

# Current approaches to infectious diseases

## PART 2



### **Current approaches to infectious diseases, Part 2**

Duration of therapy for common bacterial infections in adults

Chronic hepatitis B in BC

Epidemiology of Lyme disease and pitfalls in diagnostics

Travel-acquired infections and illnesses in British Columbians



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*Chronic hepatitis B is caused by the hepatitis B virus, a member of the Hepadnaviridae family. It is a common infection with a worldwide prevalence of more than 250 million people.*

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### ON THE COVER

Without a concerted societal effort, antimicrobial resistance is predicted to kill more people than cancer by the year 2050. Theme issue begins on page 206.

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*Changes over the last 2 years have resulted in a permanent shift to virtual-enabled health care, accelerating transformation of BC's health care system faster than we ever imagined possible. Article begins on page 201.*

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# Valuing time and care

**M**orale of the average family physician of the longitudinal full-service variety is at a very low level in our province. In fact, fatigue from the pandemic, demands from stressed patients, increased paperwork, and rising overhead costs are all factors causing *many* BC physicians' morale to drop, not only full-service longitudinal-care family physicians. These physicians are crying foul at the stagnation in their take-home pay relative to other physicians, other health care providers, and other occupations.

I don't begrudge my hardworking colleagues who are earning more than I am, and I certainly don't want to divide our profession. At present, there is no incentive for family physicians to work in a practice that provides full-service longitudinal care. First, we are not trained in medical school to run a small business. Second, overhead costs are rising at a much faster rate than our fee schedule. This point is very important, I believe, and applies to all physicians running their own offices.

A number of years ago, Doctors of BC (then the BCMA), set an hourly rate (currently \$160) intended to compensate family physicians for the work they did outside of their practice—for example, committee work for the association. This rate is now used as a guideline for contracts with family physicians working as hospitalists or in urgent and primary care clinics. What seems to have been forgotten is that the hourly rate was originally designed to include an amount for office overhead costs, based on the premise that our office overhead continues whether we are in our offices or not. I am not suggesting that hospitalists be paid less. My hospitalist colleagues work hard and deserve every penny they earn. What I am suggesting is that the puny Business Cost Premium does not even come close to compensating us for the added costs of running an office

practice, over and above what family physicians who don't have business costs earn.

Newly qualified family physicians are voting with their feet. Very few are heading into office-based practices with overhead. Family physicians with years of experience are doing likewise by working less or shutting down their offices in favor of retirement or other work—for example, as hospitalists or as urgent and primary care clinic physicians. As a result, the number of unattached patients is growing steadily. It's ironic that urgent and primary care clinics were meant to be the government's solution to the growing number of unattached patients.

As Doctors of BC and the BC government negotiate a new Physician Master Agreement, they need to come up with creative ways of compensating physicians who own and work in their practices, which differentiates them from physicians who don't pay business costs. This compensation should not be available to medical clinic owners who do not work as physicians in those clinics, and it should reward full-service longitudinal family physicians fairly, relative to their colleagues who provide episodic care, those who don't operate small businesses, and those who offer only virtual care.

Ultimately, it comes down to what each person at the negotiating table wants from their family physician. What I want from my family physician is someone who has the time to get to know me and care about me, and someone who is not stressed by having to run their own practice with rising business costs and increasing intensity of their work.

I can't write such a gloomy editorial without throwing in a small piece of humanity. I was standing in a long line at the bank recently, when an elderly lady holding a cane took her place behind me in the line. I offered to let her go ahead of me. She was quite feisty and asked

me why I thought that she deserved to go ahead of me in line. I told her it was because she was holding a cane. Her response, with a cheeky grin, was that she was just holding it, and that she didn't need to use it. She eventually took me up on my offer and moved ahead of me.

A few minutes later, a very frail-looking elderly lady with a cane joined the line. She could barely stand and was leaning heavily on her cane and the railing. I assisted her to the front of the line and into the bank, where a bank employee found her a chair. As I walked back to my place in line, the first lady I had helped remarked that there was always someone worse off than oneself. Despite my sombre tone, I am always cognizant of the fact that there are many people worse off than I am. ■

—David Chapman, MBChB


**Newly qualified family physicians are voting with their feet. Very few are heading into office-based practices with overhead.**

Attn: BC Doctors


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# Carpe diem?

I am rethinking *carpe diem* (seize the day). We who have a career in medicine have a clear understanding of the long haul—planning years in advance the steps we need to take, where we need to be, who we need to find, and how long we will need to work before seeing the end of the tunnel. We knowingly walk our particular fork in the road, weary head down and eyes focused, miles before even the potential of seeing if the destination is as wonderful as we expect it to be.

Straying off the line, especially in competitive fields, may have led to questions about a lack of commitment or focus. There was always an exam to prepare for, a talk to attend, a procedure to learn, a teachable moment, a new rotation. When I finished my Royal College exams, I realized it was the first time since

high school that I didn't have my next month programmed for me.

If I'm recognizing it correctly, there is a decidedly different mood now. Many in my kids' generation realistically believe that the Earth as we know it may cease to exist within their lifetimes. They are not as interested in the long haul if it means sacrificing too much of the now. They will probably not be able to afford a house, and having a basic university degree may not give them enough career advantage to balance the incurred debt, both financial and temporal. Many don't drive. Many won't have kids. There is a highly subscribed-to Reddit site called FI/RE (Financial Independence/Retiring Early) where people look

for ways to *not* have long careers. What many appear to be doing differently from my generation is taking control of their paths in ways we had been programmed to think were short-sighted and only immediately gratifying.

The pandemic has been a big wake-up. We can now *really* see how little friggin' control we have, how vulnerable our pithy plans are. How a tiny particle that didn't exist 5 years ago can upend the world economy, our work, our political activity, our family structure, our *plans*. How even when being careful and vaccinated and masked people could die as a result of their short-term choices. The novel downtime we had for retrospection during the beginning of lockdown let us recognize that we hadn't sufficiently appreciated the time we had with our friends and families, that we should have taken that trip instead of working, that nurses deserve neighborhood applause, that live entertainment is in fact something special, that *now* contains so much short-term joy.

I am realizing that we studiously looked away so as to keep to our path. People and wonderful moments are truly fleeting, and we may even miss missing them if we don't look

up enough. Beyond the pandemic, there are accidents and diseases; beloved family members are lost to malignancy or sudden vascular events; a war breaks out somewhere in the world, and opportunities and lives are lost in the time it takes a missile to land.

We take for granted that we will one day enjoy all the little things again. I hope not to regret too much that all those little things may no longer be there to enjoy.

I used to think that *carpe diem* was a kind of admonishment for us to not waste time off our path. To not procrastinate in striving for our goals. What I am being taught by my kids' generation and by this horrible viral particle is that what we should

seize might be more *off* the path than on it.

Maybe our kids are better at balancing what they are willing to invest and recognize that nihilism is okay during a time of no control and perhaps no guaranteed future. The minutes spent sleeping in, cuddling with a partner or a pet, or lounging with friends doing absolutely nothing might be the best parts of the day to seize.

There is a corollary aphorism that counsels *carpe omnia*. Seize it all. Be present in everything. Find joy and relationships in all parts of life. Don't wait until your ducks are in a row. I don't know if I would have had the courage to live that way when I was young and focused on "getting there," but I am definitely more sympathetic to millennials looking off the path that we followed.

Be kind to yourself, present and future. *Carpe omnia*. ■

—Cynthia Verchere, MD

**People and wonderful moments are truly fleeting, and we may even miss missing them if we don't look up enough.**

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## Re: Our impact can live on forever

I found our president's message [*BCMJ* 2022;64:55] fresh, daring, and inspiring. So, I have been contemplating "Why are you?" My logical mind took me all the way from nihilism to eternalism on a somewhat philosophical/spiritual tangent. However, when I stayed with it, I sank into a quieter presence, more relaxed but still precise. Here I seemed to feel the question and opened to it with amazing curiosity as answers came through from a space that was cheerful, uplifted, and unbounded, yet deeply interconnected. So, I thank you, Dr Dosanjh.

I presume this is the inner space of "direct knowing" that drives many Indigenous wisdom-based healing systems, and I wonder if it's time to explore and hopefully enrich both ourselves and our practices by adding this inner, more subjective point of view, along the lines of "Physician, heal thyself," particularly in this time of groundlessness with its accompanying vulnerability and helplessness.

I have a sign in my office drawer that I bring out once in a while: "You can't fix stupid." Maybe it's time the evidence-based double-blind accompanies the Indigenous and more intuitive "Two-Eyed Seeing" view of reality. In Chinese medicine, it is only the heart that can embrace coexisting opposites.

—Jim Tucker, MD  
Victoria

## "Just a GP"

"Just a GP" is a telling statement that reflects a mindset of inferiority, being second best, and being not that valuable. You do small stuff, write prescriptions, look at sore throats, and refer people to specialists. Who would choose this as a career? Especially when you also have to run a business, something you are clueless about, having spent all your time learning the language of medicine.

By the way, you also have to:

- Be available 24/7/365.
- Manage every patient issue that comes through your door, which includes their examinations, tests, investigations, and procedures, including surgeries, referrals, results, charting, and paperwork.
- In many places, work in your emergency room.
- Visit and care for your inpatients in hospital.
- Help deliver your patients' babies.
- Anesthetize patients for your surgeon.
- Care for your patients in long-term care institutions.
- Make home visits for complex health care.
- Manage your dying patients in palliative care.
- Work in opioid agonist clinics.
- Work in doctor-in-school clinics.
- Work at a Foundry centre (if you have one).
- Provide medical assistance in dying services.
- Provide Diabetes Day Program expertise.
- Provide chemotherapy services.
- Offer group cognitive-behavioral therapy mental health services.
- Offer input to divisions of family practice and medical staff hospital associations.
- Contribute to primary care network development in your community.
- Keep up with your CME to meet your credits and stay up to date on rapidly changing medical knowledge.
- Provide multiple other niche services that fill the needs of the communities, large and small, in which we provide the bedrock of our health care system.

In addition, could you also please increase your patient attachment numbers, because we don't have enough family practitioners to meet the needs of our communities?

You are rewarded with a fee-for-service system that encourages a high-volume practice, so spend as little time as possible with each patient.

We are discouraged, exhausted, and looking for alternatives in this increasingly stifling environment.

Do we, as family doctors, and do our society and our health care system truly recognize and value the critical role we play and have played for generations in this system?

As with everything, we must value ourselves first as creating the bedrock of our health care system with the incredible and creative roles we play in this system.

We are not just GPs. We are specialists in longitudinal comprehensive care. We need to value this indispensable role in our health care system while we also accommodate the other evolving and more specific family physician roles we perform.

Until we believe this, we will allow inequity to continue. Our education system, our health care system, and our society will define us as "just GPs," and our medical students, residents, and practising family physicians will keep voting with their feet by choosing or changing directions to something more encouraging and rewarding.

We are in a time of transition in which physicians are seeking a healthier balance in their lives between satisfaction from their work and whatever creative pursuits and relationships bring them joy in the rest of their lives.

If we want to—and we *must*—increase the work-satisfaction part of that equation, let our voices be heard in valuing our offerings as family physicians, let us embrace the multiple and specific roles we fulfill, and let us reward the essential family physician role of a longitudinal comprehensive community primary-care (and sometimes secondary- and tertiary-care) provider. We are not replaceable, and we provide incredible value for money.

*Continued on page 202*



## How crisis can be an impetus for positive change

**T**he challenges we face as a profession are immense. The challenges within our health care system are daunting. There is no sugarcoating it. The health care system is in crisis. We are a profession in crisis. The current sentiment throughout our profession appears to be one of anger. Despite our relentless efforts, advances, and innovations, there are parts of our broken health care system that need a desperate overhaul, which is inciting anger. Anger is a common expressed secondary emotion but can have underlying rooted origins in fear, resentment, frustration, or sadness. Lately, it seems that our amygdala and orbitofrontal cortex are in overdrive in medicine. One thing is for certain: our outpouring of emotions on display is reflective of what is intolerable.

Frustration that has been building, especially during the pandemic, has morphed into outright anger. And when we are angry, we lash out—at the government, at the professional associations we feel should be doing a better job of representing us, and sometimes at each other.

Anger has its place. It can be a constructive force, a catalyst to bring about needed changes. The tremendous outpouring of anger from the public toward government with respect to the shortage of family doctors, for example, is creating a pivotal opportunity to make real change. So is the fact that many doctors are closing their offices in response to the broken system and suboptimal conditions.

If we are truly invested in the future of our profession, it is up to us to use this as fuel to create our revival. It has been years of disparities, inequities, unmet needs, and short-term bandage solutions that got us here. If we want to advance our health care system, improve

our morbidity and mortality rates, and provide preventive care and medicine indicative of the 21st century, now is the time to use our anguish. No longer will we settle for substandard care or outcomes, no longer will we be divided or pushed into inequities, and no longer will we accept the status quo.

Doctors of BC is committed to doing the right thing when times are tough; through adversity and uncertainty, we will continue to strive, as we are better together. We support all our members to be able to provide the care they wish to deliver. For example, within the current primary care crisis, we are strongly fighting for the things we need to attract and retain family doctors, so that our doctors can be supported to provide the care our patients need and deserve.

We are pressing on the need for quick action on many fronts: for new and expanded contract models that will address the rising costs of doing business and the additional time and energy required to provide longitudinal patient care, and for steps to relieve physician burdens so that we can relieve ourselves of administrative burdens and spend more time doing what we love—providing patient care.

To this extent, we want to see more and better support for after-hours care, more support for locums, and an easing of administrative burdens. We recognize the need for and deserve a healthy and safe working environment, and we are pressing on the government to approach this with urgency and an understanding of the need to act promptly.

This is just one example of how we are advocating for you. Many colleagues outside of primary care are facing critical challenges as well. The long wait times for surgery in our province are unacceptable. All doctors, irrespective of their expertise or geographical location in the province, need to have a voice and real influence in health authority decision making. Physicians have valuable frontline experience and understanding and should play a

pivotal role in formulating solutions. Doctors of BC continues to advocate strongly on these fronts—directly with government and health authorities—and by supporting medical staff associations and empowering them in their relationships with health

authorities. The same is true for family doctors who are empowered by divisions of family practice at the grassroots level. Many don't realize that the divisions are funded by Doctors of BC and the BC government, as part of the Physician Master Agreement.

We are also advocating for you in other areas that you have told us are priorities for you through surveys; through your divisions, medical staff associations, and the Joint Collaborative Committees; and through engagement with Doctors of BC. We are listening to all of you, who are also passionate about social determinants of health—considering the impacts of poverty, inequality, discrimination, climate change, and other factors on health outcomes, particularly for our children. We are actively advocating with the public, the media, and

**We want to see more and better support for after-hours care, more support for locums, and an easing of administrative burdens.**

*Continued on page 202*



# The integration of virtual care: Where to go from here?

As we transition out of the pandemic, we need a collective effort and thoughtful, deliberate planning about the role of virtual care in British Columbia and the future of work for BC physicians.

Renee Fernandez, MD, CCFP

**I**n March 2020, patients and physicians quickly adapted to the new realities of medical care in a global pandemic. Virtual care was implemented nearly overnight as a stopgap emergency measure to meet the immediate health care needs of British Columbians. There was no time for thoughtful, deliberate planning about the role of virtual care then, but we have an opportunity for that now.

Changes over the last 2 years have resulted in a permanent shift to virtual-enabled health care, accelerating transformation of BC's health care system faster than we ever imagined possible. As we begin pandemic recovery, now is the time to reflect on the lessons of COVID-19 to build a more sustainable health care workforce and system in BC. We have the opportunity to reimagine the future of care for British Columbians and the future of work for BC physicians.

This is not a simple undertaking. The integration of virtual care has far-reaching implications, including updating regulatory standards, care guidelines, patient education, and funding. Simply put, we need a province-wide integrated approach for the future of virtual care based on the vision of an equitable, modern health care system in a province recovering from a multiyear global pandemic.

