BC MEDICAL JOURNAL
60 YEARS OF PUBLISHING

BCMJ
BC Medical Journal

May 2018; 60:4
Pages 181–232

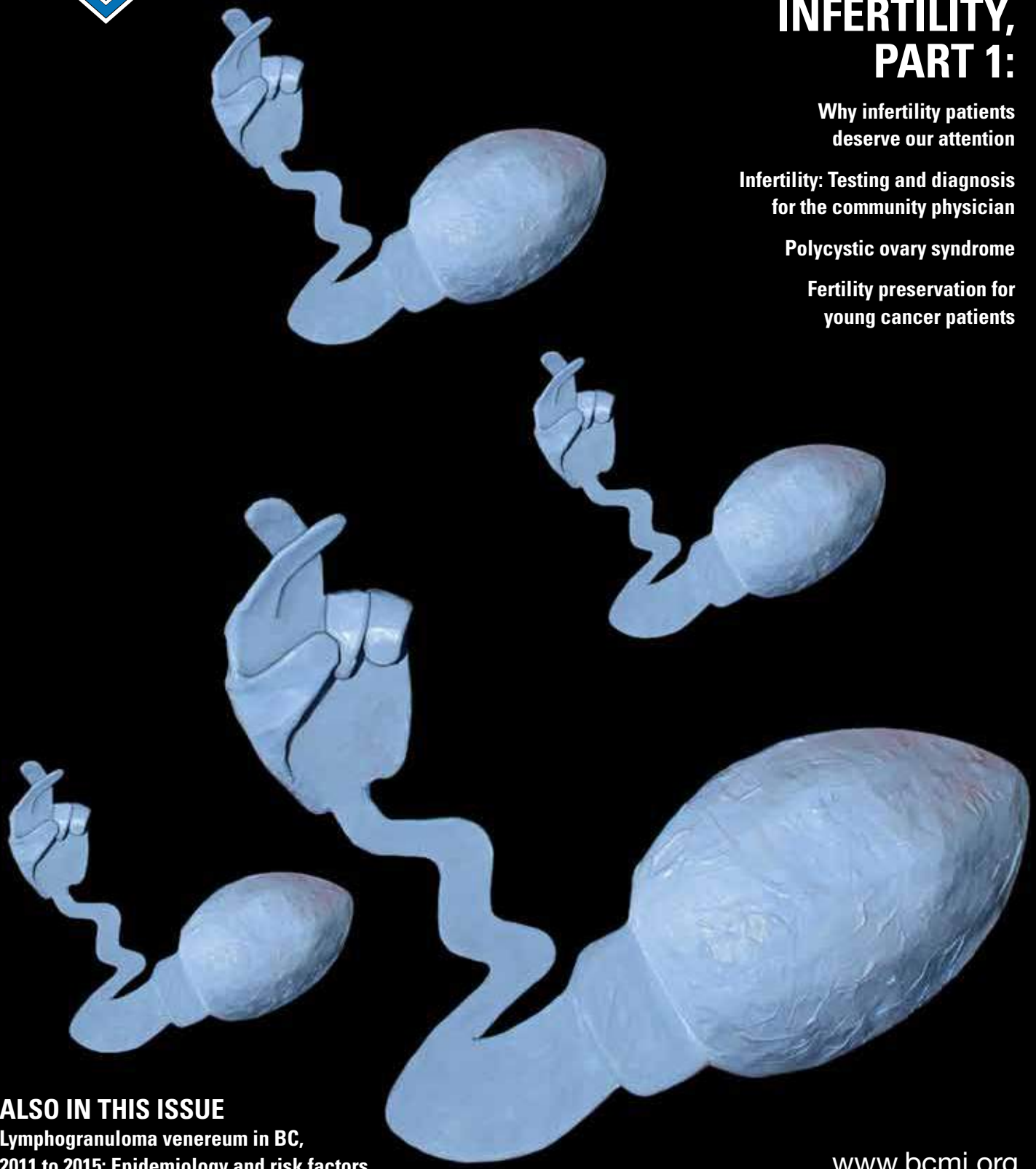
INFERTILITY, PART 1:

Why infertility patients deserve our attention

Infertility: Testing and diagnosis for the community physician

Polycystic ovary syndrome

Fertility preservation for young cancer patients



ALSO IN THIS ISSUE

Lymphogranuloma venereum in BC, 2011 to 2015: Epidemiology and risk factors

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ON THE COVER

Infertility is a condition commonly encountered by family physicians in the community. Timely diagnosis and treatement of infertility can help to mitigate the clinical and emotional consequences for the patient and her partner. Series begins on page 202.

The *BCMJ* is published by Doctors of BC. The journal provides peer-reviewed clinical and review articles written primarily by BC physicians, for BC physicians, along with debate on medicine and medical politics in editorials, letters, and essays; BC medical news; career and CME listings; physician profiles; and regular columns.

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Acronyms 2: The return

I'm overdue for a good rant. Synonyms for the word *rant* include *shout*, *wild*, *impassioned*, *fulminate, vociferate, diatribe, sound off, spout, pontificate, bluster, tirade, yell*, and *bellow*. Who wouldn't feel better after all of that is said and done?

At the *BCMJ* we review all sorts of submissions for publication. I remain in awe of authors who put themselves out there and take the time to craft a scientific paper, letter, or opinion piece. Risking rejection, the creative individuals writing scientific papers design and complete studies, analyze the data, organize it into a paper with a discussion and conclusion, and support it all with references. I appreciate the time, effort, and energy this process requires. However, there are certain things that drive us crazy at the *BCMJ* Editorial Board, and I hope that by ranting about one of them, change will follow.

I think I have night terrors about acronyms. For some reason many authors feel they must use acronyms wherever possible. I addressed this issue in a previous tongue-in-cheek editorial (www.bcmj.org/editorials/do-abbrs-bother-u) in the hope of eradicating this trend. Alas, little changed after my editorial's publication (cementing my conviction that readership of my editorials consists more of family members than *BCMJ* authors). I am asking, pleading, and begging on behalf of the Editorial Board for authors to cease and desist.

Numerous acronyms in a manuscript make it difficult to read and detract from its message. I'm not talking about commonly used acronyms we all understand like DM for diabetes mellitus or CAD for coronary artery disease. I am talking about the obscure ones that not even the most scholarly readers understand. On brief perusal of last month's manuscript submissions I found RB, ICC, LIC, CAS, APSF, ELC, DLC, DALY, YLL, YLD, DAD, ERAT, SBIRT, HDSA, and CMHA. Perhaps I'm not up to speed, but I don't think this list contains any generally accepted frequent flyers. It is much better to use the actual words than an acronym because surely the objective is to convey meaning, not save space in the *BCMJ* or avoid the nuisance of typing? Also, for the love of everything holy, please don't use an acronym for a two-word phrase such as FD for family doctor or ED for emergency department (most of us middle-aged men think ED stands for something else anyway). Finally, to prevent me from having a hypertensive stroke, don't create an acronym for a phrase if is only used once in a manuscript.

I have night terrors about acronyms.

I'm not trying to deter prospective authors, but I am striving to reduce the total number of Editorial Board member facial tics that develop each time another unnecessary acronym is used. Remember that at the *BCMJ* we really do appreciate and look forward to the submissions that we receive, so keep up the good work.

For my next rant perhaps I will focus on low response rate survey studies?

—DRR, FD, ED

Time's up, Doc

If you have ever ordered a pneumoencephalogram, administered an aminophylline drip, cross-eyed stereo-viewed a cerebral angiogram, or used Tensilon to convert paroxysmal atrial tachycardia, then you are likely retired or in the retirement-contemplative stage. So it is with me. After 40 years in medicine it's time to retire and also step down from my 10-year membership on the *BCMJ* Editorial Board, which of all the committees I've served on has been my favorite.

The membership of the Editorial Board is composed of a diverse group of talented physicians and staff who, while not always like-minded, have always been able to achieve consensus on which articles would be of value and interest to BC physicians. The fact that the *BCMJ* is celebrating its 60th anniversary is a testament to its continued popularity.

It is always interesting to reflect on one's past view of the future, versus today's reality. For instance, I never saw the coming of plastic water bottles, Starbucks coffee, yoga, or that being tattoo-positive did not equate with being MSP-negative. I've always believed that patient autonomy and self-determination would extend to the end of life, and am relieved that medical assistance in dying has finally been decriminalized. I never saw the value of medical marijuana, but never saw the harm in decriminalizing marijuana, even if I don't like the smell of a skunk. For many decades my dream was to have a fully functional integrated EMR complete with lab and diagnostic imaging results, patient scheduling, data tracking, and prescribing software. Many years and dollars later I came to sympathize with the builders of the Tower of Babel. I'm hopeful for the day that all physicians can truly say that their EMR has resulted in delivery of safer and more efficient care.

In all its marvels we must remember that technology is our servant, not our master. We serve our patients, not our computers. No technology will ever replace our care.

If I may also reflect on the future of medicine, I see it as promising, exciting, and somewhat daunting, particularly with regard to technological changes that will challenge most physicians' ability to remain current. Advances in laboratory medicine, genetics, diagnostic imaging, and informatics are staggering, but in all its marvels we must remember that technology is our servant, not our master. We serve our patients, not our computers. No technology will ever replace our care.

There are also political, economic, and societal pressures that will change the way we practise medicine. For instance, our role in being accountable to only our own patients is increasingly being challenged. We must be cognizant of the provincial government's frustration that despite huge financial expenditures there is a perception that collectively we sit on the sidelines while patients are unable to access timely medical care. In Quebec this has resulted in draconian incursions into physician autonomy by the introduction of Bill 130, which includes physicians having to guarantee availability of service. While in BC we may feel that we are doing enough by collaborating with government on initiatives such as the General Practice Services and Specialist Services committees, there are many poorly accessible services. We must vigorously promote and publicize our collaborative engagements, and barriers when they exist, "in matters relating to public health, health education, environmental protection, legislation, function, and improvement of health services."[1]

Just as I never envisioned retiring from medicine, someday, if you are lucky, that day will arrive for you. It might seem far away for some, but it's not. Plan for it just as diligently as you planned your career. Ask yourself, aside from medicine, what gives you the joy, excitement, and purpose that will fuel your retirement years.

I have been very privileged to have been part of this Editorial Board. Thank you.

—WRV

1. Canadian Medical Association. CMA code of ethics (2004): 42. Responsibilities to society. Accessed 19 March 2018. www.cma.ca/En/Pages/code-of-ethics.aspx.

It's not about the destination, it's about the journey. Or is it?

I like to travel. I like to drive and I like to fly. From the airplane I like to look down on snow-covered mountain peaks, deep valleys, mountain passes, and little winding roads. But travel isn't always reliable. Bad weather can be notorious for causing flights to be canceled or road conditions to be treacherous. For me, the worst that can happen in these situations is that I need to cancel a meeting or event, or I arrive late. But what if the journey is time-sensitive—a life or death situation? What if we we're talking about the challenge of moving a critically ill or injured patient from a location that can't provide definitive care to one that can? All of a sudden the terrain isn't a beautiful view from above, but rather a transportation challenge where travel delays aren't just inconvenient, they're possibly fatal.

Red transfers are classified as those involving life or limb-threatening conditions. In rural communities the issues and processes around red transfers have been identified as some of the biggest stressors that rural physicians face. Dealing with any serious illness or severe trauma is stressful for most physicians, but particularly so when you practise in a low-resource environment and such cases are infrequent. The basic approach is the same—assess, resuscitate, stabilize, and arrange for definitive care. But the last item on that list generally involves a journey by either ground or air ambulance to a tertiary care hospital, and this is where we run into trouble.

Identifying the preferred destination and convincing them to take your patient is only the first step, and often there is a major impediment. We all know our hospitals are constantly overcapacity. Most often this overcapacity isn't due to very sick patients, but rather those who can't go home and are awaiting other sorts of arrangements. Many health authorities have developed no-refusal policies for the extremely ill, and this is a crucial requirement if we are to develop a truly patient-centred health care system. But it still takes too long to find an accepting hospital, delaying transfers in a dangerous way.

The second problem is access to and availability of the proper mode of transport and the personnel to physically move the patient from point A to B. Our ambulance system works extremely hard with the resources it has, but there aren't enough planes in the right places, enough helicopters, or enough ground ambulances to move all the patients quickly and efficiently. We also don't have enough of the right paramedics and other transport personnel in the right places at the right times.

Issues and processes around red transfers have been identified as some of the biggest stressors that rural physicians face.

A review published by the Applied Policy Research Unit at UBC analyzed best practices and generated suggestions for an evidence-based reorganization of the system. The work was supported by the Rural and Remote Division of Family Practice and the Rural Coordinating Centre of BC, both of which are funded through Doctors of BC and the Ministry of Health. Several ongoing projects arose from this work, one with Northern Health and BC Emergency Health Services, and a Rural Patient Transfer and Transport Working Group that reports to the Ministry of Health Select Standing Committee on Population Health Services. The Community Paramedicine Program is another program designed to address some of these needs. So while much work is in progress, only time will tell if the commitment to changing and improving the system in BC produces visible results.

Trauma and extreme illness are unpredictable. Too much of our health care planning involves implementing resources and personnel to the bare minimum required. It is done because of cost constraints and because in our publicly funded system we have a responsibility to account for the spending of taxpayer money. But in health, ultimately, this is a false economy. Timely initial treatment is crucial for potential recovery. The slower our response and the more delays in treatment, the more it costs us in actual health care dollars and in human suffering downstream. When it comes to patient care, the journey needs to be seamless, skilled, and efficient, because the destination matters if we are to provide the *right* care at the *right* place at the *right* time for *all* citizens in British Columbia.

As this is my last *BCMJ* President's Comment, I want to say that the job of president has been an amazing journey. I want to thank you all for giving me the opportunity to travel with you this year. Together we can make these journeys for our patients better and work to transform the health care system in BC to one we can all be proud of.

—Trina Larsen Soles, MD
Doctors of BC President

letters to the editor

We welcome original letters of less than 300 words; they may be edited for clarity and length. Letters may be emailed to journal@doctorsofbc.ca, submitted online at bcmj.org/content/contribute, or sent through the post and must include your mailing address, telephone number, and e-mail address.

Re: Two-for-one private health care: A Canadian compromise

I would disagree with Dr Kotaska's opinion that charging double the cost for medically necessary treatment is a justified social policy. If medical care is a right and not a privilege, then imposing financial barriers of double the actual cost to subsidize a failing public system is mercenary. With competition and a market economy, costs approach value. Circumventing the Supreme Court's decision that prohibiting necessary care is unethical with a scheme to charge double the actual cost for medically necessary care is illegal because the Canada Health Act prohibits extra billing. Charging double is also unethical since it runs counter to the prime directive and first order of the Doctors of BC Code of Ethics (www.doctorsofbc.ca/code-ethics) to "Consider first the well-being of the patient." Any financial policy that delays treatment and prolongs suffering for an individual patient because they are unable to pay twice what the service is worth violates this edict. It's also very optimistic to imagine a 100% tax would generate a net payoff. It's like doubling down on a losing hand with stolen money.

—Mike Figurski, MD, CPHIMS
Big Whitear

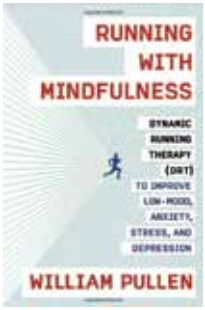
Re: Two-for-one private health care: A Canadian compromise. Author replies

Dr Figurski says that I suggest imposing financial barriers that would delay treatment and impose suffering on patients. I do nothing of the sort. I propose offering affluent patients expedited service for an additional fee that will be specifically applied to providing services for patients with lesser means. This is the fundamental basis of a progressive taxation system. The net result will be additional capacity and shorter waiting lists for procedures undersupplied by the public health care system. The approach is ethically sound and improves the well-being of all patients compared with the status quo. With competition, market forces will indeed come to bear. For the system, private facilities may increase efficiency. For patients, as the service in economy class gets faster, fewer will choose to fly first class.

Dr Figurski seemingly defends and derides the Canada Health Act, yet does not appear to understand the conflict with the Charter of Rights and Freedoms that engendered my suggestion in the first place. The Supreme Court has not doubled down on the Canada Health Act: it has declared it unconstitutional. Free health care is not enshrined in the Charter. As the growing myriad of current violations demonstrate, the Canada Health Act is on life support. Some would happily see it die; however, I believe that most Canadians would prefer a measured compromise to the Wild West of unregulated private health care.

—Andrew Kotaska, MD
Yellowknife, NWT

Book review: *Running with Mindfulness: Dynamic Running Therapy (DRT) to Improve Low-Mood, Anxiety, Stress, and Depression*



By William Pullen. New York: Penguin Life, 2017. ISBN-10: 0735219796. Paperback, 224 pages.

For as long as I can remember, running has been a part of my life. I chose to review this book, *Running with Mindfulness,* thinking it would improve my running—in particular, getting into "the zone" and being surprised when reaching my destination without recollection of pain, exhaustion, or the environment. However, that would be *mindless* running. Mindful running is just the opposite and focuses on the immediate present. In order to review this book I solicited the opinions of a few of my colleagues who are more conversant with mindfulness therapy.

The author is a psychotherapist who, based on his own life struggles, developed a program to improve low-mood, anxiety, stress, and depression. It is aimed at anyone who is feeling stuck and is interested in exploring self-awareness through exercise, either alone or preferably with a partner.

The first part of the book includes a useful review and description of mindfulness. The start of one's session (or run) begins with a four-stage grounding exercise. The reader is directed to focus on a question to explore during the physical activity: "moving with intention." Finally, the reader is to make notes.

Although this book is labeled *running* with mindfulness, I think it might better be labeled *exercising* with mindfulness. The techniques in the book can readily be applied to any exercise that leads to the achievement of "flow," a state of complete absorption in the activity.

The author encourages the reader to find a suitable partner willing to undertake the journey and to be a non-judgmental listener. This would not work for everyone, but could be useful for some.

