given multiple cases of angiographic string sign revealing a carotid dissection. He was able to correlate these cases pathologically in less than 48 hours.[6]

Interpretation of any phenomenon requires picking out the relevant foreground details while eliminating the noisy background. An admiring Henri Meige wrote of Charcot, "the ability to discern the essential elements in a landscape or a human form, to seize immediately the total picture and to isolate from it the essential elements, this was a skill that Charcot possessed to a remarkable degree."[9] Both Charcot and Fisher modelled for their students how to distill complex phenomena into a unifying theory.

The Medical Record

Recording by photograph or drawing captures details vividly and avoids tedious verbal description. Charcot categorized the thousands of patients he saw at the Salpêtrière through unified case folders which contained drawings, lengthy descriptions, photographs, and painted footprint gait records. These were paired with posthumous anatomic and microscopic drawings, journal clippings, and letters about similar cases.[14] Charcot turned to a large group of artists and photographers to supplement his work, instituting a photographic service at the Salpêtrière under Londe and Richer.[15] His appreciation of this new technology was evident from his description of his own career, where he indicated that he was "absolutely nothing but a photographer".[4] Charcot employed slide projectors, statues, photographs, patients, and pantomime to illustrate clinical syndromes for a global audience, using a medium which transcended linguistic barriers.[16] In the introduction to Charcot's *Nouvelle Iconographie de la Salpêtrière*, a journal centred around photographic or drawn images, the editors seem to boast:

> *When a patient demonstrates signs of particular interest – various atrophies, contractures, special postures or deformities – he is immediately drawn or photographed. With the aid of this immediate record, we are able to freeze the abnormality, to decompose the various abnormal movements one by one, and thereby capture the disorder with precision.*[5]

Likewise, Fisher advised that precision in recording was paramount. He taught his students that a reproducible visual description of a patient allowed for much greater reliability than nebulous encoding.[17] His extensive file folder collection demonstrated a catalogue of many curious presentations. Some intriguing titles included "abulia and the telephone", "burning feet of undetermined etiology in older people", "unusual [sic] difficult to identify muscular jerking during action in limbs following a stroke", and "post-operative hallucinations on eye closure". The advent of the computed tomography scan in the 1970s and magnetic resonance imaging in the 1980s provided Fisher with an analogous advance to study pathology *in vivo*. Though he applauded advances in medical imaging, he was always an advocate for simple and direct tissue visualization. Armed with a hand-held magnifying glass and an angiogram, he invited clinicians to examine and diagnose a congophilic amyloid angiopathy for themselves. One month before his death, while discussing a complex patient with ambiguous MRI findings, he concluded that "you have to have pathology".[8]

The World as Spectacle and Classroom

For Charcot and Fisher, people everywhere presented the opportunity to observe humankind and to study disease. Just as James Parkinson's early field observations informed his case reports in his *Essay on the Shaking Palsy*, Charcot noticed and sketched Parkinsonian patients even while on vacation.[19] While walking past the bell tower of the Santa Maria Formosa, a Venetian church, Charcot made the fortuitous recognition of a glossolabial hemifacial spasm engraved just above the door. This grotesque mascaron reminded him of cases presented just a few days earlier at the Salpêtrière and prompted his subsequent compilation of other depictions of disease in art in his book, *Les Difformes et les Malades dans l'art*. Charcot shared Leonardo da Vinci's view of science and art as united in their representation of reality.[20] A rare autobiographical glimpse into Charcot's personal life comes from a journal entry written while on summer holiday in Morocco in 1887. Even here he saw medical cases such as eczema, arthritis, failed circumcisions, a hysterical mute, and a "beautiful case of Parkinson's". Charcot's wish, even while on vacation, was to capture an "indelible visual impression" of the world around him.[21]

Fisher also loved to accrue knowledge wherever he went. Throughout his career, he collected information about people who piqued his interest. This included patients with unusual movements ipsilateral to a cerebral lesion, mumblers, a man strong enough to lift a small car, families with a history of impressive longevity, obese individuals who enjoyed excellent health, and people who succeeded at unusual occupations. Even those he deemed to be "normal" were subject to his intense scrutiny as controls.[14,18] Unlike Charcot, who rarely commented on his personal life, Fisher relied on self-report and introspection to record observations of his own migraines, postoperative delirium, and difficulty recalling people's names. As a captured prisoner of war, Fisher took the opportunity to learn German, read medical literature, learn about Strachan syndrome from his fellow malnourished prisoners, and treat those in need. As a practising clinician, Fisher frequented Boston libraries late into the night to gain insight from the past, noting that each generation cannot afford to rediscover the history of neurology. His diverse interests included hysteria and human free will.[23-25] Well after his retirement in 1983, Fisher continued his relentless search for answers to the "puzzling cases", and he continued to round regularly at the Massachusetts General Hospital. Toward the final years of his life, despite having his vision reduced to a small temporal field in the left eye, he continued to be an active reader, writer, and explorer.[26]

Legacy and Challenge

Jean-Martin Charcot and Charles Miller Fisher are a glowing inspiration for all practitioners of the physical examination. Their example challenges clinicians everywhere to observe their patients humbly while not letting past assumptions overshadow what is directly observed through a continuous process of comparison and contrast. Recording their data with vivid precision, they exhibited a boundless and contagious curiosity. Their tireless efforts to explain complex human behaviour led them both to postulate and continually refine new hypotheses, which are still valuable to this day. For Fisher, "neurology abounds in phenomena created by nature's experiments that invite the attention of neurologists interested in the neural activity that underlies or, more accurately, that is human experience." The success of keen observation allowed him, along with Charcot, to dream of the day when the foundations of complex and psychiatric disease such as hysteria would reveal their clinical and anatomical secrets. Until then, Charcot offers a stirring soliloquy on the importance of observing and listening to patients:

> *Locomotor ataxia after all is not new. It probably existed at the time of the Greek siege of Troy, and Hippocrates' tabes was likely locomotor ataxia. But it was recognized for the first time by a doctor who knew how to do only one thing – observe and describe what he saw. Such men are the real doctors, those who really contribute the most, those we call observers.*[5]

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