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*Dr Fernandez is a practising family doctor in Vancouver and the executive director of BC Family Doctors. She believes in the power of physician advocacy and community to achieve meaningful change.*

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*This article has been peer reviewed.*

## Priorities for the future of virtual care

I believe that our approach to virtual care needs to be based on shared values and priorities for patient care. As the executive director of BC Family Doctors, I have worked with our Board and members to determine our priorities for the future of virtual care. While our conversations have focused on family medicine, I believe these priorities extend beyond our specialty.

### Equity

Every virtual care policy decision must be made with an equity-first lens so that it does not exacerbate inequities among underserved and marginalized communities. For example, physicians learned during the pandemic that the telephone is an important modality of care, providing equitable access and reducing the digital divide. We learned that the patients who most stand to benefit are also those least able to use technology such as video platforms.

### Patient and physician experience of care

COVID-19 reinforced the lesson that “one size fits no one.” Patients need different levels and types of health care services at different times of their lives. The integration of virtual care provides an opportunity to design a health care system that is truly focused on the needs of the patient. In addition, many physicians are experiencing significant strain on their mental health, professional work, and personal lives. Coming out of the pandemic, virtual care can be one element that helps with creating more humane working environments for physicians.

### Care is care

It's time to recognize that care is care, whether it is delivered in person or via telephone, video,

or another modality. What is important is the ability to meet a patient's needs, not the delivery modality. The choice of modality needs to be made by the patient and physician together, with physicians supported to use the tools that best fit the clinical, social, and cultural needs of their patients.

### Quality and safety

The pandemic has shown that virtual care is best used as a complement to in-person care. As we move from pandemic-appropriate care to postpandemic-appropriate care, the use of virtual care will change as we learn how to use various modalities of care outside of a public health emergency. We must develop a shared understanding between patients, physicians, and other stakeholders about how in-person and virtual care can together support safe, high-quality care.

### The longitudinal care relationship

Clearly, virtual care cannot replace in-person visits in many clinical situations. However, the integration of virtual and in-person care over time within a longitudinal doctor-patient relationship is vastly different from the use of virtual care by episodic virtual care providers. Episodic care has an important role to play, especially for the more than 750 000 British Columbians who do not have a family doctor. We cannot, however, consider episodic care in the same light as longitudinal care, given the limited knowledge of the patient's health and social situation and the lack of access to the patient's continuing care record in those settings.

## PREMISE

### A new era of care

COVID-19 forced the modernization of our health care system; however, physicians, patients, and policymakers are still struggling to manage the evolving changes in the way we deliver care. As we transition out of the pandemic and into our next normal, we need a collective effort and phased approach to virtual care. Taking a phased approach will smooth the transition through the COVID-19 recovery period for both patients and physicians. It will give physicians time to recover from the strain of providing care during the pandemic. It will allow us to stabilize and support the health care system as we emerge from this collective disruption to our lives.

I believe we need to consider the future of virtual care alongside the reforms necessary to ensure the sustainability of our profession. We need time to focus on system modernization, with associated reform of fee-for-service and other payment models. The pandemic and the resultant explosion in the use of virtual care highlight the need to modernize the Medical Services Commission Payment Schedule to align with current standards of care, advancements in technology, and contemporary service delivery. Maintaining the current virtual care fee codes during the initial postpandemic period will allow for thoughtful decisions about the future of care, by virtual and in-person means.

We cannot go back to our prepandemic normal in health care, because normal wasn't good enough for patients or for physicians. Yet, I do have faith that it is possible to design a modernized health care system based on shared values and priorities. Each small action that we take as we emerge from the pandemic will add up to the world that we're creating.

Now is the time to rebuild, to foster new ways of working together, and to establish new supports for the delivery of health care. The collaborative efforts of physicians, government, and patients are required for the many changes and challenges ahead. Together, we can create a better tomorrow for all British Columbians. ■

## LETTERS

Continued from page 199

If we do this, the foot-voting will turn back in the direction of family practice, particularly longitudinal comprehensive family practice. If we further increase the satisfaction level of family physicians with business support, with a funding system that rewards comprehensive care while maintaining physician independence, with our primary care networks' efforts of team-based care again, and with a funding and communication system that promotes this teamwork, our chronic problems of access and attachment will naturally start to resolve themselves.

I believe that at this point in time our government understands these issues and is open to addressing our critical needs in family medicine. As our General Practice Services Committee grapples with this and as we negotiate our Physician Master Agreement, please lend your support to the voice of family doctors and fix this crisis in health care that is eroding its foundation.

Let us make family practice an irresistible choice and confirm that we value ourselves and the essential role we play in a system that could not function without us.

We may just start to find real joy again in the amazing work we do.

—Rob Lehman, MD, CCFP, MCISc, FCFP(LM)  
Roberts Creek

### Re: The crisis that COVID-19 exposed, highlighted, and worsened (but did not cause)

I have been working as a family physician for 45 years, mostly in Nanaimo, BC. I agree with Dr Day's editorial in the March issue of the *BCMj* [2022;64:53-54]—having to deal with a shortage of hospital beds, overcrowded emergency rooms, long wait lists, and needing to fight for my patients to get proper medical care.

I am frustrated with the several BC governments that have not done anything to address these problems, not taken responsibility for their actions, and not listened to doctors about how to improve our health system.

—Barbara Macleod, Licentiate  
Nanaimo

## PRESIDENT'S COMMENT

Continued from page 200

key stakeholder partners. A working group through the Council on Health Economics and Policy is working on a policy statement on gender equity that will be coming to the Board later this year, part of our commitment to address equity, diversity, and cultural safety/humility.

We are fierce in our advocacy for you and your patients. We are doing this on many different fronts. Let's use our anger to seek solutions together and promote change. We all have a role to play in navigating the challenging terrain ahead of us. We can no longer be silent; our voices will not be muffled, for what we speak of and stand for is the betterment of all our patients and British Columbians. When we mobilize together and act as one, we have our biggest opportunity to make positive change. We must seize the moment, together, now. ■

—Ramneek Dosanjh, MD  
Doctors of BC President



The screenshot shows a tweet from the BC Medical Journal (@BCMj). The tweet text reads: "BC #youth are in a #MentalHealthCrisis—we must invest in prevention. The US Surgeon General recently issued an advisory on the youth #MentalHealth crisis, which was worsened by #COVID19. The situation in BC is similar. Read the article: [bcmj.org/cohp/bc-youth-are-mental-health-crisis-we-must-invest-prevention](https://bcmj.org/cohp/bc-youth-are-mental-health-crisis-we-must-invest-prevention)". Below the text is a photograph of a young man sitting on concrete steps, looking down with a distressed expression. The tweet includes a "Follow" button and a link to the article.

# News

**We welcome news items of less than 300 words; we may edit them for clarity and length.** News items should be emailed to [journal@doctorsofbc.ca](mailto:journal@doctorsofbc.ca) and must include your mailing address, telephone number, and email address. All writers should disclose any competing interests.

## Business Pathways introduces HR toolkit to help physicians hire, onboard office staff

Business Pathways is a new program from Doctors of BC dedicated to helping members navigate the operational side of running a practice—a one-stop shop to access targeted resources based on practice needs during all stages of a medical career.

With the launch of the program, Business Pathways is introducing the first of three HR toolkits that will help with all aspects of managing staff. The first toolkit, available now at [www.doctorsofbc.ca/managing-your-practice/](http://www.doctorsofbc.ca/managing-your-practice/)

[business-pathways/managing-your-office/human-resources-toolkit](http://www.doctorsofbc.ca/managing-your-office/human-resources-toolkit), delves into best practices for recruiting and hiring staff. HR management is an area of particular importance to doctors, and more in-depth toolkits for other key aspects of managing office staff will be released as soon as possible.

Also available are exclusive deals in partnership with Club MD ([www.doctorsofbc.ca/your-benefits/discount-programs/club-md](http://www.doctorsofbc.ca/your-benefits/discount-programs/club-md)), for legal and financial services from MD Financial Management and MNP LLP, and from other business partners like TopStack and Staples (member login required).

There are guides, resources, and other toolkits as well, which include support for:

- Transitioning to medical practice: [www.doctorsofbc.ca/managing-your-practice/business-pathways/starting-your-practice](http://www.doctorsofbc.ca/managing-your-practice/business-pathways/starting-your-practice).
- Contingency and emergency planning: [www.doctorsofbc.ca/contingency-planning](http://www.doctorsofbc.ca/contingency-planning).
- Protecting yourself and staff against physical and online violence: [www.doctorsofbc.ca/sites/default/files/human\\_safety\\_optimization\\_tip\\_sheet.pdf](http://www.doctorsofbc.ca/sites/default/files/human_safety_optimization_tip_sheet.pdf).

More tools, resources, and educational opportunities will be released on an ongoing basis. Business Pathways is here to help doctors optimize their practice, every step of the way. Access all resources at [www.doctorsofbc.ca/managing-your-practice/business-pathways](http://www.doctorsofbc.ca/managing-your-practice/business-pathways).

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## BCMJ survey results 2022: What we heard

In January the *BCMJ* conducted an online readership survey to gauge how well the journal is meeting the needs of BC doctors. We conduct these surveys approximately every 5 years to explore new ideas and ensure the journal is succeeding in its mission.

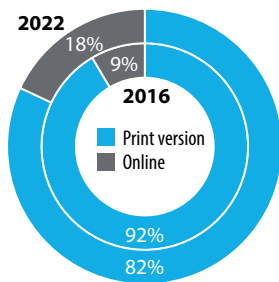
The 1400 responses we received were from a mix of physicians (39% family physicians, 37% specialists, 13% students/residents, 11% retired) across the age spectrum, so we are confident that these findings are representative. Here are some of the key findings (percentages have been rounded to the nearest whole number).



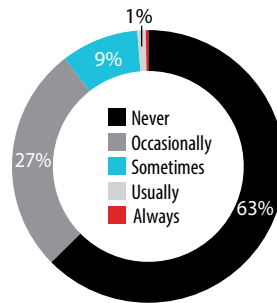
### Print and web

In 2016 we asked doctors whether they read the *BCMJ* in print or online, and we were surprised at how many chose print (92%), a preference that held regardless of age. This year, while there was some change, print's dominance over online remains—82% of respondents continue to read the print version, with 18% choosing online.

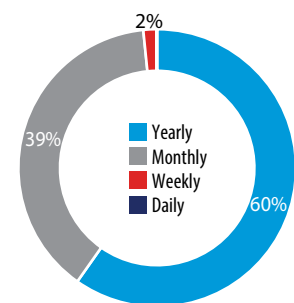
The majority of respondents (63%) who read the *BCMJ* in print never go to the website, with the remaining 37% going at least occasionally. Of those who use the website, a significant number (approximately 40%) visit monthly or more often to find and read content.



"I primarily read the *BCMJ*..."  
(print version or web version)



Do you ever go to the *BCMJ* website?  
(Base: All "print" respondents)



I visit the website...  
(Base: All but "never" respondents)

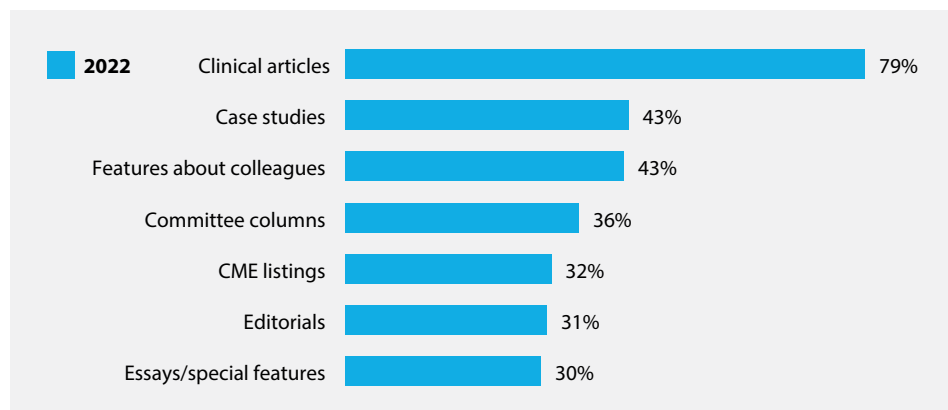


### The *BCMJ*'s niche

Readers' favorite content type continues to be clinical articles, head and shoulders above the rest at 79% of people's top five favorite sections. Case studies, features about colleagues, committee columns, CME listings, editorials, and essays/special features are also favorites. These findings hold when the survey data are sorted by frequency of reading, practice type, age, and setting (i.e., whether in a community, hospital, or academic setting). A strong majority of members believe that the *BCMJ* is a good place to have physicians' voices shared (66% agree) and a good place for learning about what is happening in medicine in BC (76% agree).

This survey shows that the *BCMJ*'s niche is BC medicine—it's where members feel the journal is the strongest, the most useful, and the most relevant. The 2022 survey confirms our impression that the journal acts as a "doctors' lounge" (as one

respondent said in the comments), a comfortable place where doctors go to hear from colleagues, pick up some best practices, and learn about changes in the medical system here in British Columbia.



Of these *BCMJ* content types, which are you most interested in (pick up to 5)? (Base: All respondents)



### Apps and social media

The survey revealed that BC physicians are increasingly using their smart phones

when looking for BC medical news or articles online (31%, up from 20% in 2016). We asked whether physicians would use an app to make reading the *BCMJ* on their phone easier. Forty-six percent of readers said “no,” 33% were in favor of an app, and 21% were undecided.

Those who responded to the survey have little use for social media for professional reasons (12%), though personal use is higher, with 49% using Facebook and 36% using Instagram. In fact, more doctors report not using social media at all (29%) than using Twitter (21%).



### Room for improvement

Overall we found that survey respondents are a little less satisfied with the journal

compared with 2016 results. Though the *BCMJ* is a general medical journal that seeks to be useful to all BC physicians, it cannot satisfy everyone all the time because BC physicians are not homogenous. The survey results underscore this: there are passionate comments for and against print, those telling us to carry on with climate and social justice issues and those telling us to stay out of them, those who think the covers are wonderful and those who think otherwise.



### Methodology

This online survey was completed by 1403 physicians of a possible

15 561 active, full Doctors of BC members, students, residents, and retired members. This provides a 9% response rate, estimated to be valid 19 times out of 20, within a margin of +/- 2.50%. Participants were given the opportunity to enter an optional draw to win one of two AirPods Pro as an incentive to participate. The survey was conducted 17–31 January 2022 by TWI Surveys.

## How to withdraw from your child's RESP effectively

You've spent years saving for your child's post-secondary education. What happens when it's time to use the money?

In Canada, the most popular education savings vehicle is the Registered Education Savings Plan (RESP). That's because the government offers a 20% grant called the Canada Education Savings Grant (CESG), to a lifetime maximum of \$7200 per child. In addition, modest-income families can qualify for the Canada Learning Bond (CLB).

Ultimately, when your child begins their postsecondary education, money must be withdrawn from their RESP account. Because of the rules for RESP withdrawals, you should consider some strategies to make your withdrawals as efficient as possible and to avoid paying back unused funds to the government.

### Understand what to withdraw first

There are different types of money in an RESP account: the original contributions to the plan, any grants and bonds received, and investment growth on all funds in the account.

When you withdraw, the original contributions (called Post-Secondary Education withdrawals) are not taxable. But the CESG, CLB, and any investment growth (called the Educational Assistance Payment [EAP]) are taxable.

What's more, if your child finishes school and there is still money in their RESP, any CESG or CLB money remaining in the plan must be paid back to the government. To avoid a potential CESG or CLB payback, be sure to withdraw as much EAP as possible before withdrawing your original contributions.

What to do: On your RESP withdrawal form, you can indicate which money you're withdrawing: your original contributions (PSE) or grants and investment growth (EAP). Choose the EAP first.

### Understand how much you can withdraw

In your child's first 13 weeks of postsecondary education, you can withdraw a maximum of \$5000 in EAP money. After that, there's no restriction on how much you can withdraw.

What to do: The EAP is taxable in the hands of the student. Most students have little

to no income, and they get the basic personal income tax exemption (which means they won't pay tax on the first \$14 398 of their income in 2022) as well as tuition tax credits. Make sure that you're not withdrawing too much of the EAP in a year, especially if your child has a part-time job or other source of income.