After the first three chapters on the basics, the book is divided into chapters on anxiety, depression, anger, relationships, and decision making. Each chapter has several questions to explore while exercising, along with space to record one's thoughts and conclusions. The author encourages note-making as being therapeutic.

I particularly enjoyed the chapter on parents and kids. It gave me some conversation ideas to explore when running with my grandchildren.

I enjoyed this book, which reinforced what I already know about the benefits of running. It also gave me ideas to focus on during runs, rather than being mindless.

Given the beneficial effect of exercise on the mind, the incorporation of mindfulness therapy makes this an even better resource to recommend to patients who are struggling with anxiety, depression, and relationship issues, and it may eliminate the need for medication.

—WRV

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Facility Engagement in Interior Health

I have been actively involved with the Facility Engagement Initiative within Interior Health (IH) since it began. My involvement has been as both the IH Facility Engagement physician liaison and chair of the Kelowna General Hospital Facility Engagement working group. As of 2018, 20 facilities across IH have initiated more than 200 Facility Engagement activities. In short, the initiative at Interior Health is flourishing.

When I think about where we started only a few years ago, I'm very excited to see that our sites are brimming with enthusiasm, particularly since there are a wide variety of projects underway, and the physician engagement among the groups continue to be excellent and growing.

Facility Engagement (www.facilityengagement.ca) is a provincial initiative that originates from the 2014–19 Physician Master Agreement. It aims to strengthen relationships, communication, and collaboration between health authorities and facility-based physicians to improve the physician work environment and the delivery of patient care.

To me, one of the positive impacts of this project has been the interdivisional and interdepartmental opportunities to regularly collaborate, such as pediatrics meeting with emergency or radiology meeting with surgery; these cross-collaborations are new. Getting physicians together to discuss common issues is very positive step.

Interior Health has committed to supporting Facility Engagement, both with my liaison position and with Dr Harsh Hundal as an executive medical director who has this initiative as an important part of his portfolio.

Last December, physician representatives from each IH facility, health administrators and executives, and representatives from HEABC and the Specialist Services Committee (SSC) met for the Interior Health Facility Engagement Symposium. The event was an excellent opportunity for learning and dialogue, to exchange ideas, to build relationships, and for everyone to get a feel for the initiatives underway at other IH sites.

While all Facility Engagement projects are unique and vary in length, they share a common theme, which is to give physicians a meaningful voice to address issues that affect them. For example, the Lillooet hospital physician group has increased mental health care access for children and youth with mental health issues. Initiated by Dr Nancy Humber, the project has physicians working together with local and regional Interior Health representatives, along with schools, Indigenous counselors, and other community members. Two child and youth psychiatrists provide outreach clinics to Lillooet and surrounding area.

At Vernon Jubilee Hospital, Dr Jason Doyle expressed concerns about redundant laboratory testing. In collaboration with the Vernon Jubilee Hospital Physician Society, they examined laboratory utilization and developed recurrent laboratory testing guidelines for inpatients. As a result of the changes, we hope that patients will experience less anxiety and discomfort and avoid unnecessary tests, and that cost savings will be realized.

These are just some of the many impressive projects happening across the health authority and I am ecstatic that IH is using the Facility Engagement Initiative to improve areas in need .

—John Falconer MD, FRCPC
Interior Health Facility Engagement Physician Liaison
Chair, Kelowna General Hospital Facility Engagement Working Group

Recently deceased physicians

If a BC physician you knew well is recently deceased, consider submitting a piece for our "In Memoriam" section in the *BCMJ*. Include the deceased's dates of birth and death, full name and the name the deceased was best known by, key hospital and professional affiliations, relevant biographical data, and a high-resolution photo. Please limit your submission to a maximum of 500 words. Send the content and photo by e-mail to journal@doctorsofbc.ca.

BCMJ
BC Medical Journal

Daily ibuprofen may prevent Alzheimer disease

Studies carried out by Vancouver-based researchers led by Dr Patrick McGeer suggest that if started early enough, a daily regimen of the nonprescription NSAID ibuprofen could prevent the onset of Alzheimer disease (AD).

As of 2016, an estimated 564 000 Canadians live with dementia (expected to rise to 937 000 by 2031). The combined health care system and out-of-pocket costs of dementia is estimated at $10.4 billion—estimated to increase by 60% to $16.6 billion by 2031.

The laboratory of Drs Patrick and Edith McGeer is renowned for 30 years of work in neuroinflammation and neurodegenerative diseases, particularly AD. A paper detailing the McGeer's most recent discoveries ("Alzheimer's Disease Can Be Spared by Nonsteroidal Anti-Inflammatory Drugs") was published in the *Journal of Alzheimer's Disease*.

In 2016, Dr McGeer and his team announced that they had developed a simple saliva test that can diagnose AD, as well as predict its future onset. The test is based on measuring the concentration of the peptide amyloid beta protein 42 (Abeta42) secreted in saliva. In most individuals, the rate of Abeta42 production is almost exactly the same regardless of sex or age. However, if that rate of production is 2 to 3 times higher, those individuals are destined to develop AD. Abeta42 is a relatively insoluble material made everywhere in the body but deposits of it occur only in the brain, causing neuroinflammation, which destroys neurons in the brains of people with AD.

Dr McGeer's team demonstrated that the peptide is made in all organs of the body and is secreted in saliva from the submandibular gland. As a result, with one teaspoon of saliva it is possible to predict whether an individual is destined to develop AD. This allows the opportunity to begin taking early preventive measures such as consuming nonprescription nonsteroidal drugs such as ibuprofen.

Knowing that the prevalence of clinical Alzheimer disease commences at age 65, Dr McGeer recommends that people get tested 10 years prior, at age 55, when the onset of AD would typically begin. If they exhibit elevated Abeta42 levels then, that is the time to begin taking daily ibuprofen to ward off the disease.

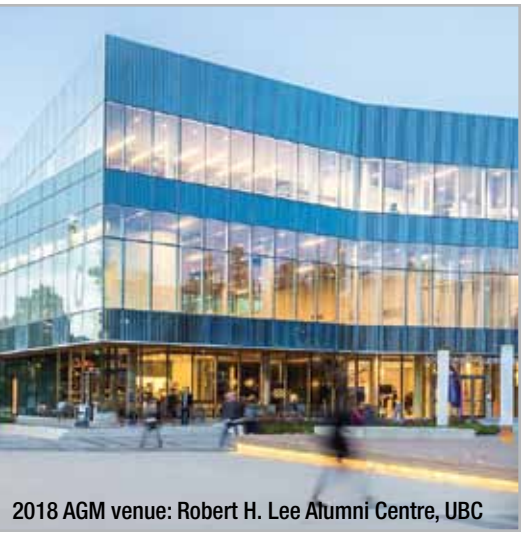
News continued on page 193

Doctors of BC 2018 annual general meeting

Doctors of BC members are invited to attend the 2018 annual general meeting (AGM) on 2 June 2018 at the Robert H. Lee Alumni Centre (UBC Campus, 6163 University Blvd., Vancouver). Onsite registration opens at 8:15 a.m. and the AGM will begin at 9:30 a.m. in Jack Poole Hall.

The evening events will be held at the Sheraton Vancouver Wall Centre, commencing at 5:15 p.m. with a reception, followed by the Doctors of BC annual awards ceremony at 6:00 p.m., including installation of officers. Register to attend the three-course President's Dinner, with an address given by the new president, Dr Eric Cadesky.

To register, or for more information, go to www.doctorsofbc.ca/news-events/event/2018-doctors-bc-annual-general-meeting.



2018 AGM venue: Robert H. Lee Alumni Centre, UBC

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The importance of expediency in writing the APS

An attending physician's statement (APS) is a common requirement for insurance underwriting. Insurers will order an APS as part of standard age and coverage amount requirements or to explore information received from an applicant's telephone interview or paramedical testing. The insurer's underwriting vendor will generally contact a physician's office to verify that the applicant is a patient, then send a request for file information. The vendor will follow up regularly by email, fax, or phone, as long as the APS remains outstanding. After several follow-ups, the insurer will contact the insurance advisor, and perhaps the applicant, to request their intervention with the physician. If an APS remains outstanding, the insurance application may be closed.

Underwriters can usually expect to wait a minimum of 2 to 3 weeks to receive an APS. Wait times can be influenced by factors such as a physician's patient volume or absence from the office.

A delay in receiving the APS can significantly lengthen insurance underwriting time. It is not uncommon for a motivated applicant to complete the underwriting requirements within 2 to 3 weeks and then spend an additional 6 weeks waiting for the physician to provide the APS. The underwriter must then review the APS and may need to request further information from the original physician or another source, adding another wait period to the process.

Longer underwriting can increase expense to the insurance applicant. For instance, if applicants are obtaining term life insurance to replace an existing policy that has renewed at higher rates, they must continue paying to maintain that coverage until they are approved for a less-expensive replacement policy. Even a month of delay may mean thousands of dollars in renewal premiums for insurance that could otherwise have been canceled sooner.

Further, a delay in underwriting may impact an applicant's ability to qualify for insurance. When signing for an approved individual insurance policy, the applicant must disclose any personal health changes since the date of the application. Even a seemingly benign event may cause the underwriter to postpone settlement of coverage and conduct a review. If the applicant has had a routine physical or visited her family doctor with flu symptoms, the underwriter will seek details on any recommended follow-up. Our administrators see multiple cases each year where a member applies for insurance, submits underwriting requirements and is approved for coverage, then advises during policy delivery that the applicant sought treatment for indigestion, chest pain, or a minor injury. Each additional week of underwriting is another week in which the applicant may slip on icy pavement or suffer a heart attack, and the consequences for an insurance application can range from further delay in settling coverage to withdrawal of the insurer's offer. If the member does obtain coverage, it may then be more expensive or have significant restrictions. In a worst-case scenario the member may be declined for coverage altogether and will remain uninsured. Efficient underwriting, with all requirements including the APS promptly supplied, reduces the member's risk of becoming uninsurable while waiting for insurance to be approved.

—Laura McLean
Client Services Administrator,
Doctors of BC

Potential effects of drugs on divers

Prescription, over-the-counter, herbal, homeopathic, and street drugs can have known and unknown side effects that can be drug or individual specific. For individuals who dive for recreation or for work, the unique nature of the hyperbaric environment can add complexity to the side effects experienced. Changes in ambient pressure, temperature, or gas levels can lead to changes in physiological mechanisms in the body at depth or on resurfacing. As well, the diver's gas mixture, which might differ from ambient air, could be a factor. You should be aware of these potential effects on your diver patients.

In a recent WorkSafeBC case, a commercial diver, who also works in a restaurant, injured his back. Through his rehabilitation process he noted to his general practitioner that he used high levels of marijuana daily for recreation and to control his pain. In addition, he was taking synthetic opioids and NSAIDs. His family physician declared him fit to return to work without considering the diving environment in declaring fitness. Because he was unfit for diving work, the worker's certificate of medical fitness to dive was revoked by WorkSafeBC until he could demonstrate that he was no longer using marijuana or opioids, and a dive physician assessed him. (A list of physicians with training and expertise in dive/hyperbaric medicine can be found on www.worksafebc.com.)

Several commonly used over-the-counter medications can impair a diver's ability to interact in their environment. For example:

- Antihistamines, particularly older-generation ones, can cause drowsiness and reduced secretions that could be compounded under water. Hydration is important to minimize effects of hyperbaric changes in oxygen saturation, bubble formation, and nitrogen narcosis.
- Decongestants can cause vasoconstriction leading to reduced blood flow, which can compound diving injuries. In addition, certain decongestants, including those that contain pseudoephedrine, can have a "rebound effect" resulting in reverse changes leading to problems on ascent. Others can have adrenaline-like effects that can have adverse effects on congestion.
- Anti-motion-sickness preparations can cause drowsiness.
- Analgesics and anti-inflammatories can alter hemodynamics.

Any medication that affects hydration, blood pressure, blood flow, or sedation should be avoided while diving. Consider the active half-life of any medication and, if necessary, explore alternatives. If certain medications are required to control a condition, the diver would have to forgo medical certification to dive until the medication is no longer required.

Many cardiac, neurological, and psychiatric drugs can have a variety of effects on the surface, which can be compounded at depth. Alcohol and street drugs are strictly prohibited in diving because they can impair judgment, cognition, and alertness.

Before supporting the use of any medication by a recreation or commercial diver, please consider the condition or illness the medication is being used for; side effects that may affect consciousness or decision making, or may impair physical or mental function; and the complex relationship between medications, drugs, the individual, and the individual's environment. Also, please test the medication on land and under controlled conditions to ensure that no undesired or potentially dangerous side effects occur. Counsel diver patients that using any form of recreational or street drug is contraindicated in diving.

For more information

If you are ever concerned about a medication or medical condition that may affect a patient working as a diver or an individual's ability to dive safely, please consult one of the dive physicians listed on www.worksafebc.com, a medical advisor in your nearest WorkSafeBC office, or Dr Steve Martin at Steve.Martin@worksafebc.com or 250 704-4226.

—Steve Martin, MD, CCFP, MScOH, FCBOM, DipSportMed

This article is the opinion of WorkSafeBC and has not been peer reviewed by the BCMJ *Editorial Board.*

Water, water everywhere but not a drop to drink!

The causes of clean-water insecurity for the Indigenous peoples of Canada.

Imagine living in a state of uncertainty about whether your drinking water is contaminated, whether this essential source is safe for you or your loved ones to use. This is the reality for many Indigenous communities across Canada.

Clean-water security consists of access to sufficient clean water and safe waste-water management. Access to clean and affordable water should be a basic right for every Canadian, regardless of heritage, skin hue, or address. Why is this access not possible for every Canadian? The effects of clean-water insecurity are myriad and well documented and include infections, mental and physical stress, diabetes, and dental caries.[1]

Canada is called a first-world country, but within Canada parity in living standards does not exist. Within this first world, many subpopulations of Indigenous peoples live in a fourth world.[1] This fourth world is defined as a place where subpopulations of a developed country live, in marginalized and substandard living conditions, similar to that of a developing country. Bradford and colleagues state that provincial water regulations, such as they are, do not apply to Indigenous communities, and that the complex interdepartmental regulatory structure hinders safe delivery of clean water, as well as forcing local communities to pay 20% of the costs for infrastructure, operations, and maintenance, including monitoring water safety and assuring availability of trained personnel.[2]

It is estimated that people living on reserve are 90 times more likely to lack running water than other Canadians.[3] Boyd notes that the "disparity between water quality on and off reserve in Canada has been criticized by the UN Committee on Economic and Social and Cultural Rights, the Royal Commission on Aboriginal Peoples and the Auditor General of Canada."[4] Boyd also comments that there are no national standards for drinking water in Canada; rather, there are guidelines for provinces to apply as they see fit.[4] Because of the Canada Labour Code, Health Canada has installed water treatment systems for their employees (sent to provide health care for local peoples) so that they can have access to safe drinking water in, ironically, Indigenous communities with poor water quality.[4]

The effects of clean-water insecurity are myriad and well documented and include infections, mental and physical stress, diabetes, and dental caries.

Poor infrastructure and poverty are seminal causes of clean-water insecurity. Many Indigenous communities are in remote and isolated locations. Sarkar, Hanrahan, and Hudson found that in remote Indigenous communities, people often rely on bottled water even though it is expensive and sporadically available, because the potable water dispensing units are often broken, the chlorine needed for processing the water has run out, and there are high operating costs with inconsistent funding from government.[1] What is also concerning is the frequent use of sugary drinks as a coping mechanism for the lack of clean usable water, even though sugary beverages lead to higher incidences of diabetes and dental caries in an already vulnerable population.[1]

As a first and fundamental step in improving water quality for our Indigenous fellow citizens, Bradford and colleagues suggest a database of health-outcome data linked to indicators of safe drinking water to house and the evaluation of the effects of water insecurity.[2] Indigenous peoples remain marginalized and suffer disproportionate adverse health outcomes. The health effects of clean water insecurity are another example of the marginalization of Canada's Indigenous peoples. It is time to ensure everyone in Canada has access to clean, safe drinking water.

—Charuka Maheswaran, MD

This article is the opinion of the Environmental Health Committee, a subcommittee of Doctors of BC's Council on Health Promotion, and is not necessarily the opinion of Doctors of BC. This article has not been peer reviewed by the BCMJ *Editorial Board.*

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Lymphogranuloma venereum in British Columbia, 2011 to 2015: Epidemiology and risk factors

A study comparing reports of lymphogranuloma venereum in two periods (2011 to 2014 and 2015) found that the characteristics of cases were similar, except for a decrease in patients self-identifying as Caucasian in 2015.