### Withdraw as much as possible before your child finishes school

What happens if you have money in the RESP after your child has completed their postsecondary education? If the money is considered as your original contributions, you can withdraw it without any tax consequences whatsoever. You can do whatever you'd like with the money. But if you still have CESG money, that amount must be repaid to the government.

What to do: Since there's no restriction on how much you can withdraw, make sure you're withdrawing all the EAP before your child finishes school.

If your child does not pursue or expect to complete their postsecondary education, and you still have funds in the RESP account (beyond your original contributions), you could receive those funds as an accumulated income payment (this is the investment growth). Any remaining CESG or CLB money would have to be repaid.

### Don't collapse the plan too early

If your child decides not to attend a qualifying education program, the RESP must eventually be collapsed. However, they may decide to pursue other avenues for a while and then go back to their postsecondary education at a later time. Therefore, collapsing the plan early could turn out to be a mistake, as the money may be needed later for tuition and other school-related expenses. You can keep the RESP open for up to 36 years.

Although there are other saving methods available, an RESP is the primary vehicle of choice when it comes to education savings.

—Carly Trobridge, CFP, Senior Financial Consultant, MD Management Limited

*This information should not be construed as offering specific financial, investment, foreign or domestic taxation, legal, accounting, or similar professional advice, nor is it intended to replace the advice of independent tax, accounting, or legal professionals.*

Yazdan Mirzanejad, MD, DTM&H, FRCPC, FACP

# Current approaches to infectious diseases, Part 2

“Quality means doing it right when no one is looking! As we express our gratitude, we must never forget that the highest appreciation is not to utter words, but to live by them.”  
—John F. Kennedy



Dr Yazdan Mirzanejad

Dr Mirzanejad is a clinical professor in the Division of Infectious Diseases, University of British Columbia, and an infectious diseases consultant at the Surrey campus/Jim Pattison Outpatient Care and Surgery Centre.

This editorial has been peer reviewed.

Welcome to the second of a two-part series on infectious diseases in British Columbia (part 1 appeared in the May 2022 issue of the *BCMJ*). The first article in part 2 focuses on antimicrobial stewardship (Wong and colleagues). Antibiotics prevent millions of deaths each year and remain the primary treatment for potentially fatal bacterial infections. Yet, inappropriate prescription rates and overuse of antibiotics have led to antibiotic resistance, which has created a global health emergency that kills at least 700 000 people per year. If no action is taken, this rate is predicted to increase to 10 million deaths per year by 2050. This article provides a comprehensive review of common infectious syndromes and the most up-to-date recommendations on duration of antibiotic therapy.<sup>1-4</sup>

The second article provides a comprehensive review of hepatitis B epidemiology and treatment of different stages of this hard-to-kill infection (Wong). In 2017, 4905 cases of hepatitis B virus infections were reported in Canada: 192 cases of acute infection (corresponding to a rate of 0.5 per 100 000 population), 4086 cases of chronic infection (11.4 per 100 000), and 627 cases of unspecified status. In 2017, acute hepatitis B rates were highest in males aged 30 to 39 years (1.19 per 100 000) and in females aged 25 to 29 (0.67 per 100 000). Rates of chronic hepatitis B in British Columbia (21.7 per 100 000 population) were above the national

average (11.4 per 100 000) and the average for Alberta (12.6 per 100 000), Yukon (12.6 per 100 000), and Ontario (12.5 per 100 000).<sup>5-9</sup>

The third article focuses on Lyme disease, particularly in BC (Morshed and Bowie). Lyme disease is considered the most common tick-borne disease in BC and North America. Unlike in eastern Canada, the rate of Lyme disease has remained low in BC. The infection is preventable by avoiding tick bites and removing attached ticks early. Early diagnosis and antibiotic treatment are important because Lyme disease can lead to serious complications if left untreated.

However, extreme caution needs to be applied in order to avoid overdiagnosing Lyme disease, and experts should be consulted when there is discordance between clinical and test results.<sup>10-14</sup>

The final article presents an analysis of travel-acquired infections and illnesses in British Columbians based on data from the GeoSentinel global surveillance network (Zapata-Dixon and colleagues). These data are used to alert public health and other relevant authorities during early signs of emerging infectious diseases in our province and country and in any other part of the world.<sup>15-18</sup> ■

**Welcome to the second of a two-part series on infectious diseases in British Columbia.**

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**Inappropriate prescription rates and overuse of antibiotics have led to antibiotic resistance, which has created a global health emergency that kills at least 700 000 people per year.**



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Maggie Wong, PharmD, ACPR, Tim T.Y. Lau, PharmD, ACPR, FCSHP, Victor Leung, MD, FRCPC, Kevin Afra, MD, MHA, FRCPC

# Is shorter better? Duration of therapy for common bacterial infections in adults

Randomized controlled studies conducted over the last decade have indicated that a shorter duration of antibiotic therapy is just as effective as longer treatment.

**ABSTRACT:** Antimicrobial resistance is a looming threat to our society's health. Physicians need simple strategies for antimicrobial stewardship that can be readily incorporated into everyday practice. Addressing duration of therapy is one

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*This article has been peer reviewed.*

of these key strategies. Every day of antibiotic exposure beyond that which is necessary to cure the infection increases the risk of adverse events and antimicrobial resistance without providing additional benefits. We focus on the adult population and commonly encountered conditions: community-acquired pneumonia, intra-abdominal infections, skin and soft tissue infections, osteomyelitis, complicated urinary tract infections, and gram-negative bacteremia. The treatment of these common infections overlaps in primary and acute care practices. Recent literature suggests shorter duration of therapy is as effective as longer durations for these infections.

**W**ithout a concerted societal effort, antimicrobial resistance is predicted to kill more people than cancer by the year 2050.<sup>1</sup> The human cost is staggering, with one death occurring every 3 seconds.<sup>1</sup> Appropriate use of antibiotics is one of the key strategies that can prevent this looming existential threat. Addressing the duration of treatment, and thus overall antibiotic exposure, is a simple practice change that all physicians can make. We focus on the duration of treatment for common bacterial infections in adults seen in community and hospital practices, based on the latest evidence in the literature.

## Community-acquired pneumonia

Historically, community-acquired pneumonia treatment ranged from 7 to 10 days;<sup>2</sup> however,

new data suggest that shorter durations of therapy are as effective. In 2007, the Infectious Diseases Society of America community-acquired pneumonia guidelines recommended that 5 days of treatment may be adequate in patients who are afebrile for 48 to 72 hours, and who do not have more than one of the following clinical signs of instability: heart rate greater than 100 beats/minute, respiratory rate greater than 24 breaths/minute, systolic blood pressure less than 90 mmHg, or arterial oxygen saturation less than 90% on room air.<sup>3</sup>

These recommendations were validated by a multicentre, randomized, noninferiority trial in Spain.<sup>4</sup> Noninferiority trials compare the effectiveness of a new regimen against a standard therapy; if the new regimen is not worse than the comparator within a defined amount, it is considered “noninferior” to the standard therapy and can be recommended for use. At day 5, hospitalized patients were randomly assigned to an intervention group or a control group. In the intervention group, researchers stopped giving antibiotics if patients reached clinical stability based on the Infectious Diseases Society of America guidelines; in the control group, the treatment duration was determined by physicians per usual practice. Primary outcome was defined as improvement in or resolution of signs and symptoms of community-acquired pneumonia at day 10 and day 30. Median duration of therapy was 5 days in the intervention group versus 10 days in the



control group. Clinical success at day 30 was similar between the two groups. These results demonstrated that Infectious Diseases Society of America community-acquired pneumonia guideline recommendations regarding shorter duration can be safely implemented in many hospitalized patients.<sup>4</sup>

In 2018, a meta-analysis of 21 clinical studies, 19 of which were randomized controlled trials, that involved 4861 patients demonstrated that a short course of antibiotics ( $\leq 6$  days) was just as effective as longer treatment durations, regardless of the type of antibiotic used. The analysis included inpatient and outpatient studies of treatment with various antibiotics, such as azithromycin, quinolones, and  $\beta$ -lactams; there were no differences in clinical cure or relapses. In addition, patients who received a shorter course of treatment had lower mortality, likely due to fewer serious adverse effects from antibiotics.<sup>5</sup>

Most recently, Dinh and colleagues demonstrated that 3 days of therapy was noninferior to 8 days of therapy in non-ICU patients with moderately severe community-acquired pneumonia. This multicentre, double-blind, randomized, placebo-controlled trial was conducted in France. Patients with lung abscess, massive pleural effusion, known immunosuppression, health care-associated pneumonia, or aspiration pneumonia were excluded. Patients who achieved clinical stability after 3 days of treatment with  $\beta$ -lactams were then randomly assigned to receive a placebo or amoxicillin plus clavulanate for 5 additional days. Clinical cure by day 15 was similar between the placebo and treatment groups, and there was no difference in 30-day mortality rate.<sup>6</sup>

### Synopsis

Based on cumulative research in the past 20 years, a short duration of therapy for community-acquired pneumonia (minimum of 3 days) is as effective as longer durations for most patients in outpatient or inpatient settings, and reduces the risk of adverse drug reactions. This applies to non-ICU hospitalized patients with clinical improvement by day 3, without known immunosuppression, lung abscess, or empyema. In the outpatient setting, it is important for clinicians to reassess patients

between days 3 and 5 in the clinic or by phone to ensure they are clinically stable and can safely stop their antibiotics.

### Intra-abdominal infections

According to the 2010 Infectious Diseases Society of America guidelines, the recommended duration of treatment for established intra-abdominal infections is 4 to 7 days unless adequate source control is not achievable.<sup>7</sup> In clinical practice, however, many patients are typically treated for 10 to 14 days.

## Without a concerted societal effort, antimicrobial resistance is predicted to kill more people than cancer by the year 2050.

In 2015, the STOP-IT trial determined that outcomes were similar between patients who received antibiotics for 4 days after source control and those who had a longer course of therapy (median duration of 8 days). This was an open-label trial that included 23 sites across the United States and Canada. Patients were enrolled if they had leukocytosis, fever, or gastrointestinal dysfunction due to peritonitis with adequate surgical source control. They were randomly assigned to receive antibiotics until 2 days after resolution of fever, leukocytosis, and ileus (control group) or to receive a fixed duration of 4 days post source control (intervention). The maximum duration of therapy was capped at 10 days for the control group. The mean Acute Physiologic Assessment and Chronic Health Evaluation (APACHE) II score was 10 (approximately 10% risk of mortality), and one-third of the patients had intra-abdominal infections related to the colon or rectum. One-third of the patients underwent percutaneous drainage as their primary source control procedure. Outcomes were similar between the groups for the composite primary endpoint (consisting of surgical-site infection, recurrent intra-abdominal infection, and death).<sup>8</sup> In a post-hoc analysis, patients with colonic source

of infection, steroid use, APACHE II score greater than 15, and hospital-acquired infections had an increased risk of treatment failure; however, this was not prevented by longer antibiotic duration.<sup>9</sup> A prospective, open-label study by Montravers and colleagues showed that even for critically ill ICU patients, longer duration of treatment did not provide additional benefits once surgical source control was achieved.<sup>10</sup>

### Synopsis

Most patients with intra-abdominal infection benefit from a shorter duration of antibiotics (between 4 and 7 days) after source control is achieved. Those who are immunocompromised or do not have adequate source control may require a longer duration of treatment depending on individual clinical scenarios.

### Skin and soft tissue infections

Skin and soft tissue infections include a broad range of presentations from cellulitis and abscess to necrotizing fasciitis. In general, the 2014 Infectious Diseases Society of America guidelines recommended that most skin and soft tissue infections be treated for 5 to 10 days.<sup>11</sup> In clinical practice, however, patients often receive antibiotics for longer periods than recommended. A retrospective analysis of 322 hospitalized patients conducted by Jenkins and colleagues in 2010 indicated that the median duration of antibiotic treatment for cellulitis and cutaneous abscess was 13 days; however, the authors felt that half these patients could have benefited from a shorter duration of treatment because they did not have complicating factors.<sup>12</sup>

In a double-blind, placebo-controlled trial by Hepburn and colleagues, 87 patients were randomly assigned to receive 5 days versus 10 days of antibiotics for uncomplicated cellulitis. Patients were recruited from primary care clinics and the emergency department of a tertiary care hospital, and were excluded if they had bacteraemia, sepsis, or deep-seated skin and soft tissue infections, such as abscess, fasciitis, myositis, osteomyelitis, or septic arthritis. The primary outcome was resolution of infection by day 14 and no recurrence by day 28. In both groups, 98% of patients improved by day 14 without further relapse. The authors concluded that there was no difference in clinical outcome in patients

who received 5 versus 10 days of therapy, and found that even though many patients still had substantial edema and erythema at day 5, it appeared to resolve on its own as long as improvement was seen within the first 5 days.<sup>13</sup>

### Synopsis

Five days of treatment with antibiotics can be considered for patients with uncomplicated cellulitis with clinical improvement. In the outpatient setting, it is recommended that the patient be reassessed in person or by phone on day 5 to ensure there is clinical improvement prior to stopping the antibiotics. Patients with complicating factors such as deep-seated infections (e.g., abscess, osteomyelitis), immunosuppression, diabetic foot infection with poor source control, peripheral arterial disease, or persistent ulcers may require longer therapy.<sup>13</sup>

### Osteomyelitis

Traditionally, patients receive at least 4 to 6 weeks of antibiotics for osteomyelitis. This practice stems from clinical studies dating back to the 1970s.<sup>14</sup> Occasionally, up to 3 months of treatment may be recommended for diabetic foot osteomyelitis without surgical debridement.<sup>15</sup> These recommendations are often based on retrospective observational studies, some of which are of low quality.

A meta-analysis of 15 studies, which was published in 2019, summarized the latest evidence on this controversial topic. Five of the studies were randomized controlled trials, but only two focused on adult patients. Of the other 10 retrospective observational studies, only three were graded as good quality. When all the studies were combined, there was no significant difference in treatment failure rates between short and long durations of therapy (> 4 to 6 weeks).<sup>15</sup> However, given the pathophysiological and therapeutic differences between pediatric and adult osteomyelitis, we focus only on the two adult randomized controlled trials.

The first trial by Tone and colleagues compared 6 versus 12 weeks of antibiotic treatment for diabetic foot osteomyelitis without surgical intervention in 40 patients. Patients with peripheral arterial disease or gangrene and those who required bone resection were excluded. The primary outcome was remission of diabetic

foot osteomyelitis within 12 months. There was no difference in remission rates between the 6-week and 12-week groups; 26 patients (65%) were in remission. However, patients in the 12-week group experienced more gastrointestinal side effects from antibiotics. The main

## In 2018, a meta-analysis of 21 clinical studies ... that involved 4861 patients demonstrated that a short course of antibiotics ... was just as effective as longer treatment durations, regardless of the type of antibiotic used.

limitation of this study was the small number of patients included, which may have affected its power to detect a difference between the two groups.<sup>16</sup>

The second trial, a multicentre, open-label, noninferiority, randomized controlled study compared 6 weeks versus 12 weeks of antibiotic treatment in patients with pyogenic vertebral osteomyelitis. The primary outcome was remission, defined as sustained lack of fever, pain, and inflammatory syndrome (C-reactive protein < 10 mg/L) 12 months after the end of treatment; this was determined by an independent committee that was not aware of the duration of treatment each patient received. In the trial, 359 patients were randomly assigned to the treatment groups. Clinical cure at 1 year was achieved in 91% of patients in each group. However, those with *Staphylococcus aureus* infection had a higher risk of failure, regardless of treatment duration.<sup>17</sup>

Additionally, a pilot, prospective, randomized noninferiority trial by Gariani and colleagues published in 2020 was the first study to show that 3 weeks of antibiotic therapy after partial surgical debridement was noninferior to 6 weeks for diabetic foot osteomyelitis in terms of remission rate. The trial included 93 patients, and the median number of surgical

debridement was one. After a median follow-up period of 11 months, 78% of the patients remained in remission. The two treatment groups had similar results. The authors plan to conduct a follow-up randomized controlled trial with a larger number of patients and a smaller margin of difference (10% instead of 25%) to validate the results of this study.<sup>18</sup>

### Synopsis

Six weeks of antibiotic treatment is likely sufficient for most cases of osteomyelitis. Emerging evidence suggests that durations as short as 3 weeks of antibiotic treatment may be sufficient in patients with partial surgical debridement for diabetic foot osteomyelitis.<sup>18</sup>

### Complicated urinary tract infections

Short-duration antibiotic treatment for female uncomplicated cystitis is well established in the Infectious Diseases Society of America 2011 guidelines.<sup>19</sup> Conversely, the duration of treatment for complicated urinary tract infections (pyelonephritis and male cystitis) is less clear.