ABSTRACT

Background: **Lymphogranuloma venereum (LGV) is a sexually transmitted infection with potentially serious sequelae. We sought to describe the epidemiology of this infection in BC and explore reasons for the doubling of cases seen when data from 2015 were compared with data from 2011 to 2014.**

Methods: **All cases of LGV reported in BC from 2011 to 2015 were identified through surveillance and laboratory databases. The characteristics of cases, including patient risk factors, and the positivity rate for LGV test results in 2011 to 2014 and 2015 were assessed using descriptive statistics.**

Results: **From 2011 to 2015, 125 cases of LGV were reported in BC. The characteristics of cases reported in 2011 to 2014 and in 2015 were not significantly different, except for a decrease in cases involving patients self-identifying as Caucasian (62% in 2015 versus 76% in 2011 to 2014). There was a trend toward an increase in the proportion of cases with asymptomatic presentation (*P* = .20) and patients residing outside Vancouver Coastal Health (*P* = .06). The positivity rate for LGV test results in 2011 to 2014 was similar to that of 2015 (*P* = .78).**

Conclusions: **Lymphogranuloma venereum cases continue to increase in BC, likely in part because of increased awareness and testing. Primary care providers should consider this infection in the differential diagnosis and screen for LGV in high-risk subpopulations.**

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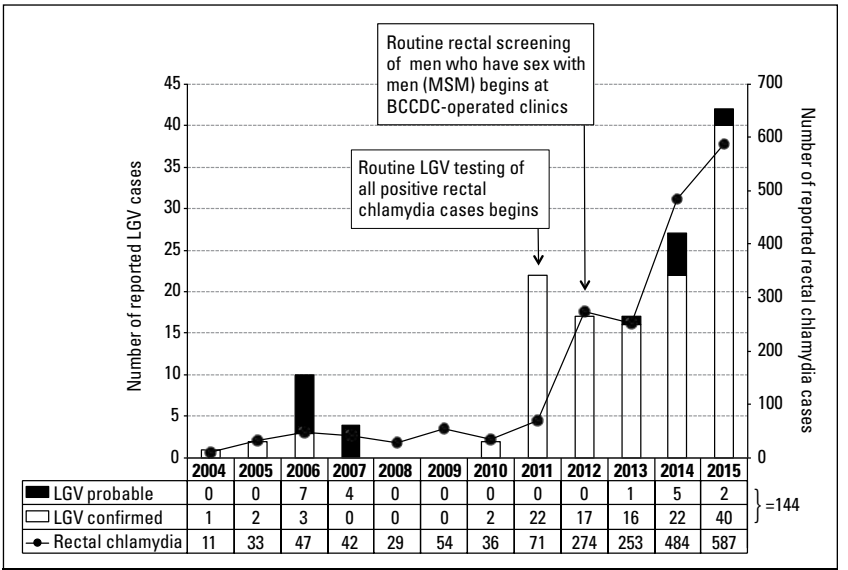
This article has been peer reviewed.

Background

Lymphogranuloma venereum (LGV) is a sexually transmitted infection (STI) caused by *Chlamydia trachomatis* serovars L1, L2, L2b, and L3. These serovars preferentially target lymph tissues, often leading to symptoms more severe than those presented by non-LGV chlamydia. Clinical presentation of LGV may include genital ulcers, inguinal lymphadenopathy, and hemorrhagic proctitis. Left untreated, LGV may lead to serious sequelae such as lymphatic obstruction, chronic ulcerations, abscesses, or colorectal strictures and fistulae.

LGV is endemic in many tropical and subtropical countries, but generally rare in Canada. Local transmission of LGV was first reported in Canada in 2003 and in BC in 2004. Over the past decade, LGV has become increasingly common in North America[1-3] and Europe[4-7] among gay, bisexual, and other men who have sex with men (MSM). These epidemics were caused almost exclusively by the L2b serovar.[8,9]

Since 2004, there have been 144 LGV cases (probable and confirmed) reported in BC (**Figure**). From 2004 to 2010, 2.7 LGV cases, on average, were reported each year. During this time, LGV serovar testing was performed only at the request of a clinician. Since July 2011, rectal specimens positive for chlamydia were routinely forwarded to the National Microbiology Laboratory (NML) for LGV serovar testing in an effort to increase detection of LGV. In addition, since 2012, clinics operated by the BC Centre for Disease Control (BCCDC), some of which serve MSM patients predominantly, have been routinely screening for chlamydia from pharyngeal and rectal sites when patients report behaviors that may put them at risk for infections at these sites. From 2011 to 2014, there were 83 cases of LGV reported (mean, 21 cases per year). However, in 2015, reports of LGV doubled to 42 cases.



	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
LGV probable	0	0	7	4	0	0	0	0	0	1	5	2
LGV confirmed	1	2	3	0	0	0	2	22	17	16	22	40
Rectal chlamydia	11	33	47	42	29	54	36	71	274	253	484	587

=144

Figure. Reported cases of lymphogranuloma venereum (LGV) and rectal chlamydia in British Columbia, 2004 to 2015.

Given the substantial increase in LGV cases reported, we sought to characterize LGV cases in BC since 2011 when the current LGV serovar testing process was implemented, and explore possible reasons for the increase in LGV observed.

Methods

A confirmed case of LGV is defined as one with a specimen testing positive by DNA sequencing for *C. trachomatis* serovars L1, L2, L2b, or L3. In Canada, all LGV serovar testing is performed by the NML.[10,11] A probable case of LGV is defined as one with a positive nucleic acid amplification test (NAAT) or culture for *C. trachomatis* and either proctitis, inguinal or femoral lymphadenopathy, a suspicious lesion, or reports of a sexual partner confirmed or likely to have LGV or with clinical symptoms consistent with LGV and reports of a sexual partner confirmed or likely to have LGV.

Case-finding and data collection

All genital chlamydia diagnoses, including LGV, are reportable under the BC Public Health Act and recorded in the provincial STI Information System (STI-IS). Since July 2011, rectal specimens that test positive for chlamydia in BC are routinely forwarded to the NML for LGV serovar testing via the BCCDC Public Health Laboratory (PHL), regardless of which laboratory performed the chlamydia testing.

All LGV cases diagnosed in BC are followed up by public health nurses located at the BCCDC. These nurses notify the patient and/or the testing clinician and collect demographic and behavioral information using an enhanced case report form and document findings in the STI-IS.

All confirmed and probable cases of LGV recorded in the STI-IS from 1 January 2011 to 31 December 2015 were included in the study. Laboratory data from the BCCDC PHL during this period were also reviewed for cases that may have been missed.

Data analysis

Descriptive statistics were used to summarize demographic, clinical, and behavioral characteristics of LGV cases in two reporting periods: 2011 to 2014 and 2015. Changes in characteristics of LGV cases were assessed using the chi-square test or Fisher exact test for categorical variables and the Wilcoxon rank sum test for continuous variables.

LGV positivity rate was calculated as the number of LGV cases (probable and confirmed) over the LGV test volume each year. LGV test volumes were defined as the number of specimens sent to NML for LGV testing in the BCCDC PHL database. Differences in positivity rates were assessed using a two-sided proportion *z* test.

Data were analyzed using R-Studio 3.2.1 (RStudio Inc, Boston MA). A P value of $< .05$ was considered statistically significant.

This study was undertaken to understand the provincial epidemiology of LGV, which falls under the BCCDC public health mandate. Thus, institutional ethics review was not required. Data for this study are under the stewardship of the BCCDC and BCCDC PHL.

Results

All 125 cases of LGV identified from 2011 to 2015 involved men who have sex with men. **Table 1** describes the characteristics of 83 LGV cases reported in 2011 to 2014 and 42 cases reported in 2015.

Characteristics and risk factors of LGV cases diagnosed in both periods were similar, with the exception of ethnicity. When comparing the two periods, 76% of patients (63 of 83) self-identified as Caucasian in 2011 to 2014, while only 62% of patients (26 of 42) self-identified as Caucasian in 2015 ($P = .004$). An increas-

Table 1. Characteristics of 83 lymphogranuloma venereum (LGV) cases reported in British Columbia in 2011 to 2014 and 42 cases reported in 2015.

Characteristics		2011–2014 n (%)	2015 n (%)	*P*-value
Laboratory results	LGV confirmed	77 (93)	40 (95)	.72
	LGV probable	6 (7)	2 (5)	
Gender	Male	83 (100)	42 (100)	
	Female	0 (0)	0 (0)	
Gender of sexual partners	Male only	78 (94)	40 (95)	1
	Male and female	5 (6)	2 (5)	
Age group (in years)	20–24	6 (7)	2 (5)	.42
	25–29	7 (8)	6 (14)	
	30–39	11 (13)	10 (24)	
	40–59	54 (65)	22 (52)	
	60+	5 (6)	2 (5)	
	Median age (interquartile range)	46 years (36–51)	44 years (31–48)	.18
Ethnicity (self-identified)	Caucasian	63 (76)	26 (62)	.004
	Aboriginal	6 (7)	0 (0)	
	Hispanic	2 (2)	8 (19)	
	Asian	8 (10)	3 (7)	
	Other (a)	3 (4)	4 (10)	
	Unknown	1 (1)	1 (2)	
Residence by health authority	Interior	0 (0)	3 (7)	.06
	Fraser	7 (8)	5 (12)	
	Vancouver Coastal	69 (83)	29 (69)	
	Vancouver Island	7 (8)	5 (12)	
Signs and symptoms (b)	Proctitis (c)	57 (69)	24 (57)	.2
	Asymptomatic (d)	7 (8)	8 (19)	
	Inguinal lymphadenopathy	10 (12)	6 (14)	
	Lesion	3 (4)	1 (2)	
	Other	1 (1)	0 (0)	
	Unknown	5 (6)	3 (7)	
HIV status	Positive	54 (65)	25 (60)	.61
	Negative	25 (30)	16 (38)	
	Unknown	4 (5)	1 (2)	
HIV viral load (e) in LGV cases co-infected with HIV	Undetectable (< 40 copies/mL)	34 (63)	18 (72)	.38
	Low (40–1000 copies/mL)	11 (20)	2 (8)	
	High (> 1000 copies/mL)	2 (4)	3 (12)	
	Unknown	7 (13)	2 (8)	
Co-infection (f)	Genital gonorrhea only	12 (14)	8 (19)	.74
	Infectious syphilis only	7 (8)	4 (10)	
	Genital gonorrhea and infectious syphilis	2 (2)	2 (5)	
	None	62 (75)	28 (67)	
Recreational drug use	By rectal route	Data not available	11 (26)	
	Not by rectal route		20 (48)	
	Unknown		11 (26)	

(a) Other ethnicity refers to Arab, Black, South Asian, and other/mixed ethnicity.
(b) Signs and symptoms categorized in accordance with the hierarchy: (1) inguinal lymphadenopathy, (2) lesion, (3) proctitis, and (4) other
(c) Proctitis includes the clinical diagnosis of proctitis and/or ≥ 1 of the following anal/rectal symptoms: mucous discharge, bleeding, frequent bowel movements, persistent diarrhea, constipation, bloody stools, burning or itchiness, pain, lesions, or discomfort.
(d) Phrase "asymptomatic" or "no symptoms" was documented in case chart.
(e) Viral load collection date was 3 months prior or after rectal specimen collection date for initial *Chlamydia trachomatis*.
(f) Co-infection defined as genital gonorrhea and/or infectious syphilis reported into the provincial STI Information System at time of LGV diagnosis or ± 7 days of LGV specimen collection date.

ing proportion of LGV cases involved asymptomatic patients and patients residing outside of Vancouver Coastal Health, although these increases were not statistically significant. Over one-third of cases involving recreational drug use in 2015 (11 of 31 cases) reported administration by rectal route. Data for this were not collected previously, however, so a comparison with past years was not possible.

The positivity rate for LGV was highest at 51.2% in 2011, the same year routine LGV testing of positive rectal chlamydia samples was implemented, then fell to 6.4% in 2012 to 2014 (**Table 2**). Overall, the positivity rate for LGV in 2011 to 2014 was similar to that of 2015 ($P = .78$), and the difference between rates for 2012 to 2014 and 2015 was not statistically significant ($P = .27$).

Conclusions

In 2015, the number of LGV cases reported in BC reached an all-time high of 42. The *C. trachomatis* serovar identified in all LGV cases was L2b, consistent with LGV cases reported for MSM in other jurisdictions.[1,2,4-7] Characteristics and risk factors for LGV cases reported in 2011 to 2014 were similar when compared to those of cases reported in 2015, with the exception of ethnicity. The proportion of cases reporting an ethnic identity other than Caucasian was higher in 2015 than in 2011 to 2014. This pattern mirrors the epidemiology data of both infectious syphilis[12] and HIV[13] in BC, which may be the result of increased testing in non-Caucasian populations, a greater proportion of ethnic minorities engaging in higher-risk sexual behaviors,[14,15] or tightly interconnected sexual networks of same-ethnicity partners among non-Caucasians.[16]

The positivity rate for LGV was highest in 2011 when routine LGV testing of rectal chlamydia samples was implemented, but fell in 2012 when routine screening for rectal STIs commenced. Since 2012, the increase in LGV diagnoses has generally followed the increase in LGV testing, suggesting that increased screening for rectal STIs may be the reason for the greater number of cases reported. This is consistent with a lack of change in the characteristics of LGV cases in recent years, and an increase in the proportion of asymptomatic cases.

The increase in LGV cases among MSM mirrors increases in other STIs in BC. While the reason for these increases is not definitively known, increased awareness and regular screening may be increasing detection of STIs. Changes in sexual practices in response to reduced anxiety about HIV transmission and acquisition with the availability of highly effective antiretroviral therapy (i.e., HIV treatment optimism) may also be increasing STI transmission.[17,18]

A substantial proportion of cases in 2015 involved rectal use of recreational drugs. Other jurisdictions have reported similar findings.[19,20] This practice may have a synergistic effect on STI transmission, with the presence of drugs in the rectum causing trauma to the rectal mucosae or condom breakage that can lead to an increased risk of transmitting or acquiring LGV. Sexual practices such as anal enema use, anoreceptive sharing of sex toys, and being fisted may also cause damage to the rectal mucosae.[21,22]

Almost two-thirds of patients in LGV cases were co-infected with HIV. This may be due to higher screening rates for LGV (and other STIs), but given the fact that most LGV infections are symptomatic, it is more likely that people living with HIV have a higher risk of acquiring LGV. HIV infection has been shown to affect the innate immune response.[23] Also, the practice of serosorting (choosing sexual partners with the same HIV status) may lead to reduced condom use,[24] thus increasing the transmission of other STIs.[25] While there is concern that LGV may increase the transmission of HIV, the vast majority of LGV patients co-infected with HIV in our study population had undetectable viral loads, likely making the risk of HIV transmission low. Nevertheless, the presence of mucosal inflammation from concomitant STIs such as LGV may alter the risk of HIV transmission, even with virologic suppression.[26] Further study is needed to understand LGV trends among HIV-positive MSM, who are disproportionately affected by LGV.

Table 2. Positivity rate for lymphogranuloma venereum (LVG) tests requested in British Columbia in 2011 to 2014 and in 2015.

Year	LGV tests requested	LGV cases identified	Positivity rate
2011–2014 totals	994	83	8.4%
2011	43	22	51.2%
2012	257	17	6.4%
2013	217	17	7.8%
2014	477	27	5.7%
2015 totals	529	42	7.9%

In 2015, the number of LGV cases reported in BC reached an all-time high of 42.

Study limitations

Although our findings are consistent with those reported in other LGV studies, they are subject to limitations. One limitation is that only individuals diagnosed with LGV were included in the study, which may mean that populations more likely to be screened (e.g., MSM who are "out" to their health care providers or people living with HIV) are overrepresented in the LGV case counts. Another limitation is that only rectal chlamydia specimens were routinely sent for LGV serovar testing, which may mean that LGV infections from other body sites have been missed. Lastly, the risk factor information collected was subject to recall or social desirability bias and may be inaccurate.

Summary

As in other jurisdictions, reports of LGV have been increasing in BC over the past decade. In 2015 there were 42 cases reported, twice the mean number of cases in the previous 4 years. However, the characteristics of LGV cases have generally been consistent from 2011 to 2015. The positivity rate has also been stable during this period, suggesting that the increase observed in 2015 is likely due to increased awareness and case-finding.

While the majority of cases are symptomatic, the proportion of asymptomatic cases has increased recently. Primary care providers should offer routine STI screening for sexually active patients and consider LGV in the differential diagnosis for patients in a high-risk group, such as MSM living with HIV. More study of recreational drug use, particularly around the time of sex or to enhance sex, is warranted to better understand the potentially synergistic effect of this practice on STI transmission.

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Competing interests

None declared.

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Primary care providers should offer routine STI screening for sexually active patients and consider LGV in the differential diagnosis for patients in a high-risk group, such as MSM living with HIV.

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Dr Caitlin Dunne

Infertility, Part 1: Why infertility patients deserve our attention

As a physician, I believe that prospective mothers are some of the most rewarding patients I see. There is rarely another time in a patient's life when she is so motivated to achieve a health care goal. This is even more the case with infertility patients. Often by the time a woman reaches my office she has done hours of research, taken supplements, consulted her primary care doctor many times, and perhaps even spent thousands of dollars on alternative medicine. During the years of trying for a baby, couples endure an emotional rollercoaster of monthly optimism at ovulation followed by the crash that comes with menses confirming that "it didn't work." Because of the stigma attached to infertility, many patients do not share their struggles with friends and family. The Internet offers forums, blogs, and chat groups that can be both helpful and harmful. Unscrupulous websites prey on women at this vulnerable time, offering fertility treatments not founded on scientific evidence or even physiological plausibility. As doctors we know we cannot change the fact that infertility exists. What we can change is the sense that our patients with infertility are alone. Part of helping our patients means simply starting the conversation.

The other day, waiting in the operating room lounge, I overheard two male surgeons talking about prostate specific antigen testing. One said, "Yeah, I am a little young to worry about PSA I guess, but I had mine checked last year. You know, might as well." The other responded, "Sure. Makes sense. Mine was high a few years back so . . . had to deal with that." It was a normal, casual conversation, and it struck me that we should strive to make conversations about infertility as commonplace. For example, as doctors we (and our spouses) are particularly susceptible to infertility simply because we take so many years to complete our education before we start a family. What if we talked about our anti-Müllerian hormone results the same way my fellow surgeons casually discussed PSA? Seems simple, but it would require a brave candidness to admit that women, doctors, and even *women doctors* are concerned about their future fertility.

I have had the privilege of treating medical colleagues for infertility. Most of them do not tell each other they have gone through treatment. My hope is that we, as physicians, can lead the way in adjusting how we think about infertility—that we can strip away the stigma so that the single, female surgical resident freezing her eggs does not feel she has to conceal the fact that she is thinking about one day, maybe, being a parent.

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This article has been peer reviewed.

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Infertility: Testing and diagnosis for the community physician

The workup for couples who fail to conceive should include confirmation that ovulation is occurring, measurement of hormone levels, hysterosalpingography, and semen analysis.