Eliakim-Raz and colleagues conducted a systematic review of eight randomized controlled trials with 2515 patients, which compared treatment of less than 7 days to longer treatment in both community and hospitalized patients with pyelonephritis or septic urinary tract infection. Clinical failure, defined as no resolution of signs and symptoms of urinary tract infection or need to change antibiotic at the end of treatment, was the primary outcome. No significant differences in treatment failure were found, including in those who received  $\beta$ -lactams. In a small subset of 100 patients with urogenital abnormalities, longer treatment was more favorable.<sup>20</sup>

For male patients, evidence is mounting to support a shorter duration of treatment, such as 7 days compared with 14 days. In a retrospective study by Drekonja and colleagues, the outpatient records of 33 336 male veterans were reviewed, and 4449 index cases (13.3%) had recurrences of urinary tract infection. In a multivariate logistic regression analysis, a treatment duration of less than 7 days was not associated with early recurrence of infection. However, a treatment duration of 7 days or longer was associated with

a higher risk of late recurrence (> 30 days after initial treatment). This could be due to selection bias, where patients with underlying risk factors for urinary tract infection were given longer treatments.<sup>21</sup> The results of this study were subsequently confirmed by Germanos and colleagues.<sup>22</sup> In their study, patients with any urogenital abnormality, recent surgery or catheterization, and immunosuppression were excluded. Of the 573 patients included in the study, 32 (5.6%) had recurrence of urinary tract infection. Longer treatment duration was associated with a twofold increased risk of recurrent urinary tract infection, even after the exclusion of men with urologic abnormalities. One possible explanation is that prolonged antibiotic exposure can alter the gastrointestinal microbiome, which in turn can affect urogenital flora and lead to recurrent urinary tract infection. The authors also showed that antibiotic choice was not associated with urinary tract infection recurrence; however, most patients received fluoroquinolones, and less than 5% of patients received a  $\beta$ -lactam.<sup>22</sup> Finally, an outpatient, double-blind, placebo-controlled, randomized trial by Drekonja and colleagues further supported the results of previous observational studies by illustrating that ciprofloxacin or trimethoprim/sulfamethoxazole for 7 days was noninferior to 14 days for men with afebrile urinary tract infection.<sup>23</sup> In their trial, 272 patients were randomly assigned to the treatment groups. More than 90% of patients in each group achieved symptom resolution by day 14, and recurrence of urinary tract infection symptoms was also comparable in the two groups. However, only ciprofloxacin and trimethoprim/sulfamethoxazole were used; it is unclear if the same duration applies to treatment with  $\beta$ -lactams or nitrofurantoin.<sup>23</sup>

### Synopsis

Seven days of antibiotic treatment may be adequate in complicated urinary tract infection, including pyelonephritis and male cystitis. Treatment duration in men with established prostatitis remains unclear; further studies are required.

### Uncomplicated gram-negative bacteremia

Gram-negative bacteremia accounts for 33% to 45% of hospital- and community-acquired

bacteremia, respectively.<sup>24</sup> Patients typically receive 14 days of antibiotic treatment for uncomplicated bacteremia, as durations in guidelines range from 7 to 14 days.<sup>24</sup> Clinicians often prescribe a longer duration to err on the side of caution due to the severity and potential mortality associated with bacteremia.

**The evidence is clear that overuse of antibiotics can lead to collateral damage, resulting in development of bacterial resistance.**

The first multicentre, randomized, noninferiority trial on uncomplicated bacteremia was conducted by Yahav and colleagues<sup>25</sup> in 2019. In their trial, 604 patients were randomly assigned to the short (7 day) or long (14 day) duration treatment group if they were hemodynamically stable for at least 48 hours by day 7 of their hospital stay. Immunocompromised patients, those without source control for infection, and those with polymicrobial bacteremia were excluded. The urinary tract was the main source of infection (69%), followed by intra-abdominal infections (12%). Males comprised slightly less than half of all patients. *Escherichia coli* was the most

commonly identified bacterium (63%). The primary outcome measure was 90-day all-cause mortality, relapse or complications related to initial bacteremia, hospital readmission, or prolonged hospitalization (> 14 days). The results indicated that 7 days of antibiotic treatment was noninferior to 14 days of treatment. In addition, patients in the short-duration treatment group were able to return to their baseline activities sooner than those in the long-duration treatment group. However, the results of this study may not be applicable to pathogens such as *Pseudomonas* and *Acinetobacter*, which comprised only a small percentage of those treated in this trial.<sup>25</sup>

In a second multicentre, randomized, noninferiority trial published by von Dach and colleagues in 2020, 504 patients were randomly assigned to C-reactive protein (CRP)-guided antibiotic treatment, fixed 7-day therapy, or fixed 14-day therapy (control group).<sup>26</sup> The CRP-guided group discontinued antibiotics once CRP declined by 75% from the peak level, with treatment capped at 14 days. To be enrolled, patients had to be afebrile for 24 hours by day 5 and could not have poor source control or severe immunosuppression. Median antibiotic duration was 7 days in the CRP-guided group. Similar to Yahav and colleagues, urinary tract infections were the main source of infection. Males comprised approximately one-third of all patients. Both CRP-guided and 7-day treatment strategies were noninferior to 14 days of

**TABLE.** Antibiotic treatment duration based on infection source.

Type of infection	Duration
Mild to moderate community-acquired pneumonia	3 days*
Intra-abdominal infection	4–7 days after source control attained
Skin and soft tissue infection such as cellulitis (excluding deep-seated infections)	5 days*
Osteomyelitis (diabetic foot and vertebral) <sup>†</sup>	3–6 weeks for diabetic foot osteomyelitis 6 weeks for vertebral osteomyelitis
Complicated urinary tract infection <ul style="list-style-type: none"> <li>• Pyelonephritis (male and female)</li> <li>• Male cystitis</li> </ul>	7 days 7 days
Uncomplicated gram-negative bacteremia (primarily from urinary or intra-abdominal sources, with adequate source control)	7 days*

\*applies only to patients who are clinically stable and have source control for infection

<sup>†</sup>infectious diseases consultation is strongly recommended to individualize the duration of treatment

treatment for clinical failure at 30 and 90 days. Patients with *Pseudomonas* or *Acinetobacter* infections were not included in the study.<sup>26</sup>

### Synopsis

The duration of treatment for uncomplicated gram-negative bacteremia from primarily urinary and intra-abdominal sources can be as short as 7 days in select patients who have clinical improvement by day 5, are not immunocompromised, and have adequate source control.

### Summary

The invention of antibiotics in the 1940s was accompanied by the dogma that using “too little” antibiotics may lead to bacterial resistance and recurrence of infections. As a result, prescribers often instructed their patients to complete their prescribed antibiotic course, even when they had recovered clinically. Current literature suggests the contrary; the evidence is clear that overuse of antibiotics can lead to collateral damage, resulting in development of bacterial resistance.<sup>27</sup> In the last decade, a number of randomized controlled studies have revealed that a shorter duration of antibiotic therapy is just as effective as longer treatment. This principle applies to many common infections [Table].

As the number of newly developed antibiotics declines, it is of utmost importance to preserve our present antibiotics by providing patients with appropriate durations of treatment; in most cases, the old adage “less is more” holds true for common bacterial infections. ■

### Competing interests

None declared.

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# Chronic hepatitis B in British Columbia

Chronic hepatitis B, a complex viral infection, requires longitudinal follow-up, management, and often clinical judgment on a case-to-case basis because a patient's test results may not fit perfectly within any particular phase of infection.

**ABSTRACT:** Chronic hepatitis B is caused by the hepatitis B virus, a member of the Hepadnaviridae family. It is a common infection with a worldwide prevalence of more than 250 million people. In Canada and British Columbia, it disproportionately affects immigrant groups from endemic countries, Indigenous populations, and people who inject drugs. Pregnant women in BC are universally screened for hepatitis B virus, and if positive, measures are taken to reduce vertical transmission to the neonate. Canada has a universal vaccination program for hepatitis B virus, and BC currently provides routine immunizations to neonates at 2, 4, and 6 months. The current focus for treatment of chronic hepatitis B is to prevent progression of liver inflammation and fibrosis and to prevent hepatocellular carcinoma. There currently are no treatment options that result in the complete cure of chronic hepatitis B.

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Chronic hepatitis B is caused by a small DNA virus called hepatitis B virus (HBV), a prototype member of the Hepadnaviridae family and the *Orthohepadnavirus* genus that infects mammals.<sup>1</sup> Chronic hepatitis B has a worldwide prevalence of more than 250 million people.<sup>2</sup> Areas with high endemicity include Asia, Africa, and parts of South America. In Canada, up to 480 000 people may be infected.<sup>3,4</sup> The population groups with the highest infection rates include immigrants from endemic countries, Indigenous people, and people who inject drugs.<sup>4</sup> In BC, local epidemiology is driven primarily by a large immigrant population from endemic countries in Asia.<sup>3</sup> In many endemic countries, routine screening and prophylaxis of infants at birth may not have been widely available. These individuals often become chronically infected during the perinatal period or in early childhood, as transmission during the neonatal period or at a young age leads to the highest rates of chronic infection.<sup>5,6</sup> Other modalities of HBV transmission include percutaneous, sexual, or close person-to-person contact through open cuts or sores. Infectious bodily fluids with the highest concentrations of HBV are blood, followed by semen and vaginal fluids; much lower concentrations are found in saliva secretions, and transmission is not attributable to sharing utensils.<sup>7</sup> In BC, most chronic hepatitis B cases are among East and South Asian individuals who have very low levels of illicit drug or alcohol use, major mental illness, or co-infection with HIV or hepatitis C.<sup>8</sup> In contrast, acute hepatitis B diagnoses in

BC are more often associated with individuals who have a high level of substance use and co-infection with HIV or hepatitis C, and with predominantly young Caucasian males.<sup>8</sup>

Within Asian immigrant populations in BC, knowledge of chronic hepatitis B infection, especially in relation to routes of transmission, was found to be limited.<sup>9</sup> A more recent study of a mix of Asian communities in BC, including Chinese, Korean, Filipino, South Asian, and Southeast Asian ethnic groups, showed that hepatitis B awareness was lowest in the South Asian communities.<sup>10</sup> This is a concern because HBV is the most common cause of hepatocellular carcinoma in Asian North Americans.<sup>11</sup>

## Testing for hepatitis B

The Canadian Association for the Study of the Liver guidelines recommend that those who are in high-risk groups be screened for HBV.<sup>12</sup> They include immigrants from intermediate-to high-risk countries and infants whose parents are from endemic countries and are not vaccinated [Table 1]. It is also recommended that at-risk individuals who have not received routine HBV vaccination be vaccinated if they screen negative for HBV.<sup>12</sup> The BC Centre for Disease Control *Communicable Disease Control Manual* lists groups that are recommended to receive free hepatitis B vaccination.<sup>13</sup> A study conducted in BC from 2006 to 2009 showed that only 71% of the study group's 759 adult immigrants, whose additional language was English, had undergone HBV testing, 8% had received vaccination without testing, and 21%

**TABLE 1.** At-risk groups for whom routine screening for hepatitis B virus (HBV) is recommended.

- People who were born or have resided in regions where HBV is more common (Asia, Australasia, Eastern Europe, South America, Africa, Middle East).
- Household contacts with HBV carriers.
- Sexual contacts with HBV carriers, persons with multiple sexual partners.
- People who inject illicit drugs or use them intranasally (past or present).
- People who are incarcerated.
- Patients with renal failure who require dialysis.
- Patients with signs of liver disease (i.e., abnormal liver enzyme test) or other infections (i.e., hepatitis C, HIV).
- Pregnant women.
- Patients requiring immunomodulation therapy or those who will develop immunosuppression.

Adapted from “Management of hepatitis B virus infection: 2018 guidelines from the Canadian Association for the Study of Liver Disease and Association of Medical Microbiology and Infectious Disease Canada.”<sup>12</sup>

had neither undergone testing nor received vaccination.<sup>14</sup> The authors suggested that better identification and management of chronic hepatitis B carriers was needed to improve strategies for reducing HBV transmission to others.<sup>9,14</sup> In BC, it is recommended that all pregnant women receive prenatal screening for HBV with hepatitis B surface antigen (HBsAg) during every pregnancy.<sup>12,13</sup> It is estimated that 95% to 99% of all pregnant women are routinely screened, and that 0.7% to 1.2% screen positive for HBsAg.<sup>13</sup>

**Clinical presentation of chronic hepatitis B**

The likelihood of developing chronic hepatitis B after an exposure to HBV is highly dependent on the patient’s age. Patients who acquired HBV via vertical transmission in infancy have

more than a 90% risk of developing chronic infection, but this risk decreases to less than 5% in patients who are exposed to HBV as an adult. In the latter scenario, over 95% of those infected will transition to resolved infection state (HBsAg loss).<sup>12</sup> Acute hepatitis B is usually a subclinical or self-limited illness, but in less than 1% cases, it can result in severe hepatitis and fulminant liver failure.<sup>12</sup>

Chronic hepatitis B is defined as having a positive HBsAg for 6 months or longer.<sup>15</sup> Most patients with chronic hepatitis B are asymptomatic until the liver disease becomes advanced and there is evidence of cirrhosis, or if there are extrahepatic manifestations. Some patients may also report nonspecific symptoms such as fatigue. Physical examination is often normal, but physicians should pay special attention to assessing for stigmata of chronic liver disease.

**TABLE 2.** Clinical phases in chronic hepatitis B, corresponding lab work, and serological and diagnostic tests.

Clinical phase	HBeAg*–positive chronic infection	HBeAg–positive chronic hepatitis	HBeAg–negative chronic infection	HBeAg–negative chronic hepatitis	HBsAg* negative
Synonymous terminology	• Immune tolerant	• Immune active	• Low replicative chronic HBV • Inactive carrier		• Resolved hepatitis B infection • Occult hepatitis B • Functional cure
• HBsAg*	+	+	+	+	–
• HBeAg*	+	+	–	–	–
• Anti-HBc*	+	+	+	+	+
• Anti-HBe*	–	–	+	+	+
• Anti-HBs*	–	–	–	–	+/-
Alanine aminotransferase (ALT)	Normal	Elevated or fluctuating	Normal	Elevated or fluctuating	Normal
HBV DNA (IU/mL)	> 10 <sup>7</sup>	10 <sup>4</sup> –10 <sup>7</sup>	Often < 2000	10 <sup>3</sup> –10 <sup>7</sup>	Undetectable
FibroScan	Normal	Abnormal	Usually normal	Abnormal	Normal
Monitoring lab work**	ALT and HBV DNA every 3–6 months HBeAg every 6–12 months	ALT and HBV DNA at 3 and 6 months, then every 3–6 months <sup>§</sup> HBeAg every 3–6 months	ALT and HBV DNA every 6–12 months HBsAg every 12 months	ALT and HBV DNA at 3 and 6 months, then every 3–6 months <sup>§</sup> HBsAg every 12 months	No routine lab work
Treatment recommended	No <sup>  </sup>	Yes	No <sup>  </sup>	Yes	No <sup>  </sup>
Referral to specialist	Optional	Recommended	Optional	Recommended	No <sup>#</sup>

Note: Above parameters presume no other coexisting liver comorbidities.  
 \* HBeAg: hepatitis B e-antigen; HBsAg: hepatitis B surface antigen; anti-HBc: hepatitis B core antibody; anti-HBe: hepatitis B e-antibody; anti-HBs: hepatitis B surface antibody  
 † Recommendations for lab work are variable and ultimately depend on specific patient characteristics, results and stability of previous tests, other liver comorbidities, etc.  
 ‡ Renal function lab work monitoring is recommended if using tenofovir disoproxil fumarate or adefovir  
 § Monitoring lab work can be done every 6 months if using more potent antivirals (i.e., tenofovir disoproxil fumarate or entecavir), or every 3 months if using less potent agents (i.e., lamivudine)  
 || No treatment would generally be recommended unless there was immunosuppression. Degree of immunosuppression and current phase of infection help determine whether prophylactic treatment is warranted  
 ¶ Prophylactic treatment in pregnancy would be considered  
 # Referral may be indicated if patient to undergo immunosuppressive treatment

Extrahepatic manifestations are thought to be due to circulating immune complexes, and the most common attributable to chronic hepatitis B are polyarteritis nodosa and membranous nephropathy.<sup>16</sup> Polyarteritis nodosa is a systemic necrotizing vasculitis that usually affects medium-sized arteries but sometimes can also affect small arteries. Most cases of polyarteritis nodosa are idiopathic, but traditionally, up to approximately 35% of total cases were thought to be associated with HBV.<sup>17</sup> However, with the introduction of the HBV vaccine and antiviral agents, HBV is now thought to be responsible for a much lower proportion of total cases. The classical presentation of membranous nephropathy is nephrotic range proteinuria. In children, papular acrodermatitis can occur, which causes maculopapular, erythematous, and nonpruritic lesions involving the face and extremities.<sup>16,18</sup> Only a small number of patients may recall a preceding history of acute hepatitis B. A serum sickness-like syndrome with fever, rash, and polyarteritis can occur during this phase of illness and usually precedes the onset of jaundice.<sup>16,19</sup>

### Treatment and prevention of chronic hepatitis B

Treatment goals of chronic hepatitis B have traditionally been to prevent progression of chronic inflammation to higher levels of fibrosis, and to prevent cirrhosis and hepatocellular carcinoma. The American Association for the Study of Liver Diseases, the Asian Pacific Association for the Study of the Liver, the Canadian Association for the Study of the Liver, and the European Association for the Study of the Liver all publish detailed guidelines on the treatment and management of hepatitis B.<sup>12,15,20,21</sup> Table 2 summarizes the various phases of chronic hepatitis B and situations where antiviral treatment is generally recommended. An assessment of fibrosis that is performed noninvasively is generally recommended for all patients and can be done various ways, including by FibroScan or aspartate aminotransferase to platelet ratio index score.

Within Canada, reimbursement criteria and access to antiviral agents for the treatment of hepatitis B are quite variable among

jurisdictions.<sup>3</sup> In BC, reimbursable prescription drug coverage through application for special authority request previously covered only lamivudine as a first-line option and pegylated interferon alpha in a few selected scenarios. In November 2018, BC PharmaCare added tenofovir disoproxil fumarate and entecavir as first-line options along with lamivudine. In BC, tenofovir alafenamide is not currently a covered benefit drug for the treatment of HBV, although that may change in the future. Tenofovir alafenamide is a prodrug, and has an improved side effect profile in terms of renal function and bone turnover when compared with tenofovir disoproxil fumarate.<sup>21</sup> Usual dosage information, potential side effects, and recommended monitoring of these HBV antiviral medications are listed in Table 3. In BC, application for special authority coverage for chronic hepatitis B medications is open to all medical practitioners and is not restricted to specific specialists. Clinical criteria that need to be met include an alanine aminotransferase greater than the upper limit of normal and HBV DNA greater than 2000 IU/mL. Alternatively, medication coverage is also available if there is evidence of fibrosis with stage equal to or greater than F2, which can be deduced through FibroScan,

aspartate aminotransferase to platelet ratio index, or liver biopsy. If there are circumstances in which a provider wants to prescribe antivirals for hepatitis B that are not covered by the listed indications, such as for prophylaxis in the setting of immunosuppression, additional information can be submitted along with the special authority application for consideration by the BC Hepatitis Drug Benefit Adjudication Advisory Committee.

Oral medications for chronic hepatitis B are usually well tolerated, although they often need to be taken for prolonged periods and sometimes indefinitely to prevent viral reactivation. Stopping treatment is possible for those who have hepatitis B e-antigen (HBeAg)-positive chronic hepatitis if they subsequently convert to anti-HBe positive, which suggests transition to HBeAg-negative chronic infection (also known as low replicative chronic HBV infection or inactive carrier), as long as there is close monitoring for relapse thereafter. For patients with HBeAg-negative chronic hepatitis, treatment is often indefinite. There are indicators for when antiviral medications can potentially be stopped based on close observation, such as if there is persistent loss of HBsAg; however, generally, these are the

**TABLE 3.** Dosing of common hepatitis B virus antiviral therapies.

	Dose in adults*	Potential side effects	Monitoring on treatment
Lamivudine	100 mg daily	Pancreatitis Lactic acidosis	• Amylase or lactic acid level if clinical concern
Entecavir	0.5 mg daily (1 mg daily) <sup>†</sup>	Lactic acidosis (decompensated cirrhosis only)	• Lactic acid level if clinical concern
Tenofovir disoproxil fumarate	300 mg daily	Nephropathy Fanconi syndrome Osteomalacia Lactic acidosis	• Baseline serum creatinine and phosphate, urine glucose and protein at baseline and then at least annually • Consider bone density study at baseline and during treatment in those with fractures or risk factors for osteopenia • Lactic acid if clinical concern
Tenofovir alafenamide <sup>‡</sup>	25 mg daily	Lactic acidosis	• Baseline serum creatinine and phosphate, urine glucose and protein at baseline and then as needed • Lactic acid if clinical concern

\* Dosing adjustments needed in renal dysfunction

† If lamivudine experienced or have decompensated cirrhosis

‡ Not currently a covered benefit drug for HBV treatment in BC, Canada

Adapted from "Update on prevention, diagnosis, and treatment of chronic hepatitis B: AASLD 2018 hepatitis B guidance"<sup>21</sup>

exception rather than the rule. Newer medications such as tenofovir disoproxil fumarate, tenofovir alafenamide, and entecavir have low rates of resistance, even with prolonged use. For patients who have developed resistance to other medications, tenofovir disoproxil fumarate or tenofovir alafenamide is typically the drug of choice. Long-term use of tenofovir disoproxil fumarate is generally not recommended for patients with chronic kidney disease or osteoporosis because it can worsen renal function and reduce bone mineral density. According to the 2017 European Association for the Study of the Liver guidelines, tenofovir alafenamide is recommended over tenofovir disoproxil fumarate in patients older than 60 years, those with bone disease (chronic steroid use or medications that worsen bone density, history of fragility fracture, osteoporosis), and those with renal impairment (estimated glomerular filtration rate < 60 mL/min/1.73 m<sup>2</sup>, albuminuria > 30 mg/24 h, moderate dipstick proteinuria, low phosphate < 2.5 mg/dl, or dialysis patients).<sup>20</sup> Pegylated interferon alfa has sometimes been used because it has a finite duration of treatment, although sustained response rates occur only in a minority of patients, and the medication is associated with

significant side effects and is contraindicated in patients with cirrhosis.

For pregnant patients who screen positive for HBsAg, ordering HBV DNA viral load is recommended to determine if further antiviral prophylaxis is required during pregnancy

**In Canada, BC was the first province to adopt a routine school-based program for HBV vaccination, which started in 1992.**

to reduce perinatal HBV transmission [Figure].<sup>12</sup> The 2017 Society of Obstetricians and Gynaecologists of Canada guidelines provide a level II-B recommendation for starting antiviral treatment in pregnant patients with HBV DNA viral load greater than 200 000 IU/mL starting in the third trimester (around 28 to 32 weeks) until delivery.<sup>22</sup> Typically, tenofovir disoproxil fumarate is chosen because of its safety in pregnancy and high barrier to developing resistance. In addition, to reduce the risk of HBV transmission from HBsAg-positive parents to

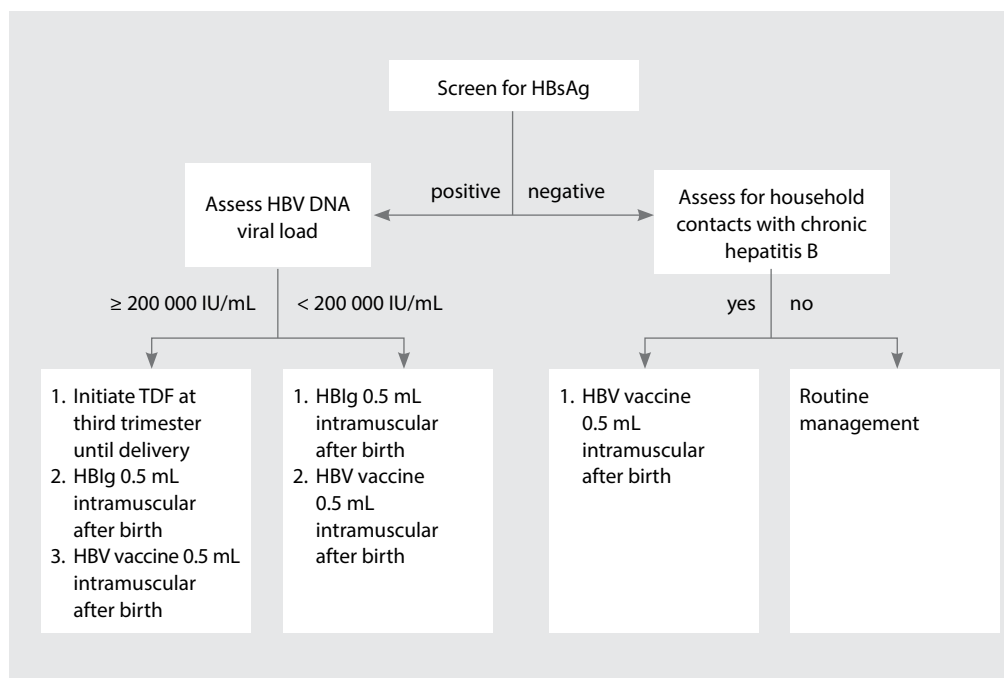
infants, hepatitis B immune globulin (HBIG) 0.5 mL intramuscular injection along with HBV vaccine 0.5 mL intramuscular injection is recommended as prophylaxis for the infant after birth.<sup>13</sup> If the mother is not HBsAg positive but the father or another household contact has chronic hepatitis B, then HBV vaccine 0.5 mL intramuscular injection is recommended for the infant after birth, but not HBIG.<sup>13</sup> Of note, all infants in BC are vaccinated for HBV as part of the diphtheria, tetanus, pertussis, hepatitis B, polio, and *Haemophilus influenzae* type B (DTaP-HB-IPV-Hib) vaccine series given at ages 2, 4, and 6 months. The prophylaxis given at birth to high-risk infants is in addition to the routine immunizations given; thus, these infants receive four doses of hepatitis B vaccination in total.

Screening for hepatocellular carcinoma is an important aspect of management. The Canadian Association for the Study of the Liver guidelines recommend surveillance ultrasound screening every 6 months for those who are at high risk. High-risk groups include Asian men aged 40 years or older, Asian women 50 years or older, African people aged 20 years or older, cirrhotic patients, those with a family history of hepatocellular carcinoma (starting at age 40 years), and all HIV-co-infected patients (starting at age 40 years).<sup>12</sup> If ultrasound is not available, then alpha-fetoprotein can be used, but it has comparably lower sensitivity and specificity.<sup>21</sup>

**Goals and future targets for chronic hepatitis B**

The United Nations' goal for HBV is to reduce new cases of HBV by 90% by 2030 (equivalent to 0.1% prevalence HBsAg in children).<sup>23,24</sup> As of 2015, the World Health Organization reported that 185 (95% of all) countries have incorporated HBV vaccination into their national infant immunization schedule.<sup>23,24</sup> In Canada, BC was the first province to adopt a routine school-based program for HBV vaccination, which started in 1992; all other provinces did so in 1998. Several provinces have now moved to a routine infant or birth HBV vaccination program; BC made this switch in 2001.

Future targets for HBV treatment will include a functional cure and, subsequently, a



**FIGURE.** Screening and management of pregnant hepatitis B-positive patients (HBsAg: hepatitis B surface antigen; HBIG: hepatitis B immune globulin; TDF: tenofovir disoproxil fumarate).



complete cure. A functional cure will allow suppression of HBV DNA and normalization of alanine aminotransferase at the end of treatment, with a loss of HBsAg. However, covalently closed circular DNA would not be eliminated in this situation; thus, there is the ongoing risk of HBV reactivation with immunosuppression. A complete cure will result in permanent HBV DNA suppression and normalization of alanine aminotransferase with the elimination of covalently closed circular DNA. Of note, neither strategy targets HBV DNA integration, and thus does not necessarily prevent hepatocellular carcinoma unless HBV treatment is initiated early before integration has occurred.<sup>25</sup> Several direct-acting drugs that target different aspects of the HBV life cycle are currently in development, although most are in preclinical phases or early phase clinical trials. These include molecules targeting viral entry, covalently closed circular DNA, capsid inhibitors, and HBsAg release inhibitors.<sup>26,27</sup>

## Summary

Chronic hepatitis B is a complex viral infection that requires longitudinal follow-up and management. Important clinical phases and recommended investigations for chronic hepatitis B are summarized in **Table 2**. Detailed management algorithms are outside the scope of this review but are well summarized in various international guidelines.<sup>12,15,20,21</sup> Not uncommonly, a patient's test results may not fit perfectly within any particular phase, and clinical judgment on a case-to-case basis is often required. Referral to an infectious diseases or hepatology specialist is reasonable, especially in situations where consideration of antiviral treatments may be warranted. ■

## Competing interests

None declared.

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# Epidemiology of Lyme disease and pitfalls in diagnostics: What practitioners need to know

Accurate clinical diagnosis of Lyme disease based on the most common finding, erythema migrans, can be challenging, but in later stages, is aided by established serologic testing.

**ABSTRACT:** Lyme disease is a tick-transmitted infection caused by *Borrelia burgdorferi*. Its prevalence is quite low in British Columbia compared with eastern North America. BC has a long history of studying Lyme disease. Extensive fieldwork and passive surveillance data clearly showed the low prevalence of this spirochete in the vector (ticks) and the predominant host (deer mice). The number of annual confirmed Lyme disease cases in BC is low, consistent with field epidemiological data. Lyme disease diagnosis is usually straightforward but can be more complex. In early Lyme disease, diagnosis is mainly clinical in patients with typical findings, a history of exposure in a Lyme-endemic region, and a history of having an attached engorged tick. For early disseminated and late Lyme disease, recommended public health laboratory tests using optimal blood samples are helpful. Recognition of erythema migrans following a tick bite is considered diagnostic; however, cor-

rect recognition of erythema migrans rash can be challenging in low-endemic areas such as BC. For serologic testing when needed, the BC Centre for Disease Control Public Health Laboratory adheres to the universally accepted Lyme disease testing guidelines, and recently introduced the newly recommended modified two-tiered test algorithm for diagnosis. There are other commercial alternative tests; however, the quality of those tests is often questionable, and their use is not recommended.

**L**yme disease is a tick-transmitted infection caused by *Borrelia burgdorferi*. It is transmitted by *Ixodes* ticks, colloquially called deer ticks. In British Columbia, the disease is transmitted predominantly by *I. pacificus*; in central and eastern Canada, it is transmitted by *I. scapularis*. Ticks have a 2-year life cycle and three stages; the second (nymph) and third (adult) stages transmit Lyme disease. Ticks are usually encountered in grassy or wooded areas. They typically must be on the host at least 24 to 72 hours to transmit infection,<sup>1-3</sup> at which stage they are engorged [Figure 1]. Often, but not always, the engorged tick is seen.