ABSTRACT: Infertility is a condition commonly encountered by family physicians in the community. Timely diagnosis and treatment of infertility can help to mitigate the clinical and emotional consequences for the patient and her partner. Investigations for infertility should be initiated after a year of trying without pregnancy, although a community physician would be advised to order testing before a year of trying in four common clinical situations: female age over 35 years, presence of oligomenorrhea, presence of risk factors for tubal disease, and suspicion of male factor infertility. Standard investigations include ovulation testing such as cycle tracking, use of ovulation predictor kits, basal body temperature charting, and serum progesterone measurement. Ovarian reserve testing should be undertaken to assess the monthly cohort of hormone-responsive (pre-antral and antral) follicles. The most common endocrine ovarian test involves measuring follicle-stimulating hormone levels on day 3 of the menstrual cycle. Additional ovarian reserve tests such as anti-Müllerian hormone assay and/or antral follicle count (done by ultrasound in a fertility clinic) can improve sensitivity, specificity, and convenience. Uterine-tubal evaluation may be undertaken with hysterosalpingography while hysteroscopy or sonohysterography can be used to further investigate the endometrial cavity as needed. Semen analysis is a fundamental part of the workup because the male factor accounts for approximately 35% of infertility. Infertility investigations should start after 6 months of trying for women over 35 years, and for women over 40 years investigations should be initiated immediately. Consultation with a gynecologist or fertility specialist is covered by provincial health insurance and should be considered for couples with abnormal test results and for couples who fail to conceive despite normal test results.

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Infertility is defined as the failure to achieve a pregnancy after 12 months of unprotected intercourse. It is a prevalent condition that affects about 15% of couples[1] and is commonly encountered by family physicians in the community. The majority of couples conceive within the first 3 months of trying, after which time the chances of pregnancy decline substantially.[1] After 1 year, 85% of couples will have achieved a pregnancy, while after another year only an additional 5% to 8% of couples will become pregnant.[2]

Peak fecundability occurs during the fertile window, which encompasses the 6 days up to and including the day of ovulation.[1] In a study of 221 couples, similar pregnancy rates were achieved with daily intercourse (37%) and intercourse every other day (33%).[1] When frequency of sexual

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intercourse was reduced to weekly, the pregnancy rate fell to 15%.[3] Pregnancies were recorded with sperm as old as 3 days, although the highest chances of conception were seen with intercourse 2 days before ovulation and on the day of ovulation itself.[1,3] Sperm has been found to survive for up to 7 days in the cervical mucus and to retain the ability to fertilize a human egg in vitro after 5 days.[4,5] Following ovulation, an egg may be ready for fertilization within 20 minutes and remains usable for 12 to 24 hours.[6] In the fertility clinic, we often tell patients that "The sperm should be waiting for the egg." A period of abstinence longer than 5 to 10 days can have detrimental effects on sperm motility and concentration.[7] Conversely, normal sperm counts can be maintained even with daily ejaculation.[7] Patients can therefore be advised that intercourse every day or every other day during the late follicular phase will optimize their chances of conceiving. Coital position does not affect the chances of conceiving and women can be safely reassured that they do not need to remain supine for any length of time after intercourse.[8] Sperm have been found within the cervical canal within seconds and in the fallopian tube within minutes of ejaculation.[8] Thereafter, the cervix may serve as a reservoir for sperm and fertilization will remain possible in the following days.

Detecting ovulation

The surest sign of ovulation is a regular menstrual cycle of 21 to 35 days. However, many women choose adjunctive methods to help them detect ovulation in order to better predict the most fertile time of each month. Numerous devices and products are available for detecting ovulation. However, if a patient finds the process stressful she should be reassured that ovulation tracking is not a requirement for conceiving and be directed to simply have regular intercourse around mid-cycle.

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Cycle tracking

Cycle tracking, otherwise known as the calendar method, is one of the oldest ways to determine when ovulation is likely to occur. A review of the normal physiology of the corpus luteum (CL) permits a better understanding of this method.

The granulosa cells of a dominant follicle—the cells responsible for making estradiol in response to follicle-stimulating hormone (FSH) in the follicular phase—undergo several important changes around the time of ovulation. First, they acquire luteinizing hormone (LH) receptors in the late follicular phase to enable them to respond to the mid-cycle LH surge and ovulate. Second, they become vascularized and therefore capable of transforming cholesterol into the principal steroid of the corpus luteum: progesterone.[6] Peak production of progesterone is achieved approximately 8 days after ovulation; at this moment the CL is one of the most vascular areas of the body.[6] The luteal phase usually lasts 14 days from the time of the LH surge. Therefore, unless the CL receives ongoing stimulation in the form of beta-human chorionic gonadotropin from a pregnancy, progesterone production ceases and menses ensues. The calendar method assumes that if you count backwards 14 days from the first day of menses you can estimate the date of ovulation in retrospect and use this information to predict future cycles. Some smart phone apps allow a woman to record her menses and then use this information to predict her fertile window using a personalized monthly average cycle length.

Use of ovulation predictor kits

Ovulation predictor kits (OPKs) available from pharmacies and online can be used to detect a high amount of luteinizing hormone in a urine sample. Follicle rupture occurs 34 to 36 hours after the onset of the LH surge at mid-cycle and LH is generally detectable in the urine for most of this time.[9] Patients are advised to test morning urine, which is the most concentrated. The LH surge is responsible for maturation of the oocyte through resumption of meiosis (from prophase I to metaphase II) and for release of the oocyte from the dominant follicle.[6] Digital ovulation kits purport to have increased accuracy by adding daily detection of a urinary metabolite of estrogen, estrone-3-glucuronide (E3G). Some brands use a smiley face to indicate when E3G levels are high (correlating with a growing dominant follicle) to identify the fertile window leading up to the LH surge and ovulation.

Basal body temperature charting

Basal body temperature (BBT) charting requires that a woman measure her temperature orally each morning before rising and before eating or exercising. The thermometer should be capable of detecting 0.1 °C increments. Daily temperature can be charted on a preprinted graph (many are available online) or using a smart phone app. A biphasic monthly temperature pattern indicates ovulation. Typically, a rise in body temperature of 0.5 °C can be seen after ovulation owing to the production of progesterone. Although this rise in BBT means a woman's most fertile days have passed, she can use this information to predict ovulation in future cycles. Around the time of ovulation a woman may also observe egg white cervical mucus that thickens and turns yellow after progesterone is produced. In mid-cycle some women experience mittelschmerz, one-sided lower abdominal pain associated with ovulation.

Serum progesterone measurement

In the mid-luteal phase (day 21 to 23 of a typical cycle) a serum progesterone level greater than 10 nmol/L is evidence of ovulation. Because progesterone is released in response to pulsatile stimulation by LH, which in turn is influenced by progesterone exposure at the level of the hypothalamus, values can fluctuate throughout the luteal phase.[6,10] Patients are thus encouraged not to dwell on the absolute value of a progesterone measurement as long as it is above 10 nmol/L.

Investigations for infertility

In addition to confirming ovulation, the basic workup for infertility includes ovarian reserve testing with a follicle-stimulating hormone test, uterine-tubal evaluation with hysterosalpingography, and semen analysis (**Box**).

It is generally recommended that investigations for infertility be initiated after a year of trying without a pregnancy. There are, however, four common clinical situations where a community physician would be advised to order testing before a year of trying: female age over 35 years, presence of oligomenorrhea, presence of risk factors for tubal disease, and suspicion of male factor infertility.

Advancing female age is becoming an increasingly prevalent cause of infertility. British Columbia has the highest age of first birth in Canada at 30.5 years versus 30.3 years in Ontario.[11] Over the past 3 decades the industrialized world has seen a dramatic increase in the age of first birth.[12,13] According to Statistics Canada, 2010 marked the first time in our history that more women in their 30s were having children than women in their 20s.[14] In 2011, there were 52.3 babies born per 1000 women age 35 to 39, compared to 45.7 per 1000 women age 20 to 24.[15] In BC, the percentage of live births to women age 35 years and older rose from 11% in 1990 to 23% in 2011, while the percentage of live births to women age 20 to 34 fell from 83% to 74% over the same period.[16] By far the most common reason women reported for not pursuing childbearing earlier was lack of a partner.[13]

The consequences of delaying childbearing are increasing rates of infertility, embryo aneuploidy, and miscarriage. These are largely attributed to aging oocytes with failing meiotic spindles and other ooplasm deficiencies such as mitochondrial dysfunction. Oocyte aging and the resulting chromosomal errors explains why miscarriage rates in natural pregnancies for women younger than age 30 are only 7% to 15% and become marginally higher for women age 30 to 34 at 8% to 21%. By age 35 to 39 the rate is 17% to 28%, and over age 40 the rate is 34% to 52%.[6] According to a computer simulation model, 32 is the maximum age at which couples should start trying to conceive in order to have a 90% chance of having a one-child family; for a two-child family the maximum age is 27; and for a three-child family the maximum age is 23.[17] For women age 35 to 40, fertility investigations are indicated after 6 months of trying and for women over 40 years they should be initiated immediately.[1]

Box. Workup for infertility

When to investigate by female age:
- After 1 year for patients < 35 years.
- After 6 months for patients 35–40 years.
- Immediately for patients > 40 years.

Clinical factors warranting earlier investigation:
- Female age > 35 years.
- Oligomenorrhea.
- Tubal risk factors.
- Male infertility risk factors.

Most common causes of infertility:
- Male factor.
- Ovulatory dysfunction.
- Tubal/pelvic disease.
- Advanced female age.

Standard investigations:
- Ovulation confirmation (serum progesterone > 10 nmol/L).
- Cycle day 3 follicle-stimulating hormone (< 7–10 IU/L) + estradiol (< 200 pmol/L).
- Hysterosalpingography.
- Semen analysis.

Additional ovarian reserve testing with anti-Müllerian hormone (AMH) assay:
- AMH reported in pmol/L in Canada and ng/mL in the US.
- Testing can be done on any day of the cycle.
- Patients must pay privately ($70).

Oligomenorrhea warrants early investigation for infertility because it is almost always the result of anovulation. If a woman's intermenstrual interval is greater than 35 to 40 days, she may be ovulating infrequently, unpredictably, or not at all. The most common causes of oligomenorrhea are polycystic ovary syndrome, perimenopause, endocrine disturbances such as thyroid disease, and endometrial pathology such as polyps, fibroids, or hyperplasia.

Ovarian reserve testing

Ovarian reserve testing aims to estimate the number of oocytes a woman has remaining. It is more accurately termed functional ovarian reserve testing because we cannot actually count the number of nongrowing primordial follicles in vivo.[18] Therefore, contemporary ovarian reserve tests assess the monthly cohort of hormone-responsive (pre-antral and antral) follicles to obtain a more accurate reflection of the true ovarian reserve.[19,20]

Female age is still one of the best predictors of oocyte quality and quantity. A female attains her lifetime maximum of oocytes (6 to 7 million) at around 20 weeks gestational age in utero.[6] By the time she is born that number has already dropped to 1 million and by the time she reaches puberty it is less than half that.[18] Oocyte number declines throughout life, dropping more rapidly after age 35 until the menopause threshold, when approximately 1000 oocytes remain.[18]

Follicle-stimulating hormone measured on day 3 of the menstrual cycle is the most common endocrine ovarian test. FSH is a gonadotropin produced by the anterior pituitary and it acts on granulosa cells in women to stimulate folliculogenesis and estrogen production.[6] Elevations in FSH were first described as a marker of ovarian aging over 40 years ago.[21] As follicular growth progresses in the early menstrual cycle, production of estradiol and inhibin B results in a negative feedback loop with the pituitary, and FSH secretion declines.[6] For this reason, it is customary to avoid falsely reassuring results when measuring day 3 FSH by checking that the estradiol level is low (less than 200 pmol/L, approximately) and FSH is not being suppressed. At menopause, when the follicular pool is depleted, FSH is no longer suppressed by estradiol and inhibin B and therefore remains indefinitely elevated. When FSH is high (above 20 IU/L) it is a reliable indicator of severely diminished ovarian reserve or perimenopause. A day 3 FSH level in the normal range (less than 10 to 15 IU/L) is not specific. While some researchers have reported on FSH thresholds, there is no level of FSH that can be considered definitively reassuring for confirming fertility potential. In a study of 3519 subfertile women, FSH levels above 8 IU/L were associated with a reduced probability of spontaneous pregnancy in the next 12 months (HR 0.93 per IU/L).[22] In cycles of in vitro fertilization (IVF), the live birth rate was maximal when the FSH level was less than 7 IU/L at all ages, and the live birth rate was below 2% when the FSH level was above 18 IU/L.[23] Measuring FSH can be inconvenient for patients since levels must be obtained on cycle days 2 to 4 and are prone to intercycle fluctuations. For this reason, offering additional ovarian reserve tests such as anti-Müllerian hormone (AMH) assay or antral follicle count (done by ultrasound in a fertility clinic) can improve sensitivity, specificity, and convenience.

Anti-Müllerian hormone has been called the "holy grail" of ovarian reserve testing.[24] The hormone was initially described in the 1940s regarding its role in sexual differentiation of the male embryo.[25] Specifically, AMH production by testis Sertoli cells in the late first trimester was shown to result in regression of the Müllerian ducts, while persistence of the Wolffian ducts was shown to result in formation of the internal male structures (epididymis, seminal vesicles, and vas deferens).[6] In 2002 it was discovered that AMH is closely correlated with the number of oocytes retrieved during an IVF cycle.[26] This led to a huge resurgence of interest in the hormone for assessing women's reproductive physiology. Although AMH is a functional ovarian reserve test, it represents a very accurate assessment of a woman's remaining egg number.[20]

A blood sample is required for an AMH assay, and in BC this test is not covered by provincial health insurance. The cost per assay is typically $70, which is paid to the collecting outpatient laboratory. AMH can be measured on any day of the menstrual cycle because it is only produced by the pre-antral and antral follicles, not the dominant follicle.[27] Some cycle-to-cycle variability of AMH does occur, but it is not significant enough to warrant repeated measurement.[28] One study found that AMH was 19% lower in users of the oral contraceptive pill compared with nonusers.[29] Other patient characteristics and lifestyle factors associated with lower AMH levels include pregnancy, African-American and Hispanic ethnicity, and obesity.[30-32] Interestingly, smoking has been consistently associated with earlier menopause but not with lower AMH values.[33,34] Research studies have incorporated AMH to improve menopause forecasting but the wide confidence intervals and marked variation between women make it difficult to use clinically.[35] The principal

utility of AMH is in assessing ovarian reserve and predicting a woman's response to controlled ovarian stimulation for an IVF cycle. AMH measurement has also been used to record ovarian reserve before and after treatments known to damage the ovary, such as chemotherapy, radiation, and ovarian surgery.

The normal values of AMH are highly age-specific and require careful interpretation. It is also important to note that Canadian labs report AMH in pmol/L, which can be multiplied by 0.14 for conversion to the American units of ng/mL. Although there is no universal definition of high AMH, a level above 21.0 pmol/L (3.0 ng/mL) is considered by many as a risk factor for hyper-response to IVF stimulation.[36] There is no upper level of AMH that is diagnostic of polycystic ovary syndrome. AMH levels below 8.0 pmol/L (0.7 to 1.1 ng/mL) are considered low and can be a marker for poor egg yield during the IVF process.[36]

Uterine-tubal evaluation

Estimates suggest that tubal and pelvic disease cause 35% of infertility.[6] In BC the most readily available test for tubal patency is hysterosalpingography (HSG), which involves transcervical instillation of radiopaque fluid and use of fluoroscopy to visualize the internal contour of the uterus and the spill of fluid through the fallopian tubes into the pelvis. HSG is generally scheduled in the follicular phase to avoid interfering with a pregnancy. Many facilities require the patient to phone for an appointment when a menstrual period begins and to perform a pregnancy test the day before HSG. For women who do not have a regular menstrual cycle, exogenous progestin can be used to induce a withdrawal bleed (e.g., 10 mg medroxyprogesterone acetate PO for 10 days). If the patient has risk factors for postprocedure infection such as hydrosalpinx or previous pelvic inflammatory disease, then antibiotic prophylaxis is recommended (e.g., 100 mg doxycycline PO, twice daily for 3 to 5 days, beginning the day before the procedure).[37] HSG is a good test for ruling out tubal pathology such as obstruction or hydosalpinx. One meta-analysis reported 65% sensitivity and 83% specificity for tubal obstruction.[38] HSG is less specific for endometrial pathology such as polyps, submucous fibroids, and adhesions. Diagnostic tests in the form of hysteroscopy or sonohysterography can be done to further investigate the endometrial cavity as needed. When a hysterosalpingogram suggests bicornuate uterine configuration, imaging of the uterine corpus must be done to differentiate between septate and bicornuate Müllerian anomalies. This can be done with 3D ultrasound, magnetic resonance imaging, or concurrent hysteroscopy with laparoscopy. Some studies have reported an increase in spontaneous pregnancy rates following HSG with water-based contrast medium,[39] although historically this benefit has been attributed to oil-based contrast HSG.[40] A recent study followed over 1000 infertile women randomly assigned to undergo HSG with water-based or oil-based contrast.[41] There were significantly more live births in the oil-based group (39% versus 28%, OR 1.38, 95% CI 1.17–1.64). The underlying mechanism for this possible benefit may involve dislodging of mucus plugs and endometrial or immunomodulatory effects.[41] In BC hysterosalpingography is usually performed with water-based contrast. The gold standard for tubal and pelvic evaluation is laparoscopy with chromopertubation. Because of the inherent risks of surgery and long wait times, however, it is not commonly performed for tubal assessment without other indications for surgery.