There are three stages of Lyme disease: early localized, early disseminated, and late Lyme. Despite the diversity of potential manifestations, there are usually three common and typical presentations and two less typical common presentations. The first, erythema migrans, is seen 3 to 30 days after infection [Figure 2]. If not treated, early disseminated manifestations arise weeks to months after the bite, and

present as a disseminated erythema migrans rash, and/or a radiculopathy, most commonly Bell palsy. Rare second stage presentations are carditis (usually heart block), meningitis, or encephalitis. There may also be polyarthralgias or a localized arthritis at this stage, but oligoarthritis, the third common presentation, is more typically seen in a third stage. Neurologic disease is also sometimes diagnosed at a later stage. Any stage, but particularly the first and second stages, may have nonspecific systemic symptoms. In reported cases of Lyme disease, patients experienced multiple signs: 70% had erythema migrans, 30% had arthritis, 9% had Bell palsy, 4% had another radiculoneuropathy, 2% had meningitis or encephalitis, and 1% had carditis.<sup>4</sup> Despite being promoted by some groups, there is no compelling evidence of serious posttreatment Lyme disease or of a host of nonspecific or other diseases caused by Lyme disease.



**FIGURE 1.** An unfed *Ixodes pacificus* female; an engorged *I. pacificus* female after a blood meal.

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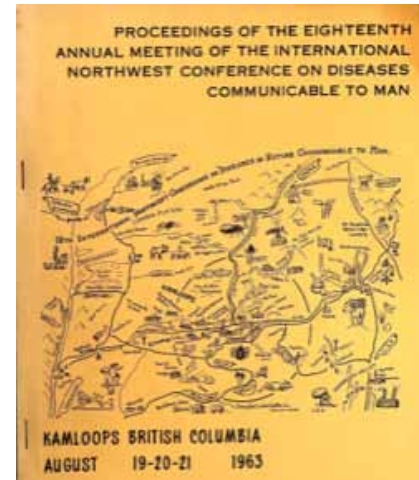
**FIGURE 2.** Different types of erythema migrans rashes on Lyme disease patients after *Borrelia burgdorferi*-carrying tick bites (courtesy of Johns Hopkins Lyme Disease Research Center).

In dealing with the consideration of Lyme disease, clinicians encounter two categories of patients. We discuss primarily the first—those with Lyme disease or probable Lyme disease. However, and particularly in BC, where Lyme disease occurs infrequently, physicians often encounter patients who think or believe they have Lyme disease in the absence of compelling evidence. They usually do not have a clear exposure history or a documented rash consistent with Lyme disease, or do not have any of the other typical objective manifestations of Lyme disease. Additionally, these patients do not have positive laboratory tests done in an accredited lab but do usually have myriad highly distressing and life-altering symptoms, have often had courses of antimicrobials and other medications that may result in a transient “response” but do not cure them, and often have a “positive” test using one of the tests that are not recommended. These individuals deserve a thorough assessment for conditions other than Lyme disease. This is discussed near the end of this article.

### Epidemiology and distribution of ticks and Lyme disease in BC

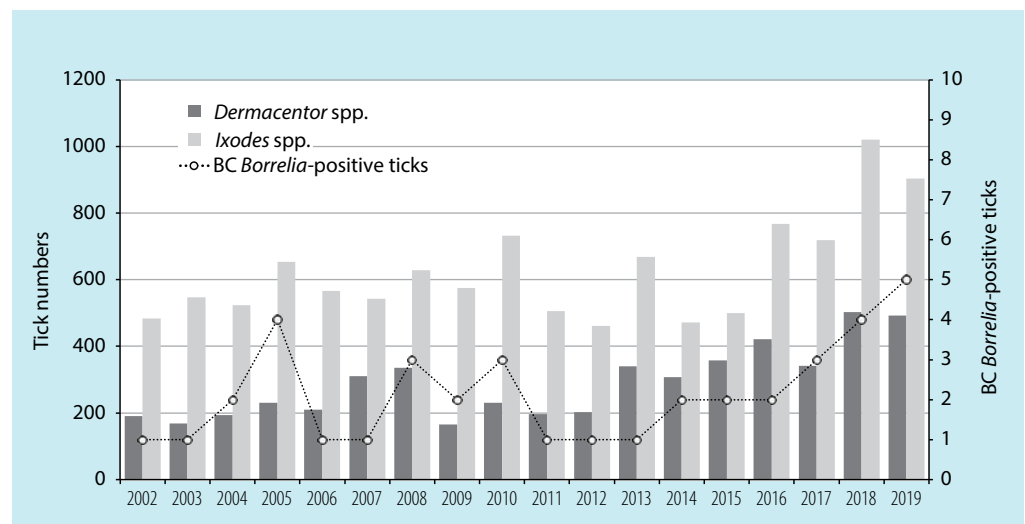
Historically, BC was well ahead of any other province in Canada in terms of studying ticks and tick-borne diseases. Tick research began in the early 1950s at the Canada Agriculture Research Station in Kamloops and played a key role in tick surveillance and determining

the distribution of vector-borne and zoonotic diseases. This is reflected in a map created by JD Gregson, which was printed in the *Proceedings of the Eighteenth Annual Meeting of the International Northwest Conference on Diseases Communicable to Man* [Figure 3]. Gregson also wrote a monograph on ticks; he found a high diversity of ticks in Canada, and particularly emphasized BC ticks.<sup>5</sup> Recently, Morshed and colleagues collated 17 years of passive tick surveillance data from 2002 to 2018 and analyzed them to determine the occurrence of tick species and the prevalence of *Borrelia* spp. in ticks in BC. The authors reported 29 different tick species distributed throughout BC.<sup>6</sup> The predominant species are *Ixodes pacificus*, *Dermacentor*



**FIGURE 3.** 1963 conference proceedings cover page showing different tick vector distributions in interior British Columbia.

*andersoni*, and *I. angustus*. *I. pacificus* is more concentrated in the Lower Mainland and on Vancouver Island, *D. andersoni* (not a competent vector for *B. burgdorferi*) is more common in the Interior, and *I. angustus* is found throughout BC but low in numbers compared with *I. pacificus* and *D. andersoni*. Both *I. pacificus* and *I. angustus* were found to carry *B. burgdorferi* and are the principal vectors for transmitting Lyme disease in BC. The number of human tick submissions increased significantly ( $P < 0.001$ ) between 2013 and 2018, but only 31 (0.28%) of 11 155 *B. burgdorferi*-carrying ticks were positive when tested either by culture or by polymerase chain reaction test.<sup>6</sup> Later, we added 2019 data [Figure 4] and found similar patterns.



**FIGURE 4.** Yearly submission of predominant ticks and number of *Borrelia burgdorferi*-carrying ticks in BC.

It is impossible to determine what percentage of tick-bitten patients will develop Lyme disease in a low-endemic area such as BC.

*I. pacificus* ticks are distributed across southern BC, predominately in the Greater Vancouver area and on Vancouver Island, but they have been detected as far north as Smithers (54°80'N, 127°20' W) based on active surveillance.<sup>7,8</sup> The deer mouse (*Peromyscus maniculatus*), the major mammalian reservoir for *B. burgdorferi* in BC, has a widespread distribution in BC and acts as a common host for larval and nymphal *I. pacificus* ticks. To determine the percentage of tick positivity for *B. burgdorferi*, 3500 deer mice were tested by culture: 30 (0.86%) were positive. In addition, 164 mice were tested for antibodies to *B. burgdorferi*: 6 (3.66%) were positive, demonstrating a low prevalence in this reservoir.<sup>9</sup> Farther inland, *I. pacificus* ticks are uncommon but may be dispersed by birds during spring migration.<sup>10-12</sup> The Rocky Mountain wood tick, *D. andersoni*, is common in southeastern BC. It is not a vector of Lyme disease<sup>13</sup> but can transmit rickettsial and bacterial pathogens.<sup>14</sup>

In BC, the first Lyme disease case was reported locally in 1988.<sup>15</sup> The first isolation of *B. burgdorferi* sensu stricto in BC was reported in an adult *I. pacificus* tick and an immature *I. angustus* tick in 1993.<sup>16</sup> Lyme disease is endemic in BC, but only a few proven cases occur every year, although a certain group believes that this is not a true reflection of Lyme disease

cases in BC. As a result, an innovative capture–recapture methodology was used to determine the true number of cases of Lyme disease from 1997 to 2008. Conservative estimates placed the true number of Lyme disease cases in BC during this period at 142 (95% CI, 111–224), indicating up to 40% underreporting of this rare disease.<sup>17</sup> Morshed and colleagues analyzed BC case numbers from 2002 to 2018, along with available Canadian positivity rates.<sup>6</sup> The case numbers in BC remained quite low, ranging from 3 to 22 cases, except in 2016, when there were 40 cases. On average, half those cases were acquired during travel outside BC (data not shown). We added 2019 data and found a similar trend [Figure 5]. The Lyme disease case number in BC is much lower than that in eastern North America (e.g., Nova Scotia, Ontario, and Quebec [data not shown]), but is similar to that in the western US (Washington, Idaho, and California).<sup>18</sup>

### Treatment

Evidence-based treatment of Lyme disease has been virtually the same for several decades, including in the 2020 guidelines by the Infectious Diseases Society of America, American Academy of Neurology, and American College of Rheumatology.<sup>19</sup> The mainstay of treatment is doxycycline 100 mg orally twice daily for 10 days, except for carditis or neurologic manifestations, in which case treatment is oral doxycycline or IV ceftriaxone for 14 to 21 days.

Recommended treatment for arthritis is 28 days of oral doxycycline.

Alternative guidelines are widely promoted by some groups, such as the International Lyme and Associated Diseases Society. They involve longer and often more complicated regimens, including with other drugs. Although such regimens have been advocated for decades, no credible evidence has been provided to demonstrate their superiority, or in some cases any efficacy, and certainly no evidence has demonstrated that their benefits exceeds their risks.

### Pitfalls in diagnosis

For most patients, Lyme disease is a clinical diagnosis in which the patient has typical manifestations, plus a history of exposure to a Lyme disease-endemic area, and a history of having an attached engorged tick. Lyme disease-carrying ticks, predominantly *Ixodes* spp., need to be attached for at least 24 to 72 hours.<sup>1-3</sup> In these clinical settings, treatment should be initiated as if the patient has Lyme disease; serologic support is not usually needed.

Ideally, early Lyme disease will be suspected based on the presence of a typical erythema migrans skin rash. In areas where Lyme disease is prevalent, such as Rhode Island, Pennsylvania, New Hampshire, Vermont, and Maine, where confirmed cases per 100 000 population ranged from 49.7 to 121.3 in 2019,<sup>18</sup> most people with such a rash will have Lyme disease. However, in low-prevalence areas such as BC (approximately 0.2 confirmed cases per 100 000 population), erythema migrans is often misdiagnosed. Typical erythema migrans arises 3 to 30 days after the bite, usually at the site of the bite, spreads slowly over days to weeks, is more than 5 cm in diameter—most typically 10 to 16 cm—and often has central clearing. In contrast, cases misdiagnosed often arise within 3 days (usually hours), are often itchy or indurated, do not reach 5 cm in diameter, and often resolve quickly. These are presumably an allergic reaction or a localized cellulitis. For example, Figure 7 shows a rash resembling erythema migrans in a patient from the West Coast, a low-prevalence area; the patient was seronegative and a diagnosis of Lyme disease was excluded. Even in Lyme-endemic areas, erythema migrans is frequently not diagnosed,

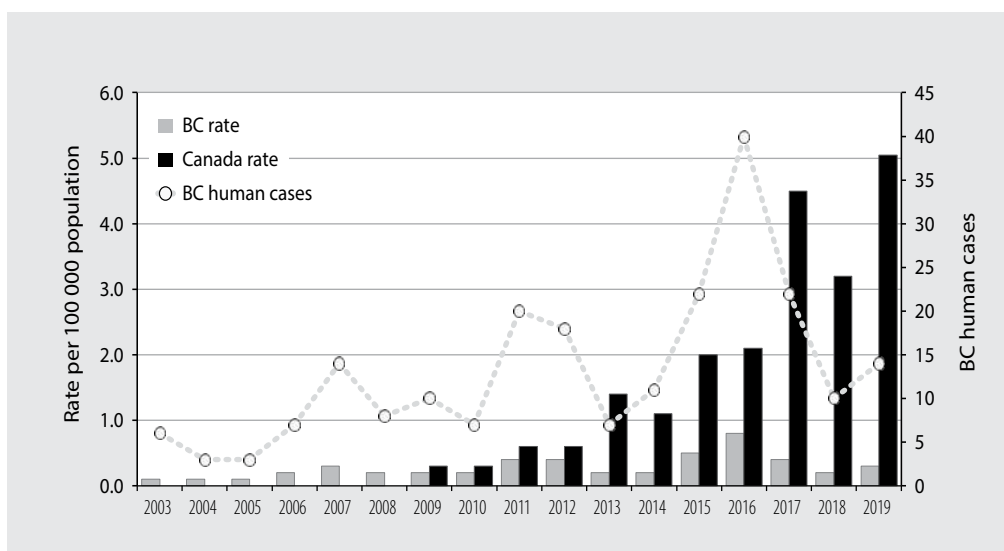


FIGURE 5. Lyme disease rate in British Columbia (BC) and Canada, and BC human cases from 2003 to 2019.

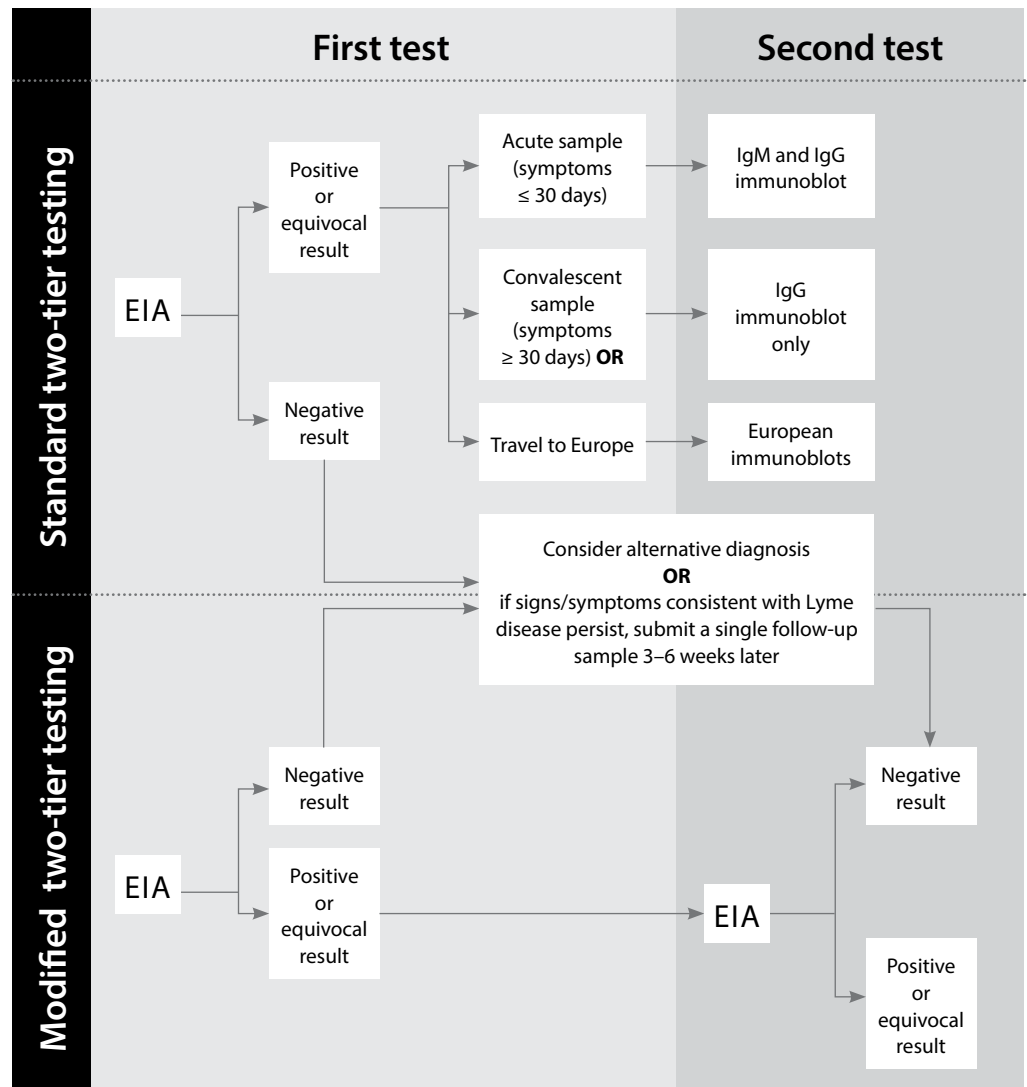
and non-erythema migrans rashes are frequently called erythema migrans.<sup>20,21</sup>

Other clinical presentations such as Bell palsy or polyarthralgias are less specific for Lyme disease, but in the correct clinical context, they should prompt suspicion of Lyme disease, and in patients with exposure history in an endemic region, should prompt empiric treatment as if the patient has Lyme disease, which, as in all infections where empiric therapy is initiated, is not the same as diagnosing the disease. When Lyme disease is specifically diagnosed or seriously considered, a careful cardiac examination and potentially an ECG is indicated. Although deaths from Lyme disease are very rare, heart block is the most common cause. It responds well to standard antimicrobial Lyme disease treatment but may need transient pacing.