Semen analysis

Semen analysis is a fundamental part of the workup because the male factor accounts for at least 35% of infertility.[6] The process of spermatogenesis takes approximately 70 days and continues throughout a man's lifetime, allowing many men to maintain fertility in perpetuity.[6] Once a spermatozoon is deposited in the vagina, it must separate itself from the seminal fluid (a product of the seminal vesicles and prostate gland) and swim through the cervical mucus and endometrial cavity to wait for the oocyte in the fallopian tube. A complex set of activities in the sperm is required for successful fertilization, including capacitation and the acrosome reaction, which allow for penetration of the cumulus oophorus and zona pellucida (egg shell).[6] Once the sperm head fuses with the oolemma it will undergo nuclear decondensation to form the male pronucleus and eventually fuse with the female pronucleus to create an embryo.[6]

An optimal sample for semen analysis is obtained after 2 to 5 days of abstinence and processed for analysis after 15 to 30 minutes of observed liquefaction. The normal values for semen parameters in the current World Health Organization (WHO) laboratory manual (5th edition) were obtained from a retrospective examination of fertile men whose partners conceived within 12 months.[42] The lowest fifth percentile was used as a cutoff. A semen analysis uses one-sided lower limits for reference: volume (1.5 mL), concentration (15 M/mL), total sperm count (39 M), total motility (40%), progressive motility (32%), vitality (58%), and morphology (4%).[43] For fertility, the chief

prognostic parameters are sperm concentration and motility, with morphology being of lesser importance. Sperm concentration can vary substantially from sample to sample in both fertile and infertile men.[42] When the concentration is lower than 15 M/mL fertility is reduced, while increases above this level are not consistently associated with better pregnancy rates.[42] Sperm motility can be affected by many factors, including duration of abstinence, age, health status, length of time to processing, and exposure to heat or toxins.[42] An abnormal test result warrants repeat testing, allowing a break of at least 2 to 3 months for any intervention aimed at improving sperm quality. Assessing morphology involves examination of at least 200 sperm under 400x or 1000x magnification to consider the head, mid-piece, and tail according to the Kruger criteria.[42] The first edition of the WHO laboratory manual required 80.5% normal-shaped sperm; over subsequent editions this was reduced to 50.0% (2nd edition), 30.0% (3rd edition), and 15.0% (4th edition). It is important when counseling patients to reassure them that even 0% normal sperm morphology does not preclude a pregnancy.[44]

Summary

Infertility is a prevalent condition that affects about 15% of couples. In BC women are delaying childbearing longer than anywhere else in the country. This makes our patient population particularly susceptible to age-related infertility. For women over 35 years, infertility investigations should be initiated after 6 months of trying to conceive, and for women over 40 years, investigations should be initiated immediately. The basic workup for infertility includes confirmation of ovulation, measurement of follicle-stimulating hormone level, hysterosalpingography, and semen analysis. Measurement of day 3 FSH should be ordered in conjunction with measurement of estradiol to confirm appropriate timing. Physicians should be aware that because FSH is a late marker of diminished ovarian reserve, there is no level of FSH considered reassuring. AMH is an accurate and convenient test, but interpretation is highly age-specific. HSG is a useful test to rule out tubal obstruction; however, any uterine abnormality should be investigated further with hysteroscopy with laparoscopy or sonohysterography. Semen analysis is a key component of the basic infertility workup, with sperm concentration being the most important predictor for fertility. Consultation with a gynecologist or fertility specialist is covered by provincial health insurance and should be considered for couples with abnormal test results and for couples who fail to conceive despite normal test results. BCMJ

Competing interests

None declared.

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Jon Havelock, MD, FRCSC

Polycystic ovary syndrome

Therapy for this reproductive and metabolic disorder remains focused on managing symptoms, including infertility caused by anovulation, and reducing long-term health risks such as endometrial cancer and type 2 diabetes.

ABSTRACT: The clinical presentation of polycystic ovary syndrome is widely variable, with complaints encompassing oligomenorrhea, infertility, obesity, hirsutism, endometrial cancer, and diabetes. Community physicians caring for reproductive-age women will invariably encounter this reproductive and metabolic disorder resulting from ovarian hyperandrogenism and insulin resistance. While community physicians should be aware of the diagnostic criteria for polycystic ovary syndrome, it is more important to have a thorough understanding of symptom management and prevention of long-term complications. Historically, clomiphene citrate has been used to address infertility by inducing ovulation, with more recent evidence supporting the use of letrozole as first-line therapy for ovulation induction. These and other mainstay treatments may be needed to address anovulation, obesity, and hirsutism. Patients should also be monitored for endometrial cancer and type 2 diabetes.

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Polycystic ovary syndrome (PCOS) is a prevalent reproductive and metabolic disorder with variable phenotypes and an underlying pathophysiology that is still not completely understood. While the earliest description of the polycystic ovary dates back to the 17th century,[1] the characterization of the present-day disorder known as PCOS was first detailed by Irving Stein and Michael Leventhal in 1935.[2] In a seminal paper, the two prominent gynecologists described a case series of seven women with enlarged ovaries associated with oligomenorrhea or amenorrhea, sterility, and clinical hyperandrogenism. Histopathologic determination of the disorder was undertaken by wedge biopsy of the ovaries. The surgical procedure that led to characterization of the disorder also serendipitously led to the first therapeutic intervention for infertile women with PCOS. Five of the seven women subsequently conceived after normalization of their menstrual cycles. One woman who did not conceive was affected by male factor infertility and the other woman was lost to follow-up.

As a result, Stein-Leventhal syndrome was the term used for more than 50 years for the heterogeneous clinical features of the disorder now known as polycystic ovary syndrome. In 1990 the first international definition of PCOS was developed, which has since been revised by various professional bodies. The lack of consensus in the definition of PCOS further highlights the uncertainty about the pathophysiology of the disorder. However, for the practising physician a thorough understanding of symptom management and prevention of long-term complications is more important than an understanding of the different diagnostic criteria for PCOS.

Pathophysiology

The abnormal findings in PCOS are a result of ovarian hyperandrogenism[3]

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and insulin resistance.[4] Evidence suggests that the ovarian hyperandrogenism in PCOS is a result of primary ovarian dysfunction and is secondary to disordered gonadotropin activity. While not included in diagnostic criteria for PCOS, the elevated level of serum luteinizing hormone (LH) in affected patients due to inappropriate secretion has long been recognized.[5] LH is the ligand for the LH receptor on the ovarian theca cells responsible for ovarian androgen production. Genome-wide association studies conducted on hyperandrogenic subjects with PCOS revealed genome-wide significance for a locus mapping to chr 11p14.1 in the region of the follicle-stimulating hormone beta polypeptide (FSHB).[6] This single-nucleotide polymorphism was associated with LH levels that result in the elevated LH:FSH ratios often seen in PCOS, providing further support for the hypothesis that dysregulated gonadotropin secretion in PCOS leads to secondary hyperandrogenism. This gonadotropin imbalance favors an exaggerated intraovarian androgen environment under the influence of LH, and impaired folliculogenesis resulting in anovulation due to a relative FSH deficiency.

Evidence also suggests that the ovarian hyperandrogenism seen in PCOS is primary, with abnormal ovarian steroidogenesis through overexpression of the *CYP17* gene being responsible for androgen biosynthesis, as well as increased expression of the LH receptor, which would potentially render the ovarian theca cells more sensitive to LH stimulation.[7,8] The ovarian hyperandrogenism appears to play a role in the appearance of the polycystic ovary on ultrasound and the follicular arrest and anovulation that is prevalent in PCOS. The ovarian phenotype may result from either endogenous or exogenous androgens, as demonstrated in the similar ultraosonographic findings and gene expression profile studies on the ovaries of women with PCOS and the ovaries of androgen-treated female-to-male transgender individuals.[9]

Evidence for the role of insulin resistance in the pathophysiology of PCOS and ovarian hyperandrogenism is demonstrated indirectly by the findings of hyperandrogenism in female subjects with type A insulin resistance syndrome, a disorder characterized by a mutation in the insulin receptor gene.[10] Insulin contributes to the biochemical and clinical hyperandrogenism by directly enhancing theca cell ovarian androgen production in concert with LH,[4] and indirectly by lowering sex hormone-binding globulin, the carrier protein responsible for reducing circulating free testosterone levels.[11] The high prevalence of impaired glucose tolerance and type 2 diabetes in women with PCOS has led researchers to consider the role of insulin sensitizers in treating PCOS.

Diagnostic criteria

Three sets of diagnostic criteria for polycystic ovary syndrome are used commonly (**Table 1**). All require the exclusion of other known disorders.

The National Institutes of Health (NIH) conference on PCOS in 1990 led to the first internationally accepted diagnostic criteria. The two criteria (clinical and/or biochemical evidence of hyperandrogenism and menstrual dysfunction) were based on expert opinion solicited through a questionnaire. In 2003 the Rotterdam criteria developed by the European Society of Human Reproduction and Embryology and the American Society for Reproductive Medicine (ESHRE/ASRM) allowed for the inclusion of polycystic-appearing ovaries on ultrasound. This was defined as 12 or more follicles measuring 2 to 9 mm in at least one ovary, or an ovarian volume greater than 10 mL in the absence of a dominant follicle. The ESHRE/ASRM diagnostic guidelines only required meeting two of three criteria (clinical and/or biochemical hyperandrogenism, oligomenorrhea and/or anovulation, and polycystic ovaries).[12] Most recently, the experts contributing to the Androgen Excess Society (AES) diagnostic guidelines required meeting two criteria (clinical and/or biochemical hyperandrogenism and either ovarian dysfunction or polycystic ovaries).[13]

Table 1. Diagnostic criteria for polycystic ovary syndrome.

National Institutes of Health criteria (1990) • Must meet both criteria	**European Society for Human Reproduction and Embryology and American Society for Reproductive Medicine Rotterdam criteria (2003)** • Must meet two of three criteria	**Androgen Excess Society criteria (2006)** • Must meet both criteria
Clinical and/or biochemical evidence of hyperandrogenism	Clinical and/or biochemical evidence of hyperandrogenism	Clinical and/or biochemical evidence of hyperandrogenism
Menstrual dysfunction	Oligoovulation or anovulation	Ovarian dysfunction or polycystic ovaries
	Polycystic ovaries	
Exclusion of other known disorders is required as well.	Exclusion of other known disorders is required as well.	Exclusion of other known disorders is required as well.

The Rotterdam criteria are the most widely used for PCOS diagnosis, and like the more liberal AES criteria they allow for different phenotypes of the disorder. Prevalence estimates for PCOS obtained using the Rotterdam and AES criteria (12% to 18%) were up to twice that obtained using the NIH criteria (9%).[14] NIH-defined PCOS is the most common phenotype, and women with this phenotype are most at risk of developing reproductive and metabolic abnormalities, specifically type 2 diabetes. Women with the Rotterdam PCOS phenotype without hyperandrogenism are least at risk of reproductive and metabolic abnormalities.[15]

Evaluation

As PCOS is ultimately a diagnosis of exclusion, other endocrinopathies that have clinical features similar to those of PCOS must be considered. If ovulatory dysfunction exists, ordering tests to rule out causes such as thyroid dysfunction and hyperprolactinemia (e.g., thyroid-stimulating hormone, prolactin assay) is imperative. Considering the possibility of other more serious causes of androgen excess, such as nonclassic congenital adrenal hyperplasia (confirmed with an elevated 17-hydroxyprogesterone level) and androgen-producing tumors (confirmed with total testosterone levels twofold above upper-normal), is also recommended. In the presence of oligomenorrhea or amenorrhea, measurement of serum FSH and estradiol may be warranted to rule out ovarian insufficiency or hypogonadotropic hypogonadism (hypogonadism of hypothalamic or pituitary origin).

The most common clinical feature of hyperandrogenism is hirsutism: the growth of excessive hair in a male-type pattern caused by the conversion of vellus hair to terminal hair under androgen effect on the pilosebacous unit. Hirsutism is most commonly assessed using the modified Ferriman-Gallwey scale to quantify the amount of hair growth on various androgen-dependent body areas. However, race and ethnicity play a significant part in hirsutism.[16] Additionally, the Ferriman-Gallwey scoring system can be somewhat impractical in everyday clinical practice, and will be affected by a patient's recent waxing, shaving, or other depilation. Practically, hirsutism remains largely a self-reported symptom. In the absence of hirsutism, acne may be considered a clinical marker of hyperandrogenism.

A strict definition of biochemical hyperandrogenism in PCOS does not exist. A free testosterone index and a free androgen index are thought to be the most sensitive markers of biochemical hypernadrogenemia by the authors of the Rotterdam criteria.[12] However, the assay methods are variable and have significant limitations. Total testosterone is not a sensitive marker of androgen excess, but measurement may be useful if an androgen-secreting neoplasm is suspected.

Irregular or absent menstrual cycles are the most common clinical finding of PCOS and are usually identified during history taking.[13] Menstrual cycle intervals longer than 35 days are often anovulatory. If menstrual cycles are absent because of ovarian insufficiency this will be indicated by a finding of significantly elevated FSH levels. In PCOS, which is characterized by euestrogenic chronic anovulation, menstrual withdrawal bleeding can typically be induced by a 5-day to10-day course of progesterone or progestin. This provides further support for anovulation being secondary to PCOS and not being the result of ovarian insufficiency or hypogonadotropic hypogonadism. In women with less severe menstrual disturbance, serum progesterone can be measured in the mid-luteal phase (day 21 to 23) of the menstrual cycle. If ovulation has occurred, the level will be 10 nmol/L or higher.

A diagnosis of PCOS rarely requires the use of ultrasound to confirm polycystic-appearing ovaries. As symptom management is the focus in PCOS, ultrasound adds little clinical value. However, ultrasound may be warranted for investigating a pelvic mass, infertility, or pelvic pain. It is important, when possible, that the ultrasound be performed with the use of an endovaginal ultrasound probe. Furthermore, obtaining an antral follicle count in each ovary (all follicles 2 to 9 mm) is important since the ultrasound diagnostic criteria for PCOS were established by reproductive endocrinologists rather than radiologists. Finally, there is a significant overlap between the diagnoses of polycystic-appearing ovaries and normal ovaries, with 30% to 50% of women younger than 30 having 12 or more follicles per ovary.[17] This indicates that a polycystic-appearing ovary is not pathognomonic of PCOS.

Management

In addition to infertility caused by anovulation, women with PCOS are at risk for obesity, hirsutism, endometrial cancer, and type 2 diabetes and should be managed accordingly (**Box**).

Anovulation

While anovulation can lead to long-term health consequences such as endometrial cancer and hyperplasia, most PCOS patients will present initially with infertility. It is reasonable to begin by ruling out male factor infertility with semen analysis and to complete fallopian tube assessment if the patient has risk factors for tubal factor infertility (prior ectopic pregnancy or gynecologic surgery, ruptured appendix, history of recurrent or

severe pelvic inflammatory disease). Ovulation induction is the simplest and least expensive infertility therapy.

For years, clomiphene, a selective estrogen receptor modulator first shown to induce ovulation in 1961, has been the mainstay of ovulation induction for PCOS. More recently, letrozole, an aromatase inhibitor, has been used off-label for ovulation induction, as first described in 2001.[18] A large, multicentre RCT comparing both medications in PCOS patients with anovulatory infertility demonstrated superior live birth rates in the letrozole arm (27.5%) compared with the clomiphene arm (19.1%), with similar twin pregnancy rates (3.9% vs 6.9%).[19] While letrozole for ovulation induction in the setting of PCOS still remains off-label use, the recent discontinuation of clomiphene production in Canada, along with the superior clinical outcomes with letrozole, has made this the first-line therapy for women with PCOS and anovulatory infertility. Typically, therapy with either agent is initiated on cycle day 3 of a spontaneous or progestin-induced menstrual bleed (**Table 2**).

As insulin resistance is a common feature of PCOS, the use of insulin sensitizing agents, particularly metformin, for treatment of anovulatory infertility is physiologically reasonable. Early studies demonstrated ovulation rates of up to 90% in women treated with metformin and clomiphene,[20] and ovulation rates of 75% in women who remained anovulatory on clomiphene single-agent therapy.[21] However, the Pregnancy in Polycystic Ovary Syndrome (PPCOS I) trial[22] comparing metformin, clomiphene, and metformin plus clomiphene found metformin alone was inferior to clomiphene alone and to metformin plus clomiphene. Metformin plus clomiphene outperformed clomiphene alone in ovulation rate, but with pregnancy and live birth rates that were similar. Thus, there appears to be no role for metformin as a single agent for ovulation induction in PCOS, and a limited role for metformin as adjuvant treatment for ovulation induction.

Obesity

Obesity is prevalent in 50% to 80% of women with PCOS.[15] Both the PPCOS I trial[22] and the PPCOS II trial[23] comparing letrozole and clomiphene demonstrated live birth rates approximately twofold higher for women with a BMI less than 30 kg/m^2 than for women with a BMI greater than 35 kg/m^2 (PPCOS I) and 39 kg/m^2 (PPCOS II). While both studies definitively demonstrated that a high BMI has an adverse effect on response to ovulation induction with oral agents, evidence of a positive effect for weight loss in women with infertility secondary to anovulation was lacking until recently. Now a trial of obese women with anovulatory infertility who were randomly assigned to either a lifestyle intervention (exercise and diet for 6 months) or no lifestyle intervention has found a significant improvement in live birth rates for women in the lifestyle intervention group (number needed to treat with lifestyle intervention to result in 1 additional spontaneous live birth without fertility therapy = 6).[24] Subjects in the lifestyle intervention group lost 4.4 kg on average during the 6-month pre-fertility treatment intervention.[25] Diet and exercise as first-line therapy for

Box. Diagnosing and managing polycystic ovary disease syndrome

- A diagnosis of polycystic ovary disease syndrome (PCOS) must exclude other causes and include two of the following:
  - Oligomenorrhea or amenorrhea.
  - Clinical or biochemical hyperandrogenism.
  - Polycystic ovaries (> 12 follicles 2–9 mm or volume > 10 mL).
- In addition to infertility caused by anovulation, women with PCOS are at risk for obesity, hirsutism, endometrial cancer, and type 2 diabetes.
- Off-label use of letrozole for ovulation induction (2.5 mg, 5.0 mg, and 7.5 mg daily, from cycle days 3–7 or 5–9) has been found to be safe and effective.
- Clomiphene citrate, the drug commonly used in the past for ovulation induction, may be difficult to obtain because the only manufacturer in Canada has stopped production.
- Oral contraceptive use remains the first-line therapy for hirsutism and has demonstrated a reduction in risk of endometrial cancer.
- Metformin use and lifestyle interventions have been found to reduce risks associated with type 2 diabetes.