### Laboratory diagnosis in BC

Serology or antibody testing is considered the test of choice for laboratory diagnosis of Lyme disease. In the early 1980s, immunofluorescence assay was used to screen Lyme disease, and all positive cases were further confirmed by western blot assay. A few years later, enzyme-linked immunosorbent assay or enzyme immunoassay replaced immunofluorescence assay because of notorious false positivity or nonspecific binding to the fluorescence dye. This enzyme-linked immunosorbent assay or enzyme immunoassay followed by western blot assay is evidence-based and was recommended at the Second National Conference on Serologic Diagnosis of Lyme Disease in October 1994<sup>22</sup> [Figure 6]<sup>23</sup>. Later, this two-tiered approach was adopted universally in North America, Europe, and Asia.

The BC Centre for Disease Control (BCCDC) Public Health Laboratory also offered this standard two-tiered test from the early 1990s to May 2021. Since June 2021, the Public Health Laboratory has adhered to a new algorithm recommended by the US Centers for Disease Control and Prevention—the modified two-tiered test.<sup>23,24</sup> As an initial test, samples are screened by an enzyme-linked immunosorbent assay test using a polyvalent antigen. This is a very sensitive test, so it will detect antibodies to Lyme disease or to other infections that are similar to Lyme disease. If the test is “positive” or “indeterminant,” the sample is further



**FIGURE 6.** Standard two-tiered testing and modified two-tiered testing serology for Lyme disease diagnosis<sup>23</sup> (reproduced with permission from the *Canada Communicable Disease Report* editorial office) (EIA: enzyme immunoassay).

tested by a specific and separate IgM and IgG enzyme immunoassay [Figure 6]. In addition, the BCCDC Public Health Laboratory uses western blots on suspected samples when the modified two-tiered test fails to provide discrete results.

### Other diagnostic testing offered/available in BC

The BCCDC Public Health Laboratory has also developed a protocol for *B. burgdorferi* culture and a number of molecular tests based on polymerase chain reaction, and provides them as adjunct tests if necessary to rule out infection upon consultation with the test-ordering

physician. Although specificity is quite good on these tests, sensitivity is less than 20%, even with the use of optimal samples, such as biopsy from the edge of erythema migrans rashes, synovial fluid from an inflamed joint, or cerebrospinal fluid from a neuro-Lyme suspected case. Positive results are rare, even in patients from highly endemic areas.

### Alternative testing

Alternatively diagnosed Lyme disease—that is, Lyme disease supposedly diagnosed on the basis of nontraditional testing using tests that have variable sensitivity but poor specificity, misinterpretation of standard serology, or purely

clinical grounds in patients with nonspecific symptoms—does not establish a diagnosis of Lyme disease. The accuracy and clinical usefulness of nontraditional tests, including urine antigen tests, immunofluorescent staining for cell wall-deficient forms of *B. burgdorferi*, lymphocyte transformation tests, CD57 natural killer cells, enzyme-linked immunosorbent spot (ELISpot) (IFN- $\gamma$  secretion by T cells), and tests for *B. burgdorferi* DNA on inappropriate specimens such as blood and urine or in house-developed western blots using different interpretation criteria, have not been adequately validated.<sup>25,26</sup> Most of the public health or accredited laboratories do not recommend using these tests for laboratory diagnosis.<sup>24</sup> Inappropriateness of alternatively diagnosed Lyme disease is particularly relevant in low-prevalence areas such as BC. This was well demonstrated in a study of patients in BC who were labeled as having chronic Lyme disease without evidence provided by standard criteria.<sup>27</sup> When assessed by numerous standard and experimental approaches, none had any evidence of infection with *B. burgdorferi*, or indeed infection at all. Most patients fulfilled criteria for chronic fatigue/myalgic encephalitis and were clinically indistinguishable from a control group of patients diagnosed with chronic fatigue syndrome. Many of these patients are highly symptomatic and severely debilitated.<sup>27</sup> They deserve concerted diagnostic and management approaches

but not long courses of putative regimens that are active against *B. burgdorferi*. The Association of Medical Microbiology and Infectious Disease Canada has strongly recommended that governments fund multidisciplinary clinics to provide comprehensive, compassionate, and evidence-based care for such individuals.

**Even in Lyme-endemic areas, erythema migrans is frequently not diagnosed, and non-erythema migrans rashes are frequently called erythema migrans.**

#### **Assessment of patients in whom Lyme disease is unlikely**

Such patients deserve a thorough assessment, both to carefully assess the likelihood of Lyme disease and to explore the cause(s) of their symptoms. Where the history, clinical findings, and sometimes laboratory tests suggest Lyme disease, these patients should be managed as discussed above, sometimes treating for Lyme disease as if they have Lyme disease—for example, those with an exposure history and new or recent typical erythema migrans rash without laboratory confirmation.

Where Lyme disease is not likely, alternative diagnoses must be considered based on a thorough history (e.g., travel, outdoor activities), examination, and consideration of other data. Most of these patients will have findings consistent with chronic fatigue/myalgic encephalitis syndrome, but there are numerous other possibilities—for example, sleep apnea, depression, substance use, multiple sclerosis, a rheumatologic condition, or cancer. The referral form for the Chronic Complex Diseases Program at BC Women's Hospital and Health Centre lists many of the more common considerations.<sup>28</sup> Investigations are warranted to assess for common conditions, but as in all testing, they should be evidence-based, not a

fishing expedition leading to significant risk of false-positive test results. Where Lyme disease is unlikely, no Lyme disease laboratory testing is warranted, and for most patients, no further testing for other pathogens (e.g., Epstein-Barr virus, *Bartonella*, *Rickettsia*) is warranted. Basic laboratory testing, as recommended for people with chronic fatigue, includes a complete blood count with differential chemistries (including glucose, electrolytes, calcium, renal, and hepatic function tests), thyroid-stimulating hormone, and creatine kinase (if muscle pain or weakness is present). Testing for HIV, syphilis, and hepatitis is warranted if results are not already known. Beyond that, investigations should be directed toward other considerations based on the patient's history and examination.

Management of Lyme disease can be difficult and time-consuming. As noted above, the Association of Medical Microbiology and Infectious Disease Canada has strongly recommended that governments fund multidisciplinary clinics to provide comprehensive, compassionate, and evidence-based care for affected individuals. The Chronic Complex Diseases Program at BC Women's is one such program.

#### **Summary**

Lyme disease is present in BC, but in low numbers. In the correct context, particularly in early Lyme disease, diagnosis is primarily clinical, without need for laboratory testing. However, in low-prevalence settings such as BC, accurate clinical diagnosis of the most common finding, erythema migrans, can be challenging. In later stages, diagnosis is aided by the use of established serologic testing, as performed by the BCCDC Public Health Laboratory. The sensitivity and specificity of these tests is well established. Alternative means of diagnosing putative Lyme disease should not be used. ■

#### **Acknowledgments**

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#### **Competing interests**

None declared.



**FIGURE 7.** A rash resembling Lyme erythema migrans rashes (courtesy of Dr Yazdan Mirzanezad).

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**Serology or antibody testing is considered the test of choice for laboratory diagnosis of Lyme disease.**

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# Travel-acquired infections and illnesses in British Columbians: Surveillance report from CanTravNet surveillance data, 2009–2018

This first published analysis of illnesses contracted by British Columbians during international travel to disease-endemic areas highlights the need to promote pretravel health advice and prompt posttravel assessment in order to reduce incidences of communicable and potentially life-threatening infectious diseases.

## ABSTRACT

**Background:** Previous studies have described travel-related infections among Canadians; however, a provincial-level analysis of British Columbians has not been published.

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*This article has been peer reviewed.*

**Methods:** We extracted and analyzed data from the Canadian Travel Medicine Network database for returning ill British Columbian travelers who presented to a GeoSentinel surveillance network site between March 2009 and September 2018.

**Results:** In total, 1153 ill travelers were assigned travel-related diagnoses; of those, 37% (n = 426) required inpatient management. The most common diagnoses (n = 1494) were tuberculosis (n = 174, 12%), malaria (n = 89, 6%), and enteric fever (n = 81, 5%). British Columbians who traveled to visit friends and relatives were disproportionately represented among travelers diagnosed with malaria (n = 35/89, 39%) and enteric fever (n = 69/81, 85%).

**Conclusions:** International travel introduces British Columbia residents to risk of communicable, preventable, and potentially life-threatening infectious diseases, which could be mitigated by promoting pretravel consultation.

## Background

The COVID-19 pandemic highlights the importance of recognizing and diagnosing travel-related infections. In 2018, 67 million passengers enplaned and deplaned in Canadian airports for international travel.<sup>1</sup> Vancouver International Airport was the point of nexus for 13 million of these international travelers,

of whom 4.9 million were returning Canadian residents.<sup>2</sup> Since 2015, transnational travel between Canada and countries other than the US has represented most of the increase in air traffic at Canadian airports.<sup>1</sup> This shift in Canada's international air travel coincided with an increased rate in Canadian population growth due to international immigration, which doubled both nationally and in British Columbia from 2015 to 2019.<sup>3</sup> In 2019, international immigration to Canada reached a record high of 436 689 people, which represented 80% of Canada's total population growth, surpassing the peak baby boom period in Canada, and was highest among all G7 countries.<sup>4</sup>

International travel to low- and middle-income countries introduces travelers and migrants to the risk of contracting communicable and preventable infectious diseases. In BC, most reported cases of shigellosis, rabies, and enteric fever are among international travelers.<sup>5</sup> International travel is associated with at least 25% of exposures to vaccine-preventable diseases, including influenza, measles, mumps, and meningococcal infections.<sup>5</sup> Multinational studies report 6% to 87% of travelers become ill during or posttravel; this estimate narrows to 43% to 79% for travelers to low-income and middle-income countries.<sup>6,7</sup> Boggild and colleagues described the diseases and syndromes acquired by



Canadian international travelers and migrants who reported to a Canadian GeoSentinel surveillance network site between September 2009 and September 2011; however, British Columbians represented only 7.3% of the travelers analyzed.<sup>8</sup> In 2019, Canadians most frequently traveled to Mexico and the UK; among BC travelers, top destinations were China and the UK.<sup>9</sup> Research on patterns of travel-related communicable diseases is hindered because the proportion of BC travelers that become ill posttravel has not been systematically assessed. The BC Centre for Disease Control collects provincial data and reports communicable diseases among British Columbians. However, if travel-related illnesses diagnosed in community laboratories are not reported to the BCCDC, travel-related illness may be underestimated, resulting in the underreporting of infections acquired by BC residents during travel.

Our analysis describes travel-related illness among British Columbians who were assessed

posttravel by infectious diseases physicians who specialize in tropical medicine at dedicated Canadian Travel Medicine Network (CanTravNet) clinics in Vancouver, Surrey, and Victoria. Our aim is to describe BC travelers who acquired illness abroad in order to further inform public health infrastructure and enhance strategies that increase the use of pretravel and posttravel/tropical medicine clinics for prospective and returning BC travelers, respectively.

## Methods

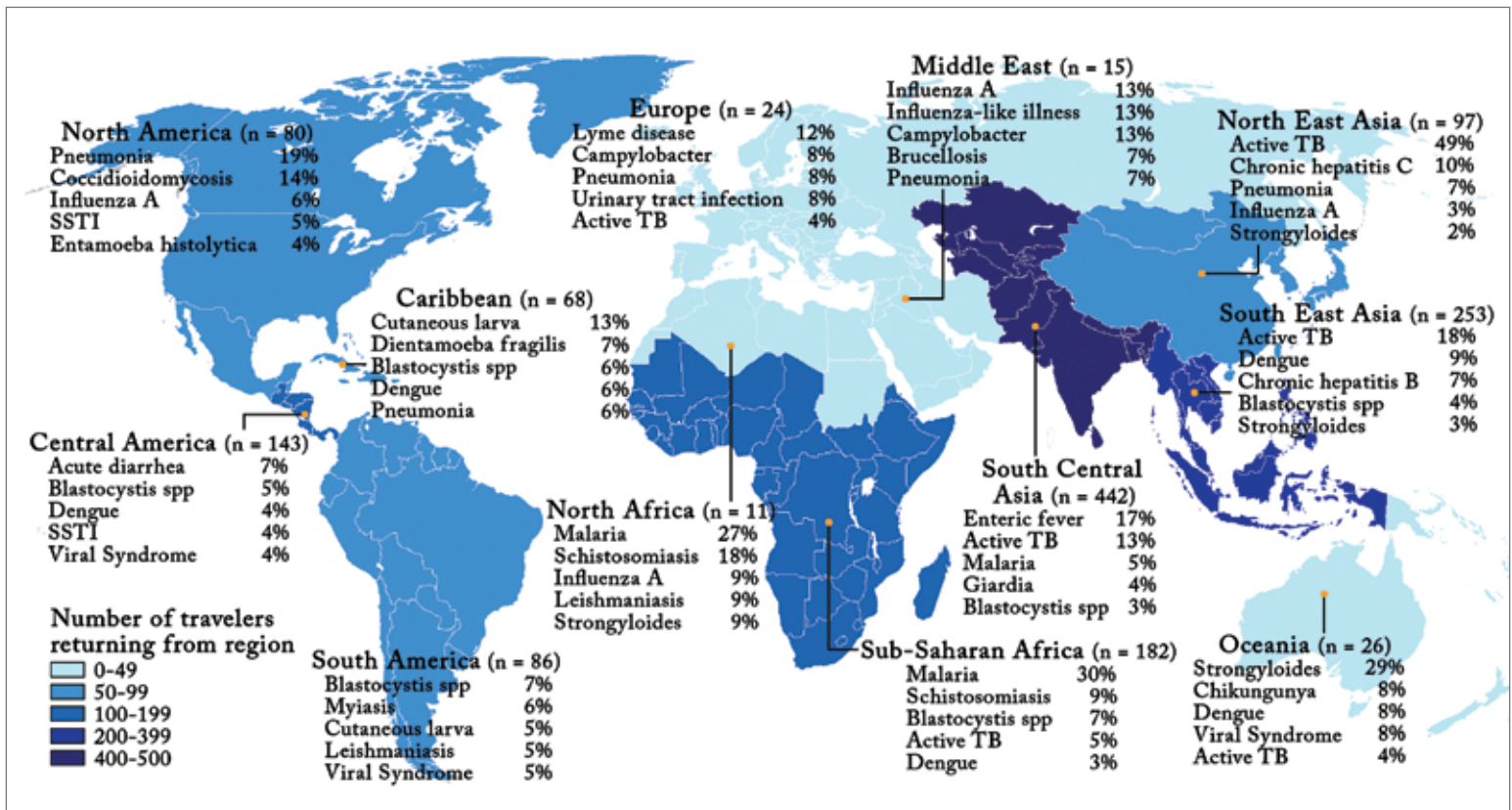
### Data source

Data were collected from the GeoSentinel global surveillance network surveillance platform ([www.istm.org/geosentinel](http://www.istm.org/geosentinel)). The US Centers for Disease Control and Prevention Institutional Review Board classifies this data collection protocol as public health surveillance. The seven Canadian GeoSentinel sites constitute CanTravNet, which works in collaboration with the Public Health Agency of Canada. The BC

CanTravNet sites consist of three referral-based posttravel outpatient clinics in Vancouver, Surrey, and Victoria that are staffed by specialists in tropical medicine. The anonymous, delinked, clinician-based travel surveillance data on ill travelers include demographics, travel details, purpose of travel, pretravel consultation, symptoms, and final diagnoses as specific etiologies and syndromes. Etiologic diagnoses are supported by microbiologic confirmation.