Table 2. Recommendations for inducing ovulation with letrozole or clomiphene.

	Letrozole	Clomiphene
Initial regimen	2.5 mg daily on cycle day 3–7 (5 days)	50 mg daily on cycle day 3–7 (5 days)
Indication for increase	Absence of ovulation	Absence of ovulation
How much to increase	2.5 mg daily increment	50 mg daily increment
Maximum daily dose	7.5 mg daily	150 mg daily
Treatment duration	6 ovulatory cycles	6 ovulatory cycles
Confirmation of ovulation	Serum progesterone > 10 nmol/L at cycle day 21–23	Serum progesterone > 10 nmol/L at cycle day 21–23

anovulatory infertility in obese women with PCOS is supported by both common sense and well-designed clinical research.

Hirsutism

Hirsutism is the result of elevated circulating free testosterone acting on the pilosebaceous unit to convert vellus hair to terminal hair. Removal of unwanted hairs by electrolysis or mechanical depilation will be a temporary solution if the underlying endocrine disorder is not treated. The androgen effect responsible for hirsutism can potentially be reduced by decreasing androgen production, increasing androgen-binding capacity to reduce circulating levels, or reducing androgen action at the androgen receptor. However, individuals with hirsutism must be counseled to be patient, as response to endocrine therapy takes at least 3 to 6 months in concordance with the hair growth cycle.

The oral contraceptive pill (OCP) remains the first-line therapy for hirsutism because of its effect on androgen production.[26] First, the estrogen component of the OCP increases sex hormone-binding globulin levels, resulting in greater androgen-binding capacity, and reducing circulating free testosterone levels. Second, the progestin component suppresses pituitary LH production, reducing the stimulation of ovarian theca cell androgen synthesis under LH stimulation. Certain OCP progestins such as drosperinone and cyproterone acetate function as androgen receptor antagonists, and have a theoretical advantage over other progestins. OCP use offers the additional benefit of reducing acne, if present, and provides protection against endometrial cancer and menstrual cycle irregularity.

As PCOS is ultimately a diagnosis of exclusion, other endocrinopathies that have clinical features similar to those of PCOS must be considered.

Women with hirsutism who do not respond adequately to OCP treatment may benefit from other anti-androgen therapies such as spironolactone or finasteride. Spironolactone is a mineralocorticoid antagonist that also functions as a weak androgen receptor antagonist. As well, spironolactone reduces the activity of 5-alpha reductase (the enzyme responsible for converting testosterone to the more potent dihydrotestosterone), and reduces testosterone biosynthesis. Daily doses of spironolactone (100 mg) for at least 6 months have been shown to reduce hirsutism.[27] Finasteride, a 5-alpha reductase inhibitor, has a theoretical role in management of hirsutism, but clinical trial results have been inconsistent.[28] When OCP use alone is ineffective, it is prudent to use anti-androgen therapies in conjunction with OCP due to the potential teratogenic effects of these agents in the case of inadvertent pregnancy.

Endometrial cancer

Endometrial cancer prevalence is documented to be significantly higher (by 2.7-fold) in women with PCOS.[29] However, it is difficult to determine whether PCOS is an independent risk factor for endometrial cancer because many of the common presenting features of PCOS (obesity, infertility, diabetes, unopposed estrogen/irregular menstrual cycles) are independent risk factors for endometrial cancer. Regardless, heightened awareness and monitoring for endometrial cancer in women with PCOS is warranted, and risk-reduction strategies should be undertaken. While weight loss and exercise are recommended for managing PCOS in obese women, evidence for these as effective therapy for protection against endometrial cancer is lacking.

Oral contraceptive use has consistently been found to reduce risk of endometrial cancer. OCP use appears to provide a risk reduction of approximately 50%, and the protective effect seems to last up to 20 years after stopping OCP use.[30] Additionally, relative reduction of endometrial cancer risk seems to be approximately two-fold lower in women who have used the OCP for 12 years compared with women using it for 4 years.[31]

Some women with PCOS and irregular menstrual cycles and anovulation resulting in unopposed estrogen may not tolerate OCP therapy, or OCP use may be contraindicated. Cyclic progesterone therapy (e.g., 200 mg Prometrium PO daily for 10 to

14 days per month, 5 to 10 mg medroxyprogesterone PO daily for 10 to 14 days per month) may be a reasonable option for inducing cyclic menses and providing progestational effect against unopposed estrogen. Alternatively, a progestin-releasing intrauterine contraceptive device may provide similar, noncontraceptive benefit.[32] While all of these therapies represent off-label use, they are generally accepted as appropriate therapy in the circumstances.

Type 2 diabetes

When controlling for other risk factors, PCOS remains an independent risk factor for developing impaired glucose tolerance (RR 2.5) and type 2 diabetes (RR 4.0).[33] Although management of diabetes is beyond the scope of this article, it is possible to recommend exercise and weight loss to reduce the risk of progression from impaired glucose tolerance to diabetes.[34] Metformin use may also be considered, given that it is known to have a modest effect despite being less effective than lifestyle intervention in reducing diabetes risk. Patients with PCOS should be monitored for diabetes if they have a BMI greater than 30 kg/m^2 (or greater than 25 kg/m^2 for Asian patients) or have a family history of diabetes, acanthosis nigricans, or hyperandrogenism with anovulation.[29]

Summary

Polycystic ovary syndrome remains a prevalent reproductive and metabolic disorder with variable phenotypes and an underlying pathophysiology that is not completely understood. Making a diagnosis of PCOS is beneficial but not essential. Therapy remains focused on managing symptoms (infertility caused by anovulation, obesity, hirsutism) and reducing long-term health risks (endometrial cancer, type 2 diabetes). BCMJ

Competing interests

Dr Havelock has received honoraria and speaking fees from EMD Serono and Merck, companies engaged in producing fertility treatments and technology. He has also received a research grant from Ferring Pharmaceuticals, a company engaged in developing and marketing products for reproductive health.

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Jeffrey E. Roberts, MD

Fertility preservation for young cancer patients

Subfertility and gonadal failure are possible after childhood exposure to chemotherapy, making future reproductive function a growing survivorship issue that must be addressed.

ABSTRACT: Recent advances in cryopreservation are providing effective fertility preservation options for young Canadians requiring chemotherapy for cancer. Both female and male patients can opt to freeze gametes before undergoing treatment. Embryo, oocyte, and ovarian tissue freezing are possible for females, and sperm freezing is possible for males. The decision to proceed with fertility preservation is made by taking into account the patient's age, diagnosis, oncology treatment plan, fertility status, and personal/social situation. Management should include surveillance of ovarian reserve, counseling on fertility and sexual health, and provision of egg and embryo banking in cases where the patient's reproductive lifespan is likely to be significantly reduced. Barriers to fertility preservation include a lack of awareness and the high cost of these services. A multidisciplinary approach to care, education of oncology professionals and patients on issues related to reproduction, and better funding can help ensure that cancer patients receive timely counseling and appropriate fertility preservation services.

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Modern chemotherapeutic protocols are highly effective at destroying malignant cells, but also damage ovaries and testicles in the process, leading to infertility in a sizable percentage of patients. This is a challenging survivorship issue faced by fertility specialists and cancer specialists alike. Most young cancer survivors desire future pregnancy, and the psychological impact of infertility can be greater than the effects of the cancer itself, with overt PTSD seen in some cases.[1] Fertility preservation treatments can increase the likelihood of future pregnancy. More importantly, they can also provide patients with hope and a positive distraction during a very negative time in their lives. Young patients often have a limited understanding of their own reproduction and what options exist through modern assisted reproductive technology (ART), and are unlikely to seek advice on fertility preservation; therefore, referral to a fertility specialist with the ability to discuss and deliver these services is critical.

Ovarian reserve testing

Ovarian reserve (the pool of primordial follicles) and reproductive potential both decline as women age.[2] The reduction in natural fertility with age is mirrored by the lower pregnancy rates with medical fertility treatments such as in vitro fertilization (IVF). Chemotherapeutic agents accelerate the age-related loss of primordial follicles through an increase in recruitment of ovarian follicles (burnout theory), apoptosis of supporting granulosa cells, and disappearance of eggs.[3,4] The toxicity of chemotherapeutic treatments varies according to the specific agents administered, dose, and protocol, and the reproductive potential of the patient at the time of treatment.[5-8] Primordial follicles are not mitotically active, so they are still sensitive to alkylating agents (a mainstay of most combination chemotherapy), which are cell cycle-independent drugs that can cause direct DNA damage.

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The clinical measure of reproductive toxicity has traditionally been ovarian failure rates, which range from less than 20% to over 80%. Regardless of the type of chemotherapeutic agent administered, at least a portion of the ovarian reserve will be lost, even if this is not immediately apparent clinically.[9,10] Ovarian failure occurs when a woman's follicle population drops to a point where hormone fluxes are inadequate to maintain a normal menstrual cycle. In terms of the capacity to conceive with her own eggs, a patient is rendered sterile at this point.

Normal menstrual function can be sustained with less than 10% of ovarian mass, making ovarian failure a very late measure of reduced fertility. Even if a patient is deemed to be at minimal risk for premature ovarian failure, it is safe to assume that her reproductive lifespan will be shorter despite the resumption of regular menstrual cycles.[4,11-15] A survey of 2532 cancer survivors between the ages of 18 and 40 showed that infertility rates were higher than rates of acute ovarian failure, highlighting the fact that the impact on fertility can be underestimated if the focus is simply on menstrual disruption.[10] For breast cancer, which is the most common cancer in reproductive-age women, chemotherapy likely advances reproductive age by at least 10 years.

The decision to proceed with fertility preservation treatments requires taking into account the patient's age, diagnosis, oncology treatment plan, fertility status, and personal/social situation. Even if not undergoing gonadotoxic treatments, all reproductive-age women now have the option to improve on the prospects of future pregnancy through ART, and the decision-making process is largely the same, albeit less urgent. In the case of breast cancer, plans must account for the 2-year period of recurrence observation following completion of chemotherapy and the lengthy delays possible when adjuvant hormone therapies are employed. It is important that the oncology team be consulted prior to initiating fertility preservation treatment. Careful coordination of the fertility preservation protocol is required to allow for the timely delivery of the cancer treatment, with a clear understanding that cure takes precedence.

For breast cancer, the most common cancer in reproductive-age women, chemotherapy likely advances reproductive age by at least 10 years.

Ovarian reserve testing is important for tailoring a woman's ovarian stimulation protocol and for providing a reasonable estimate of her likelihood of pregnancy in the future. All measures of ovarian reserve are affected by chemotherapy, and patients with a history of chemotherapy exposure appear to have a lower potential for pregnancy.[16] A cycle day 3 follicle-stimulating hormone serum level has been the standard way to evaluate ovarian reserve for many years, with anti-Müllerian hormone (AMH) level now proving to be a better predictor of reproductive outcomes and a more convenient option, as it can be performed at any time in the menstrual cycle. Unfortunately, AMH testing is not an insured service in BC, costing approximately $70. In combination with patient age, the AMH level is also useful for quantifying the effects of chemotherapy in individuals, for predicting response to ovarian stimulation, live birth rates, and for ovarian reserve surveillance.[17,18] A transvaginal pelvic ultrasound with antral follicle count is an essential part of the basic fertility assessment of these patients, and is as predictive as the AMH level for ovarian response to gonadotropins.[19]

In vitro fertilization and embryo freezing

The mainstay of fertility preservation in female patients is the freezing of egg and embryos generated through the IVF process.[20,21] It is important to minimize any delay of cancer treatments and to maximize the number of eggs without causing undue discomfort for the patient or complications such as ovarian hyperstimulation syndrome or ovarian torsion. With concurrent use of aromatase inhibitors, gonadotropins can be administered to maximize embryo yield while minimizing the normally elevated estrogen levels encountered during these

treatments, which can be particularly important for the breast cancer patient. IVF protocols are principally defined by the methods used to block the surge of luteinizing hormone. Inhibiting the ovulatory process allows for the precise timing of the egg retrieval procedure and prevents premature luteinization of the uterus to allow for transfer of fresh embryos. Gonadotropin-releasing hormone antagonist protocols provide the most flexibility for ovarian stimulation. These treatment cycles tend to be shorter, require less gonadotropin medication (which reduces costs), and can virtually eliminate the risk of ovarian hyperstimulation syndrome when a gonadotropin-releasing hormone agonist (GnRHa) is administered to trigger final maturation of eggs for harvest.[22] The ultimate goal is to maximize the number of eggs retrieved, while minimizing any risks and delay of cancer treatments.

Cryopreservation of embryos has remained the principal fertility preservation treatment for decades. It is employed by all IVF clinics for the banking of supernumerary embryos generated through IVF and for situations when pregnancy is ill-advised for medical reasons or is being delayed for social reasons. The likelihood of future pregnancy depends on the patient's age, the number of embryos obtained, and the number of IVF cycles performed. Of great importance is the growing body of evidence that demonstrates higher pregnancy rates and better perinatal outcomes when a frozen embryo transfer rather than a fresh embryo transfer is used.[18,23-27] A recent exciting advance in the technology is the use of embryo biopsy techniques for choosing embryos for use, by screening out aneuploidy (comprehensive chromosomal screening) and single gene defects (preimplantation genetic diagnosis).[28]

Oocyte and ovarian tissue freezing

For women wanting reproductive autonomy, or those without a male partner, oocyte cryopreservation has become the standard method of preserving fertility. Historically, the technique has been beset by lower pregnancy rates compared with embryo cryopreservation, but improvements have been seen with recent advances in vitrification, the flash-freezing technology now being offered by most Canadian IVF clinics. The poor outcomes of the past were related to several technical challenges inherent in freezing and thawing of oocytes, the largest human cells. Mature (meiosis II) eggs provide the best chance for pregnancy, but have several characteristics that make them susceptible to cryodamage, including large size (low surface area to volume ratio) and high water content, which makes the egg vulnerable to ice crystal formation, rupture, and limited permeability to cryoprotectant solutions. Recent studies have found pregnancy rates with frozen eggs approaching those of fresh.[29,30] Despite the potential obstacles, clinical and neonatal outcomes to date attest to the safety of this technology, and it is now recognized by the Canadian Fertility and Andrology Society as a standard of care.[31]

Reports of reduced amenorrhea rates in young women using adjuvant gonadotropin-releasing hormone agonists throughout chemotherapy have prompted research into the protective properties of GnRHa for the ovary. Proposed mechanisms of action include hypogonadotropism-induced ovarian quiescence, reduction of ovarian blood flow, and agonistic effects on ovarian receptors for gonadotropin-releasing hormone. Although not presently endorsed by the most recent guideline of the American Society of Clinical Oncology (2013) as a standard method of fertility preservation,[7] two large RCTs suggest that a reduction in the risk of premature menopause is approximately 50% in patients undergoing chemotherapy for breast cancer.[32,33] GnRHa administration prior to and during chemotherapy is presently used widely in BC.

For women wanting reproductive autonomy, or those without a male partner, oocyte cryopreservation has become the standard method of preserving fertility.

Since the first experiments with ovarian transplantation in animals, steady advances have been made in human subjects.[7] Patients receiving chemotherapy or radiotherapy that

targets the ovary can be considered candidates for ovarian tissue cryopreservation, particularly if they are undergoing abdominal surgery. At an appropriate time after completion of the patient's cancer therapy, the tissue is thawed and transplanted orthotopically or heterotopically within the pelvis. The major barrier for this technology is survival of the transplant. With fewer than 100 documented live births from transplanted ovarian tissue, the potential for reseeding of metastatic disease, and the surgical risks inherent in undergoing two procedures, ovarian transplantation is considered experimental and generally reserved for cases where oophorectomy is already planned.

Children and adolescents with cancer are frightened, but their ability to understand the impact that medical treatments will have in future should not be discounted.

Sperm freezing

For men, fertility preservation typically involves cryopreservation of ejaculated sperm.[7] Rarely, surgical collection directly from the epididymis or testicle is required. The testicle is very sensitive to even low doses of systemic chemotherapeutic agents. Additionally, cancer patients commonly present with reduced sperm counts secondary to their illness. Reduction of spermatogenesis results from effects on the epithelium. Leydig function is typically unaffected, so testosterone deficiency is uncommon. Oligospermia and azoospermia rates range from 70% to 98% depending on the follow-up period. Spermatogenesis can recover at variable times, so long-term sperm testing is recommended.[34] Some patients are rendered azoospermic for life, and one study found cancer survivors were 50% more likely to be infertile.[34,35] Importantly, fetal malformation rates are elevated for up to 2 years following chemotherapy, so sperm should be banked prior to treatment for both fertility preservation and the health of any offspring.[36] The amount of sperm required for banking will depend on the clinical scenario, timeline to treatment, and availability of the patient.

Preserving fertility in children and adolescents

Cure rates for childhood cancers exceed 80% for most types. Despite the larger ovarian reserve of most young patients going into treatment, subfertility and gonadal failure are possible after childhood exposure to chemotherapy, making future reproductive function a growing survivorship issue for these patients as they transition into adulthood. The Childhood Cancer Survivor Study, which compared patients exposed to chemotherapy with randomly selected siblings, found a thirteenfold increase in the rate of ovarian failure in female cancer survivors.[37]

Children and adolescents with cancer are frightened, but their ability to understand the impact that medical treatments will have in future should not be discounted. They typically lack knowledge about their own reproduction and existing technologies for assisting with fertility, but do eventually want children.[1] Assuming that fertility preservation procedures are technically possible, all fertility preservation techniques are available to these patients. There are no legal restrictions in Canada to the application of assisted reproductive technology in pediatric cases, so long as the reproductive material is reserved for the patient.

Decisions on proceeding with treatment need to respect the patient's level of understanding of the medical issues, as well as the risks and benefits of the technologies. For girls, challenges with vaginal procedures can often be addressed with the use of transabdominal pelvic ultrasound for monitoring of ovarian stimulation and general anesthesia for harvesting of eggs. For boys, sperm recovery will depend on their stage of sexual development. Masturbation and exposure to pornography present ethical concerns, but for the most part is the only feasible approach. Obtaining appropriate consent is critical before employing invasive techniques such as testicular sperm retrieval and electroejaculation. As well, a fair estimate of the probability of obtaining mature sperm is needed.

In terms of reproductive health, transition to adulthood is poorly addressed by our medical system. Adequate management should include ovarian reserve surveillance, counseling on fertility and sexual health, and provision of egg and embryo

banking in cases where a woman's reproductive lifespan is likely to be significantly reduced. All patients must be made aware of the fact that pregnancy is possible in the vast majority of cases, irrespective of gonadal function, through the use of egg and sperm donation technologies. In the event of premature ovarian failure, patients should be counseled on the use of hormone replacement.

Barriers to services

Recent advances in cryopreservation are providing effective fertility preservation options for Canadians, yet barriers to services exist for cancer patients. A multidisciplinary approach to care and education of oncology professionals and patients on issues related to reproduction are both required. More work is needed to increase awareness in BC and to ensure that patients receive appropriate fertility preservation counseling and services in a timely manner. The high cost of these services must also be addressed. Presently, only Ontario and Quebec provide funding for egg, sperm, and embryo banking. Fertile Future, a national charity that is committed to making these treatments affordable for cancer patients, currently provides up to $3000 toward clinical costs for female patients and $350 for male patients. The pharmaceutical companies that manufacture gonadotropins used in IVF have been providing compassionate medications for many years. No area of our profession is more in need of public support and we will continue to lobby provincially and federally for these critical services.

Summary

While modern chemotherapeutic protocols are highly effective at destroying malignant cells, they also lead to infertility in a sizable percentage of patients. This is a challenging survivorship issue for fertility specialists and cancer specialists alike. Fertility preservation for males usually involves freezing sperm, and for females involves ovarian reserve surveillance and freezing of embryos, oocytes, or ovarian tissue. Young patients with cancer should be referred to a fertility specialist with the ability to discuss and deliver these services. BCMJ

Fertility preservation for cancer patients

- Breast cancer is the most common cancer in reproductive-age woman.
- Alkylating agents used in chemotherapy are gonadotoxic.
- The ability to have children in future is important to the majority of cancer patients.
- Options for fertility preservation include:
  - Embryo freezing (with partner sperm or donor sperm).
  - Oocyte freezing.
  - Ovarian tissue freezing (experimental).
  - Sperm freezing.
- Fertility preservation can generally be performed at little or no cost to the patient through the Fertile Future Foundation.

Competing interests

None declared.

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Transition to a three-dose rotavirus vaccine in BC

Beginning April 2018, BC and other Canadian provinces and territories will begin to use the pentavalent rotavirus vaccine (RV5, RotaTeq, Merck Canada) in their immunization programs for infants, replacing the use of the monovalent live attenuated vaccine (RV1, ROTARIX, GlaxoSmithKline), which has been used in BC since the program started in January 2012. This change is a result of a federally coordinated bulk-purchasing process in which all Canadian jurisdictions participate, and the term for the new contract will be for up to 3 years.

As is RV1, the RV5 is a live orally administered vaccine with similar contraindications. Both rotavirus vaccines are recommended for use by the National Advisory Committee on Immunization, without a preferential recommendation for one or the other. Both have been used globally in national immunization programs. Comparable vaccine effectiveness (VE) for the two has been observed in postmarketing surveillance evaluation for outcomes of hospitalization, emergency department visits, and outpatient visits. In low rotavirus mortality countries such as Canada, for RV1, median VE was 84% (range, 19%–97%) in 13 studies, and for RV5, median VE was 90% (range, 63%–100%) in 20 studies.[1]

The main difference for the BC program will be the schedule of immunization: for RotaTeq, is is *three* doses, at 2, 4, and 6 months of age, whereas for ROTARIX, it was *two* doses at 2 and 4 months of age. The series can be started as early as 6 weeks of age, but Canadian recommendations are for series completion by 8 months and 0 days of age; these parameters are common to both products and are based on potential association with intussusception. Based on BC immunization registry data for participating health authorities (all but Vancouver Coastal), rotavirus vaccine 2-dose series completion rates have increased by 12% since the first year of the program. By year of birth, these rates are 70% for 2012, 75% for 2013, 79% for 2014, and 81.8% for 2016.[2] In moving to the RotaTeq product, however, providers will need to increase their efforts to achieve on-time immunization through use of reminders and recalls based on current completion rates for the coadministered DPT-containing vaccine. For infants born in 2016, while 87.6% received 2 doses of DPT-containing vaccine by 8 months of age, only 76.6% have completed 3 doses of DPT-containing vaccine by this milestone; 14.3% never started a series of rotavirus vaccine.

BC health units will be working with physician providers as they transition from RV1 to RV5, as the timing of this change will vary depending on remaining RV1 inventory at the local level. The two vaccines are not considered interchangeable and, ideally, infants who commence a series with RV1 should complete the second dose with that product. Those who must transition to RV5 after starting RV1 should receive a total of 3 doses of rotavirus vaccine.

In several prior surveys of BC parents, concern about vaccine safety has been the most frequently cited reason for refusal of vaccines. Both approved rotavirus vaccines have demonstrated high levels of safety and are well tolerated. While intussusception had been observed at a rate of about 1 in 10 000 recipients with a prior rotavirus vaccine approved in the USA in the 90s, this adverse event has not been consistently observed in all countries and studies using the RV1 and RV5 vaccines. At present and based on a large number of studies in different global settings, the generally accepted excess risk of intussusception is 1 to 2 cases per 100 000 vaccine recipients, mainly associated with the first dose.[3] This risk, however, has not been detectable in the Canadian population using administrative data on hospitalized intussusception among infants, and in that study there was no increase in the rate of intussusception following introduction of rotavirus vaccine.[4]

Finally, it is important for providers to be aware that administering the rotavirus vaccine prior to injectable vaccines given at the same visit has been demonstrated to provide comparable analgesic effect to that of orally administered sucrose solutions.[5] Both rotavirus vaccines contain similar quantities of sucrose[6,7] and this analgesic effect is expected with use of RV5 given prior to injectable vaccines, of which up to three injections are recommended for coadministration at the 2, 4, and 6 month visits, respectively.

BC resources for the use of vaccines including rotavirus are online.[8,9]

—Monika Naus, MD, MHSc, FRCPC, FACPM
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BC Centre for Disease Control

This article is the opinion of the BC Centre for Disease Control and has not been peer reviewed by the BCMJ *Editorial Board.*

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obituaries

Dr W.R.J. (Bill) Martin 1927–2017

It is with much sadness I write of the passing of my friend, a long-time colleague, Dr W.R.J. (Bill) Martin on 26 December 2017. Bill passed away peacefully in his home on Galiano Island surrounded by his beloved family. He was predeceased by his wife, Gwen, and leaves his four children, Shelley, Sandy, Craig, and Scott and their families. He also leaves two surviving siblings and numerous nieces and nephews.

Bill practised ophthalmology in Burnaby for over 30 years in conjunction with a long-term partnership with Drs Jack Siddall, Sam Gibson, Don Matheson, and later Drs Bill Pratt and Larry Daitz. Bill always put the interest of his patients first and practised medicine with a high degree of skill and integrity. Bill and Gwen were active in the medical community in Burnaby, and Bill was given a long-term service medal by Burnaby Hospital in recognition of his many years of service to that institution and the community.

Bill was born and raised in Burnaby. He and his siblings grew up during the Great Depression when money and work was scarce. Nevertheless, after the war, Bill attended the University of Oregon and UBC where he met and married the love of his life, Gwen, a romance that lasted over 60 years.

Bill was a member of the first graduating class of the medical school at UBC in 1954. He did a few years of practice with his boyhood friend, Dr Hugh Pontifex, mostly in Merritt. He loved the challenges of bringing modern medicine to what was then an isolated community.

Bill took his eye training at Vancouver General in the late 1950s, and during his residency, he was instrumental in assisting the new professor of ophthalmology, Dr AJ Elliot, in modernizing and expanding the department at Vancouver General Hospital and UBC.

Bill and Gwen retired to Galiano Island in 1991 and quickly adapted to island life. Bill spent a few years as a consultant in ophthalmology for the Workers' Compensation Board. He and Gwen traveled widely, and Bill indulged in his lifelong passion of woodworking producing many beautiful grandfather clocks and guitars, which are now family treasures.

Bill lost his beloved Gwen in 2011. His health began a slow decline and he left us gently in the last days of 2017 in his 91st year.

Bill was a man of high intelligence, great kindness, and integrity. He adored his family, and his family adored him. His was a life well lived.

Rest in peace, my friend.

—D.C. Matheson, MD, FRCSC
North Vancouver

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CHRONIC PAIN MANAGEMENT
Various locations, starting 24 Apr (Tue)
Not Just a Prescription Pad: A Multimodal Approach to Chronic Pain Management. Courses will be hosted by WorkSafeBC throughout the province. The sessions align with the College of Physician and Surgeons of BC's Standards and Guidelines for the safe prescribing of opioids and will interest physicians keen on learning more about best practices in the treatment of chronic noncancer pain. Physicians certified in addiction medicine will address issues relating to the risks and benefits of various pharmacological and nonpharmacological strategies for the treatment of chronic noncancer pain. Learn more about safe prescribing of opioids; tapering, substitution, and exit strategies; evidence for various other treatments; community and regional resources and support, including WorkSafeBC programs; and more. Dinner is included. To register or obtain more information, including other dates and locations, go to events.eply.com/chronicpain.

HOT TOPICS IN MENTAL HEALTH 2018
Vancouver, 2 Jun (Sat)
The UBC Department of Psychiatry is once again offering this popular one day update for primary care physicians and other mental health care professionals on current psychiatric topics. This course will be held at UBC Robson Square. All presentations will be very practical and relevant to daily medical practice. Participants will examine common and challenging mental health conditions and acquire evidence-based strategies to apply in practice. Don't miss out! To register and for more information visit https://ubccpd.ca/course/MH2018, or email: cpd.info@ubc.ca.

CME ON THE RUN
VGH and various videoconference locations, to 8 Jun (Fri)
CME on the Run sessions are held at the Paetzold Lecture Hall, Vancouver General Hospital, and there are opportunities to participate via videoconference from various hospital sites. Each program runs on Friday afternoons from 1 p.m. to 5 p.m. and includes great speakers and learning materials. Topics and dates: 8 June (MSK, sports medicine, and rheumatology)—Chronic foot and ankle pain; Biologics for Rheumatoid Arthritis and Beyond; Utility of Rheumatologic Lab Investigations; Osteoarthritis and Office Injection: What Works; Osteoporosis Update 2018; Evidence-based Diagnosis of Fibromyalgia; Sports Injuries of the Knee: Diagnosis and Management; MVA Office Visit: What to Assess and What to Document? What Are We Responsible For? To register and for more information, visit ubccpd.ca, call 604 875-5101, or email cpd.info@ubc.ca.

CINI 2018
Surrey, 8-11 Jun (Fri-Mon)
Canada India Networking Initiative 2018, like its predecessors in 2010 and 2014 is designed as an outcome-focused interactive conference. The context is of building a healthy civil society thorough innovation, technology, and engagement in health care. Conference sessions will comprise the sharing of work being done by the speakers to build further depth and capacity for the project. Each session is further enhanced by designated champions who are experts in their own right and committed to the area. Our partners Simon Fraser University, Fraser Health, Global Association of Physicians of Indian Origin, Canadian Association of Physicians of Indian Origin, and Physicians with Interest in South Asia will kick off the conference. Though our focus is South Asian population, the learnings are scalable and applicable to the population at large and will cover a variety of topics. The conference will end with closings session reports by the respective champions and include recommendations and next steps. The conference will focus on how we connect, build networks, and collaborate to build healthy civil society in the context of the Canada and India partnership. Facebook: Canada India Network Society; Twitter: @the cins. Full program and registration information: www.thecins.org.

PRACTICE SURVIVAL SKILLS
Vancouver, 9 Jun (Sat)
UBC CPD's 11th annual Practice Survival Skills—What I Wish I Knew in My First Years of Practice will be held at UBC Robson Square. This course will emphasize practical, nonclinical knowledge crucial for your career with topics such as billing, navigating through the medical organizations, accreditation, practice audits, medicolegal advice and report writing, job finding, office skills and management, physician resources, practice management, and avoiding physician burnout. Target audience: family physicians, specialty physicians, locums, IMGs, physicians new to BC, family practice and specialty residents, physicians working in episodic care settings. Course format: collaborative didactic lectures and interactive small-group workshops; plenty

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of networking opportunities; practice-based exhibits. Join us at the end of the day for a job fair and networking reception to meet with colleagues and make career connections! Conference information, program details, and online registration: ubccpd.ca/course/practice-survival-skills-2018. Tel 604 875-5101; fax 604 875-5078; email cpd.info@ubc.ca; web https://ubccpd.ca.

FERTILITY & REPRODUCTIVE MEDICINE SYMPOSIUM
Vancouver, 13 Jun (Wed)
This symposium is hosted by the Pacific Centre for Reproductive Medicine and will be held at the Chan Centre for Family Health, 950 W 28 Ave. The program starts with breakfast and registration at 7:30 a.m., includes a refreshment break at 9:45 a.m., lunch at 12:15 p.m., and ends with a reception at 5 p.m. Excellent local faculty featuring Drs Caitlin Dunne, Jeff Roberts, Jon Havelock, Ken Poon, Rebecca Warburton, Sabrina Gill, Sheona Mitchell, Tim Rowe, and Ken Seethram. Admission is complimentary. RSVP auni@pacificfertility.ca. Check out our physician resources page at pacificfertility.ca.

GP IN ONCOLOGY TRAINING
Vancouver, 10 Sep–21 Sep and 18 Feb–1 Mar 2019 (Mon–Fri)
The BC Cancer Agency's Family Practice Oncology Network offers an 8-week General Practitioner in Oncology training program beginning with a 2-week introductory session every spring and fall at the Vancouver Centre. This program provides an opportunity for rural family physicians, with the support of their community, to strengthen their oncology skills so that they may provide enhanced care for local cancer patients and their families. Following the introductory session, participants complete a further 30 days of customized clinic experience at the cancer centre where their patients are referred. These can be scheduled flexibly over 6 months. Participants who complete the program are eligible for credits from the College of Family Physicians of Canada. Those who are REAP-eligible receive a stipend and expense coverage through UBC's Enhanced Skills Program. For more information or to apply, visit www.fpon.ca, or contact Jennifer Wolfe at 604 219-9579.

SURVIVORSHIP CARE POSTTREATMENT FOR PROSTATE & BREAST CANCER
Vancouver, 29 Sep (Sat)
Please join us for this comprehensive update hosted by Vancouver Prostate Cancer Centre's Prostate Cancer Supportive Care Program. To be held at the JW Marriott Parq Vancouver, this conference (https://ubccpd.ca/course/

CME listings rates and details

Rates: $75 for up to 150 words (maximum), plus GST per month; there is no partial rate. If the course or event is over before an issue of the *BCMJ* comes out, there is no discount. Visa and MasterCard accepted.

Deadlines:

Online: Every Thursday (listings are posted every Friday).

Print: The first of the month 1 month prior to the issue in which you want your notice to appear, e.g., 1 February for the March issue. The *BCMJ* is distributed by second-class mail in the second week of each month except January and August.

Send material by email to journal @doctorsofbc.ca. Tel: 604 638-2815. Please provide the billing address and your complete contact information.

survivorship2018) is geared to all physicians and allied health providers dealing with survivorship issues of breast and prostate cancer patients after initial diagnosis and treatment. The seminar will review selected issues of relevance to survivors of breast and prostate cancer and will address how the primary care, family physicians, and allied health providers can help recognize and/or mitigate issues of importance relevant to these populations of cancer patients. Target audience: health professionals in primary care, family physicians, general practitioners in oncology, allied health providers, residents, and medical students. Accreditation: Up to 4.75 Mainpro+/MOC Section 1. Register: https://www.eply.com/survivorship2018.

MINDFULNESS IN MEDICINE
Molokai, HI, 13–20 Oct (Sat–Sat)
Now is the time! Join Dr Mark Sherman on the pristine Hawaiian island of Moloka'i for this 7-day mindfulness meditation retreat for physicians. The retreat is an opportunity to learn mindfulness and meditation skills, connect with fellow physicians, and to bring a restored perspective and vitality into your personal and professional life. We will offer instruction in basic and more advanced meditation practice interspersed with small group discussions and sharing, with an opportunity for self-reflection and deep rest. Please see http://livingthismoment.ca/event for more information and to register. Contact mark@livingthismoment.ca for any questions.

INFECTIOUS DISEASES SYMPOSIUM
Surrey, 20 Oct (Sat)
The 4th annual Infectious Diseases Symposium will be held at Surrey Memorial Hospital, UBC Lecture Hall, Floor-B, Critical Care Tower. Symposium chair: Dr Yazdan Mirzanejad. Topics: Adult immunization and resurgences, necrotizing fasciitis, meningitis, high-risk infection during and after pregnancy, fever in returned travelers, parasitic infections in refugees and immigrants, common infections in transplanted patients, fever in children in the office and emergency room settings, and pitfalls in interpretation of infectious diseases diagnostics. Event speakers: Drs Tony, Monika Naus (BCCDC), Drs Alissa Wright, Laura Sauve, Mike Chapman, Miguel Imperial, Katherine Plewes, Meera Anand, Julie Schalwyk, and Yazdan Mirzanejad. Further information and registration: https://events.eply.com/infectious-diseases-day-2018-10-20.

classifieds

BCMJ BC Medical Journal

CLASSIFIED ADVERTISING (limited to 700 characters)

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Doctors of BC members: $50 + GST per month for each insertion of up to 350 characters. $75 + GST for insertions of 351 to 700 characters. We will invoice on publication.
Non-members: $60 + GST per month for each insertion of up to 350 characters. $90 + GST for insertions of 351 to 700 characters. We will invoice on publication.

Deadlines: Ads must be submitted or cancelled by the first of the month preceding the month of publication, e.g., by 1 November for December publication. Please call if you have questions. Tel: 604 638-2858.
Submit requests at www.bcmj.org/classified-advertising-submission-form.

practices available

N VANCOUVER—PRACTICE TAKEOVER OPPORTUNITY
Permanent physician or long-term locum required to take over a well-established and high-revenue family practice in North Vancouver—an area known for its great lifestyle, outdoor pursuits, and wonderful community. This is a latch key practice with group support and an associated walk-in clinic. There is an established base of 2800 patients with the current physician billing $300K plus per year working 4.5 days per week. There is the opportunity to buy into the clinic if desired. Experienced MOAs, electronic records, and well-set-up supportive and harmonious working environment. Contact Dr Rockford Samborski at lvclinic@telus.net.

QUADRA ISLAND—PRACTICE FOR SALE
Family practice for sale: $1.00! The right doctor for this clinic wants a low stress, no hospital, full- or part-time practice with nurse practitioner support and rural CME and locum funding in an amazing, beautiful, small, island community a short ferry ride from Vancouver Island. Call Mary at 250 285-3540 or email office@qimc.ca.

VANCOUVER (S GRANVILLE)—FAMILY PRACTICE
Solo general practice on Granville and 16th Ave. Doctor retiring. Busy practice, attractive location. Replacement needed by 1 September. Practice could be split by 2 doctors. For information: phone 604 731-6212, fax 604 731-9703.

VANCOUVER—FP BREASTFEEDING MEDICINE
The Vancouver Breastfeeding Centre is looking for an enthusiastic physician with a special interest in breastfeeding medicine to join the clinic. The retiring MDs will offer mentorship as needed. Maternal and child health experience and IBCLC qualification are assets. Visit www.breastfeedingclinic.com for further information.

VICTORIA—OPPORTUNITY: JOIN OR BUY
Well-established, busy walk-in clinic with family practices on site. Looking to add more owners or to sell clinic outright. Attractive business/practice opportunity. Reply to victoria mdclinic@gmail.com.

employment

ABBOTSFORD—GP/WALK-IN, FT OR LOCUM
Physicians looking to start a practice or to relocate and enjoy the beauty of BC will be pleased to work in our state-of-art facility using OSLER EMR. Great working environment and well-trained staff. Compensation is fee-for-service with an estimated remuneration of 250K per year (70/30 overhead split). BC licence required. International graduates who need to work within the College of BC Guidelines welcome. Website: https://windermeremedicalclinic.ca.

ABBOTSFORD—LOCUMS
Full-service East Abbotsford walk-in clinic requires locum physicians for a variety of shifts, including weekends and evenings. Generous split; pleasant office staff and patient population. Please contact Cindy at 604 504-7145 if you are interested in obtaining more info.

ARMSTRONG—FT FAMILY PHYSICIAN
Haugen Medical Group, located in the heart of the North Okanagan, is in need of a full-time family physician to join a busy family practice group. Flexible hours, congenial peers, and competent nursing and MOA staff will provide exceptional support with very competitive overhead rates. Obstetrics, nursing home, and inpatient hospital care are not required, but remain optional. Payment schedule: fee for service. If you are looking for a fulfilling career balanced with everything the Okanagan lifestyle has to offer, please contact Maria Varga for more information at mariaka1@telus.net.

BURNABY—FAMILY PHYSICIAN, FT/PT OR LOCUM
Family practice, located across from Metrotown Mall, two-physician clinic seeking an associate to join a very busy practice with a large Cantonese/Mandarin patient base. Possibility of taking over the practice. OSCAR EMR. Convenient parking. Negotiable split. Please email bbymedclinic@gmail.com.

BURNABY—FP/WALK-IN, FT OR LOCUM
Canway Medical Centre, Burnaby, is seeking an associate to join their team of family physicians. Clinic has diverse patient population (ages and genders). We have OSCAR EMR; friendly, knowledgeable, and skilled staff. Flexibility to work full- or part-time, walk-ins or build your own practice. This clinic is bright and spacious, situated in a Burnaby neighborhood close to businesses, BCIT, and Burnaby Hospital. We have a pharmacy and free parking on site. We have an overwhelming flow of patients. If interested or for more information, call 604 428-8123, email canwaymedical@shaw.ca, or visit our website: www.canwaymedicalcentre.ca.

ELKFORD/FERNIE—LONG-TERM LOCUM
Six-month locum/vacation opportunity from Jan to July 2019. Half-time rural practice in Elkford, BC; 2.5 days/wk. Group practice clinic (ER skills required). Generously compensated. Accommodation: 4-bedroom home in ski/bike resort community of Fernie BC. Amazing opportunity for a work/play adventure! Contact kimberleyareid@hotmail.com for info.

KELOWNA—LOCUM NEEDED
Locum needed for solo practice in Lower Mission; any part or all of 29 April to 20 May 2018. Brand new office with beautiful facilities and great MOAs. If you wish to work FT hours there is plenty of work; I usually only work T-W-Th and cover about 20 nursing-home patients. No obs, no inpatients. Call Pam at 250 863-8456 or email pamandderm@gmail.com.

KELOWNA—RADIOLOGIST LOCUM
Our busy hospital and community clinic practice is in need of locum coverage from mid-

March to the end of December 2018 due to maternity leave. Short and longer terms available. Modalities covered include: fluoroscopy and DR, US with procedures, CT with biopsies, MRI, mammography and stereo biopsies. NM, angio/interventional available but not required. Contact Dr Mike Partrick at michael.partrick@interiorhealth.ca.

NANAIMO—GP
General practitioner required for locum or permanent positions. The Caledonian Clinic is located in Nanaimo on beautiful Vancouver Island. Well-established, very busy clinic with 26 general practitioners and 2 specialists. Two locations in Nanaimo; after-hours walk-in clinic in the evening and on weekends. Computerized medical records, lab, and pharmacy on site. Contact Ammy Pitt at 250 390-5228 or email ammy.pitt@caledonianclinic.ca. Visit our website at www.caledonianclinic.ca.

NANAIMO—NEW 1-YEAR CCFP-EM RESIDENCY POSITION
UBC CCFP-EM St. Paul's Program offering 1yr re-entry opportunity in Nanaimo-based pilot, 1 August 2018–19. Rotations mirror St. Paul's with increased rural/dual practice. Academic sessions conjointly with St. Paul's/locally. Successful completion allows candidate to write CCFP-EM exam. Applicants should be practising BC physicians, CCFP-qualified with interest/commitment to nonurban care. Applicants should be aware that this is a PGY3 position with corresponding benefits and responsibilities. Applications through http://postgrad.familymed.ubc.ca/enhanced-skills-program/admissions, send to Dr Tina Webber (tina.webber@ubc.ca). Closing date: 15 May 2018. Selection: 1 June, following phone/in-person interviews.

NORTH VAN—FP LOCUM
Physician required for the busiest clinic/family practice on the North Shore! Our MOAs are known to be the best, helping your day run smoothly. Lucrative 6-hour shifts and no headaches! For more information, or to book shifts online, please contact Kim Graffi at kimgraffi@hotmail.com or by phone at 604 987-0918.

PITT MEADOWS—FAMILY PHYSICIANS
We are seeking three full-time family physicians to join our team at the New Pitt Meadows Medical Clinic. We encourage physicians to have a full family practice with regular shifts in our very busy walk-in clinic. The NPMMC is a purpose built, well established, and highly reputed practice in Pitt Meadows with beautiful views. It is ideally situated between Coquitlam and Maple Ridge in a high-visibility, high-traffic location. We have excellent staff. Low overheads for full-time physicians. At present, the clinic is open 6 days per week. For further details visit www.newpittmeadowsmedicalclinic.ca or contact Dr L. Challa at 604 465-0720.

POWELL RIVER—EMERGENCY MEDICINE
Part- or full-time ER locum. Flexible shifts in single-coverage ER with good specialist back up. 50+ patient visits per day, good imaging and lab coverage (including limited CT scan coverage). Length: 2-week to 3-month locums. Powell River is a family-oriented community and an outdoor playground with multiple lakes, trails, and ocean activities. Contact Robert Head at prerscheduling@gmail.com or 604 344-0636.

POWELL RIVER—LOCUM
The Medical Clinic Associates is looking for short- and long-term locums. The medical community offers excellent specialist backup and has a well-equipped 33-bed hospital. This beautiful community offers outstanding outdoor recreation. For more information contact Laurie Fuller: 604 485-3927, email: clinic@tmca-pr.ca, website: powellrivermedicalclinic.ca.

S SURREY/WHITE ROCK—FP
Busy family/walk-in practice in South Surrey requires GP to build family practice. The community is growing rapidly and there is great need for family physicians. Close to beaches and recreational areas of Metro Vancouver. OSCAR EMR, nurses/MOAs on all shifts. CDM support available. Competitive split. Please contact Carol at Peninsulamedical@live.com or 604 916-2050.

SURREY/DELTA/ABBOTSFORD—GPS/SPECIALISTS
Considering a change of practice style or location? Or selling your practice? Group of seven locations has opportunities for family, walk-in, or specialists. Full-time, part-time, or locum doctors guaranteed to be busy. We provide administrative support. Paul Foster, 604 572-4558 or pfoster@denninghealth.ca.

TERRACE—FAMILY PHYSICIAN, NEW CLINIC
Join our new primary care office opening in Terrace, BC. Only 80 minutes north of Vancouver. Opening in August 2018, the HG Health Centre offers complete provision of medical office infrastructure to operate your own professional family practice. Outstanding specialist support: gen surg, int med, peds, OBGYN, psych, ENT, urology, ophthalmology, and oncology. Obstetrics and ER available, not mandatory. ER: uniquely APP funded, and point-of-care diagnostics. DI dept includes MRI and on-site radiology. Expand your scope and vision in your own family practice, and sculpt your personal work-life-balance in this unique opportunity. Please contact hermangreeff@gmail.com.

VANCOUVER/RICHMOND—FP/SPECIALIST
We welcome all physicians, from new graduates to semiretired, either part-time or full-time. Walk-in or full-service family medicine and all specialties. Excellent split at the busy South Vancouver and Richmond Superstore medical clinics. Efficient and customizable OSCAR EMR. Well-organized clinics. Please contact Winnie at medicalclinicbc@gmail.com.

VANCOUVER—FT/PT FAMILY PHYSICIANS & PSYCHIATRISTS
New medical office in the Fairmont Medical Building is looking for family physicians who want to move or start a practice. Office features four fully furnished exams rooms; able to accommodate both paper and EMR (Accuro) practices. Office hours are flexible and available 7 days a week (7 a.m.–7 p.m.). MOA and support staff provided. Clinic has many unattached patients looking for a family doctor, and is accompanied with available VDofP supports to help build a practice. Offering 70/30 split. Email raz@elitemedicalassociates.com.

VICTORIA—GP/WALK-IN
Shifts available at three beautiful, busy clinics: Burnside (www.burnsideclinic.ca), Tillicum (www.tillicummedicalclinic.ca), and Uptown (www.uptownmedicalclinic.ca). Regular and occasional walk-in shifts available. FT/PT GP post also available. Contact drianbridger@gmail.com.

VICTORIA—PERMANENT/P-T FP
Experienced family physician wishing to expand medical team at Mattick's Farm in beautiful Cordova Bay. Fully equipped office, OSCAR EMR, congenial staff, close to schools. Contact phoughton@shawcable.com, phone 250 658-5228.

medical office space

NEW WEST—GP FOR EST. HEALTH CLINIC
Polo Health+Longevity Centre on Columbia street in New Westminster is looking to expand our team. We are looking for a general practitioner to join our dynamic health team and integrated clinic. There is an available treatment room with a designated area at the front desk for your own personal MOA. We have our own on-site pharmacy as well. We have street parking and skytrain access. You would be joining a team of other health care providers, psychologists, medical aesthetics, and more. Please send resumes to drallanapolo@gmail.com. Visit www.polohealth.com for more information on our health centre.

SIDNEY, BC—BRIGHT CLINIC SPACE
Bright, two-op clinic space available in the heart of Sidney BC Fully furnished; waiting room, front desk area with Internet, landline, fax, two operatories, sterilization room, and restroom. Days available are flexible. To view please call 250 920-5043.

SURREY—MED OFFICE FOR LEASE
Looking to relocate or starting your own medical practice (solo or group)? Turn-key medical

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spaces available (600–2200 sq. ft.) for lease with all-inclusive low rates. Prime locations next to established pharmacies. Spaces located in Surrey, Delta, and Fleetwood. For more information, contact 604 518-1952 or email medicalspacesbc@gmail.com.

VANCOUVER (KERRISDALE)—OFFICE SPACE
Airy, spacious, quiet office available for a psychiatrist or psychologist on Fri and/or weekends. Located in Kerrisdale Prof. Bldg., an exceptionally convenient location for access by public transit or car, with a large amount of free residential parking available. Close to pharmacies, labs, a walk-in clinic, coffee shops, and restaurants—all within walking distance. The office is accessible by stairs and elevator. Consists of a waiting area that seats two people; a large reception desk; file storage room; and large, bright, comfortable interview room/office. If interested please contact Dr Lewis Pullmer at dr.pullmer@gmail.com, or contact the office directly at 604 872-3422.

VANCOUVER (MAIN STREET)—2 MED OFFICE SPACES FOR LEASE
Two separate second-floor office spaces for lease: 650 and 600 sq. ft. Both set up as general medical. Established pharmacy on main floor. Unit 1: $1500/month, waiting room, three exam or office rooms. Unit 2: $1400/month, waiting room, two exam rooms, one small office. No elevator access. Utilities and unit cleaning included, property tax $5800/year. Contact Matthew at mhuangvan@gmail.com.

VANCOUVER (W BROADWAY & CAMBIE)—MED OFFICE SPACE, SALE OR LEASE
Highly desirable Broadway and Cambie location, minutes walk to VGH and Broadway-City Hall Canada Line station. Underground visitors' parking for patients' convenience. Medical office space for sale or ease: 500 to 600 sq. ft.; lease: 3162 sq. ft. Visit www.550WestBroadway.com or call 604 505-6810 for more details.

VANCOUVER—LARGE SPACE
Very large (approx. 2400 sq. ft.), well-maintained space in a recently renovated single-level building in South Vancouver. Ideal for a walk-in clinic. Located near Champlain Mall and steps from a community centre, school, park, and other businesses. Chiropractor, dentist, and pharmacy already in the building. Street-level parking with over 20 spaces. Entrance to the building and the clinic is very accessible to patients (no stairs or elevators). Densely populated residential neighborhood. Email southvanclinic@outlook.com.

VANCOUVER—TWO RENOVATED OFFICES CLOSE TO VGH
Two fully renovated office spaces available close to VGH with city views. Close to the Broadway–City Hall Canada Line station on Cambie for your patients' convenience. The offices are suitable for psychiatrists, psychologists, or counselors. New furniture, including in the waiting area. Customize your office and bring in your phone, fax machine, etc. Offices are available immediately on a 1-year lease basis; however, will consider other options. Negotiable and reasonable rent. Call or text 604 970-6600 or e-mail wahan.wanis@ubc.ca.

vacation properties

PROVENCE, FRANCE—YOUR VILLA
Les Geraniums, a luxury 3-bedroom, 2½ bath villa, is your home in the heart of Provence. Expansive terrace with pool and panoramic views. New kitchen and bathrooms. Walk to lovely market town. One hour to Aix and Nice. Come and enjoy the sun of southern France! 604 522-5196. villavar@telus.net.

SHUSWAP LAKE—COTTAGE, WATER ACCESS ONLY
Rent by the week or buy the lease to this idyllic summer retreat. View photos on OKhome seller.com, #26805. Call or text Mike Stanger 1 250 361-6115.

miscellaneous

CANADA-WIDE—MED TRANSCRIPTION
Medical transcription specialists since 2002, Canada wide. Excellent quality and turnaround. All specialties, family practice, and IME reports. Telephone or digital recorder. Fully confidential, PIPEDA compliant. Dictation tips at www.2ascribe.com/tips. Contact us at www.2ascribe.com, info@2ascribe.com, or toll free at 1 866 503-4003.

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MILL BAY (BRENTWOOD COLLEGE WATERFRONT)—HOME & COTTAGE FOR SALE (1.38 ACRES)
Nature's paradise. True oceanfront in the finest natural setting on Vancouver Island offering over an acre of land with mature douglas fir and native arbutus trees. South-facing seafront at the end of a quiet road; 2900 sq. ft. home is a detailed work of art tastefully updated with every consideration given to modern lifestyle comforts; impressive wildlife-viewing master bedroom with 5-piece ensuite. Relaxing hot tub a few steps to restored historic 800 sq. ft. guest cottage set at ocean's edge. Up-close wildlife viewing for nature lovers. Minutes to Mill Bay Village, the Marina, and Brentwood College. Contact Suzanne Bowen 250 360-7557.

PATIENT RECORD STORAGE—FREE
Retiring, moving, or closing your family or general practice, physician's estate? DOCUdavit Medical Solutions provides free storage for your active paper or electronic patient records with no hidden costs, including a patient mailing and doctor's web page. Contact Sid Soil at DOCUdavit Solutions today at 1 888 781-9083, ext. 105, or email ssoil@docudavit.com. We also provide great rates for closing specialists.

VANCOUVER—TAX & ACCOUNTING SVCS
Rod McNeil, CPA, CGA: Tax, accounting, and business solutions for medical and health professionals (corporate and personal). Specializing in health professionals for the past 11 years, and the tax and financial issues facing them at various career and professional stages. The tax area is complex, and practitioners are often not aware of solutions available to them and which avenues to take. My goal is to help you navigate and keep more of what you earn by minimizing overall tax burdens where possible, while at the same time providing you with personalized service. Website: www.rwmcga.com, email: rodney@rwmcga.com, phone: 778 552-0229.

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Delta Hotel Vancouver

Newly renovated guest suites just steps from historic Gastown and Vancouver's waterfront. Starting at **$174/night**. Call 1 844 254 5048 and ask for the Doctors of BC Corporate Rate.

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