### Definitions

The primary purpose for travel designations include tourism, immigration, visiting friends and relatives, missionary and volunteer work, business, and other. Immigration-related travel was designated regardless of migration status. Visiting friends and relatives was defined as first-generation and second-generation immigrants traveling from a high-income country of current residence to a low-income country of origin for the purpose of visiting friends



**FIGURE.** Regional exposure for returning British Columbia travelers (2009–2018).

TB: *Mycobacterium tuberculosis*; SSTI: skin and soft tissue infection. Proportions shown represent the proportion of each diagnosis per total number of diagnoses within each region. There were 67 diagnoses that were not assigned a region; indeterminate/multiple regions of travel (n = 33), not ascertainable (n = 8), and missing data (n = 26).

Base map adapted from PresentationLoad PowerPoint Maps: [www.presentationload.com/powerpoint-maps/](http://www.presentationload.com/powerpoint-maps/).

and relatives. “Other” includes seasonal or temporary work, education, military service, and medical tourism travel purposes. Countries were grouped into 12 regions: North America, Central America, the Caribbean, South America, Europe, North Africa, Sub-Saharan Africa, the Middle East, South Central Asia, Northeast Asia, Southeast Asia, and Oceania.

**Inclusion criteria**

The study group included all patients with travel-related diagnoses recorded in the

GeoSentinel database after assessment at a BC CanTravNet site from 30 March 2009 to 12 September 2018.

**Statistical analysis**

Extracted data were managed in a Microsoft Access database. Statistical analyses were performed using SPSS Statistics 25 software (SPSS Inc.).

**Results**

In total, 1153 travelers with travel-related diagnoses were evaluated by CanTravNet sites in

BC during the 9-year surveillance period. There were 1494 diagnoses from the 1153 travelers examined: 891 travelers (77%) had a single diagnosis, and 262 (23%) had multiple diagnoses. The most common diagnoses overall (n = 1494) were tuberculosis (n = 174/1494, 12%), malaria (n = 89/1494, 6%), and enteric fever (n = 81/1494, 5%) [Table 1]. The most common syndromic diagnoses were febrile syndromes (30%), gastrointestinal syndromes (22%), respiratory syndromes (16%), dermatologic syndromes (9%), and genitourinary syndromes (3%).

**TABLE 1. Top 10 syndromic and etiologic diagnoses from 1153 ill returning travelers, by reason for travel (2009–2018).**

Rank	All travelers (n = 1153)	Immigration (n = 236)	Tourism (n = 424)	Visiting friends and family (n = 324)	Missionary and volunteer (n = 80)	Business (n = 61)	Other* (n = 28)
Total number of travel-related diagnoses	(n = 1494)	(n = 323)	(n = 555)	(n = 382)	(n = 115)	(n = 82)	(n = 37)
1	Active TB†	Active TB	<i>Blastocystis</i> spp.	Enteric fever	Malaria	Malaria	Malaria
	174 (12%)	145 (45%)	32 (6%)	69 (18%)	15 (13%)	13 (16%)	3 (8%)
2	Malaria	Chronic hepatitis B	Pneumonia	Malaria	<i>Blastocystis</i> spp.	Pneumonia	Active TB
	89 (6%)	29 (9%)	32 (6%)	35 (9%)	12 (10%)	5 (6%)	3 (8%)
3	Enteric fever	<i>Strongyloides</i>	Dengue	Active TB	Schistosomiasis	Active TB	Bacteremia
	81 (5%)	19 (6%)	32 (6%)	18 (5%)	7 (6%)	4 (5%)	2 (5%)
4	<i>Blastocystis</i> spp.	Chronic hepatitis C	Cutaneous larva migrans	Dengue	Dengue	Dengue	<i>Blastocystis</i> spp.
	60 (4%)	16 (5%)	20 (4%)	15 (4%)	6 (5%)	4 (5%)	2 (5%)
5	Dengue	Malaria	Viral syndrome	<i>Entamoeba histolytica</i>	<i>Entamoeba histolytica</i>	<i>Blastocystis</i> spp.	Leishmaniasis
	55 (4%)	9 (3%)	20 (4%)	11 (3%)	6 (5%)	4 (5%)	2 (5%)
6	Pneumonia	Schistosomiasis	Acute diarrhea	Acute diarrhea	Febrile illness	Influenza-like illness	Schistosomiasis
	51 (3%)	9 (3%)	19 (3%)	11 (3%)	5 (4%)	4 (5%)	2 (5%)
7	Acute diarrhea	Latent TB	SSTI‡	Brucellosis	<i>Giardia</i>	SSTI	<i>Shigella</i>
	35 (2%)	7 (2%)	18 (3%)	9 (2%)	4 (4%)	4 (5%)	2 (5%)
8	Chronic hepatitis B	Echinococcosis	<i>Giardia</i>	Urinary tract infection	<i>Rickettsia</i>	Influenza A	SSTI
	33 (2%)	4 (1%)	16 (3%)	9 (2%)	3 (3%)	3 (4%)	2 (5%)
9	<i>Entamoeba histolytica</i>	Leprosy	Insect bite	<i>Blastocystis</i> spp.	Enteric fever	<i>Campylobacter</i>	Urinary tract infection
	32 (2%)	4 (1%)	15 (3%)	8 (2%)	2 (2%)	2 (2%)	2 (5%)
10	<i>Strongyloides</i>	<i>Dientamoeba fragilis</i>	Malaria	<i>Giardia</i>	<i>Campylobacter</i>	Coccidioidomycosis	Viral syndrome
	31 (2%)	3 (1%)	14 (3%)	7 (2%)	2 (2%)	2 (2%)	2 (5%)

\* Other: includes reason for travel related to military, education/student, or planned medical care

† TB: tuberculosis

‡ SSTI: skin and soft tissue infection

A total of 620 diagnoses were assigned to 426 patients who required inpatient management: the most common inpatient diagnoses were active TB (n = 147/620, 24%), malaria (n = 49/620, 8%), pneumonia (n = 45/620, 7%), enteric fever (n = 41/620, 7%), and dengue (n = 18/620, 3%) [Table 2].

Among travelers who required outpatient management, the most common etiologic diagnoses were *Blastocystis* spp. infection (n = 57/874, 7%), enteric fever (n = 40/874, 5%), malaria (n = 40/874, 5%), dengue (n = 39/874,

5%), and chronic hepatitis B (n = 28/874, 3%).

Among all 1153 travelers, the top reasons for travel were tourism (n = 424, 37%), visiting friends and relatives (n = 324, 28%), immigration (n = 236, 21%), missionary and volunteer work (n = 80, 7%), and business (n = 61, 5%). Among nonimmigration travelers, the most common diagnoses were enteric fever (7%), malaria (7%), *Blastocystis* spp. infection (5%), dengue (5%), and pneumonia (4%). The Figure summarizes the top five diagnoses per region of exposure: the most common regions of exposure

overall were South Central Asia, Southeast Asia, and Sub-Saharan Africa.

### Tuberculosis

Active tuberculosis was the most common diagnosis among all travelers [Table 1]; most cases were diagnosed among those traveling for immigration purposes (145/174, 83%). Hospitalization was required for 84% (147/174) of all active tuberculosis diagnoses. Five patients with tuberculosis (3%) were diagnosed with drug-resistant tuberculosis; additional

**TABLE 2.** Top five syndromic or etiologic diagnoses from 1153 ill returning travelers, by posttravel level of care required (2009–2018).

Diagnosis	Total number of diagnoses in database (n = 1494)	Total number of diagnoses requiring hospitalization (n = 620)	Three most common source countries
<b>Active TB*</b>	<b>174</b>	<b>147 (84%)</b>	<b>India, China, Philippines</b>
Pulmonary	111	106 (95%)	India, China, Philippines
Extrapulmonary	51	29 (57%)	India, China, Vietnam
Intracranial TB	26	13 (50%)	India, Philippines, China
Abdominal	14	9 (64%)	India, China, Vietnam
Skeletal	5	4 (80%)	China, Pakistan, Vietnam
Other	6	3 (50%)	Philippines, China, India
Miliary	7	7 (100%)	India, Hong Kong, Vietnam
XDR/MDR†	5	5 (100%)	China, Philippines, Vietnam
<b>Malaria</b>	<b>89</b>	<b>49 (55%)</b>	<b>India, Nigeria, Uganda</b>
<i>Plasmodium falciparum</i>	46	35 (76%)	Nigeria, Uganda, Kenya
<i>P. vivax</i>	27	9 (33%)	India, Indonesia, Pakistan
<i>P. ovale</i>	5	2 (40%)	Uganda, Ghana, Sierra Leone
<i>Plasmodium</i> spp.‡	11	3 (27%)	Nigeria, India, Ghana
<b>Pneumonia</b>	<b>51</b>	<b>45 (88%)</b>	<b>United States, China, India</b>
Lobar	32	29 (91%)	United States, China, India
Atypical	13	11 (85%)	United States, China, India
Other	6	5 (83%)	US, Hong Kong, Dominican Republic
<b>Enteric fever</b>	<b>81</b>	<b>41 (51%)</b>	<b>India, Mexico, Pakistan</b>
<i>Salmonella</i> Typhi	42	25 (60%)	India, Pakistan
<i>Salmonella</i> Paratyphi	23	12 (52%)	India, Mexico, Pakistan
Unspeciated	16	4 (25%)	India
<b>Dengue</b>	<b>55</b>	<b>18 (33%)</b>	<b>India, Indonesia, Philippines</b>

\*TB: *Mycobacterium tuberculosis*

†XDR: extensively drug-resistant tuberculosis/MDR: multidrug-resistant tuberculosis

‡unspeciated *Plasmodium* spp. infections

resistance to rifabutin was identified in one patient, another patient was resistant to streptomycin, and one patient was resistant to streptomycin, pyrazinamide, and rifabutin. The most common regions of exposure to tuberculosis were South Central Asia (n = 56/174, 32%), Northeast Asia (n = 48/174, 28%), and Southeast Asia (n = 47/174, 27%). Three countries accounted for most (71%) of the active tuberculosis exposures [Table 2]: India (n = 50, 29%), China (n = 45, 26%), and the Philippines (n = 27, 16%).

### Malaria

Malaria was the second-most common diagnosis among all travelers, most of whom were traveling for visiting friends and relatives (35/89, 39%), missionary and volunteer work (15/89, 17%), tourism (14/89, 16%), or business (13/89, 15%) [Table 1]. Table 2 shows the *Plasmodium* species of infection, the proportions of malaria cases requiring hospitalization, and the top countries of exposure for all malaria diagnoses. Nine patients (10%) were diagnosed with severe malaria: one due to infection with *P. vivax* acquired in India, seven due to infection with *P. falciparum* acquired in Sub-Saharan Africa, and one case was unspciated. The three most common regions of exposure to malaria were Sub-Saharan Africa (n = 54, 61%), South Central Asia (n = 22, 25%), and Southeast Asia (n = 5, 6%). Three countries accounted for nearly half (44%) of the malaria exposures [Table 2]: India (n = 19, 21%), Nigeria (n = 11, 12%), and Uganda (n = 10, 11%).

### Enteric fever

Enteric fever was the third-most common diagnosis, with nonimmigration travelers accounting for all diagnoses. Those traveling to visit friends and relatives accounted for 85% (69/81) of all enteric fever diagnoses [Table 1]. *Salmonella enterica* serotype Typhi and Paratyphi were isolated from blood and/or stool in 42 (52%) and 23 (28%) patients, respectively; the remaining cases of typhoidal *Salmonella* isolates were unspecified. The three most common regions of exposure to enteric fever were South Central Asia (n = 75, 93%), Central America (n = 5, 6%), and Southeast Asia (n = 1, 1%). Three countries accounted for most (93%) of the active enteric

fever exposures [Table 2]: India (n = 70, 86%), Mexico (n = 3, 4%), and Pakistan (n = 2, 3%).

### Pediatric diagnoses

Children and adolescents aged 18 years and younger (n = 49) accounted for 4% (n = 61/1494) of all diagnoses. The most common diagnoses were enteric fever (n = 8, 13%), malaria (n = 5, 8%), and active tuberculosis (n = 4, 7%). Inpatient management was required in 31% of children and adolescents (15/49). The

**This analysis showed that potentially life-threatening infections were commonly acquired by British Columbians during travel abroad. Active tuberculosis, malaria, and enteric fever were encountered most frequently, with clear overrepresentation among specific cohorts of travelers and geographic regions.**

most common diagnoses among those hospitalized were enteric fever caused by *Salmonella* Typhi (n = 5), falciparum malaria (n = 2), dengue (n = 2), and active tuberculosis (n = 2); one pediatric patient was hospitalized with melioidosis.

Young people aged 16 to 18 years were more commonly diagnosed with travel-related illness (n = 34, 56%) than those aged 0 to 5 years (n = 12, 20%) and 6 to 10 years (n = 10, 16%). Among those aged 0 to 10 years, visiting friends and family and tourism represented all reasons for travel. Children older than 10 years increasingly traveled for missionary and volunteer work (7/39, 18%). India was the most common source country for illness among those aged 0 to 10 years and 16 to 18 years; Thailand was the most common source country for illness among 11- to 15-year-olds.

### Discussion

This analysis showed that potentially life-threatening infections were commonly acquired by British Columbians during travel abroad. Active tuberculosis, malaria, and enteric fever were encountered most frequently, with clear overrepresentation among specific cohorts of travelers and geographic regions. Inpatient management was required for 37% of travelers, among whom the most common diagnoses were active tuberculosis, followed by malaria, pneumonia, enteric fever, and dengue.

Travel-related active TB was disproportionately represented in those who traveled for immigration. This is consistent with active TB incidence reported by the BCCDC.<sup>10</sup> The Canadian tuberculosis standards identify individual and public health benefits of latent TB infection treatment for individuals migrating from countries with a high incidence of TB.<sup>11</sup> Our analysis found that 70% of tuberculosis diagnoses occurred among immigrants who originated from three countries: India, China, and the Philippines. This highlights the need for proactive measures for those who might benefit from latent TB infection treatment in order to prevent treatable and potentially serious pulmonary and extrapulmonary TB infections.

Malaria due to *P. falciparum* infection, which can cause severe and potentially fatal disease, was reported in more than half of ill returning travelers who had malaria. While malaria infections due to *P. vivax* less commonly cause severe disease, it is notable that one-third of *P. vivax* infections required hospitalization. Of the 10% of malaria-infected travelers who had severe malaria, most cases were acquired by those traveling for business or tourism in Sub-Saharan Africa; however, there was one severe malaria case caused by *P. vivax*, which was acquired in India. Although there were no deaths among the severe malaria cases, one to two Canadians die annually due to delayed diagnosis or treatment.<sup>12</sup> Overall, most travel-related malaria was acquired by those traveling to visit friends and relatives, followed by missionary or volunteer work, tourism, and business travel. Our analysis showed that *P. falciparum* malaria was most commonly acquired in Sub-Saharan Africa, whereas *P. vivax* malaria was most commonly acquired in South Asia and Indonesia, consistent with the

literature on malaria acquired by travelers.<sup>8,13</sup> Targeted strategies are needed to increase appropriate malaria prophylaxis prescribing and adherence among these differing populations of travelers to high-risk malaria endemic regions in order to reduce malaria infections.

Enteric fever was among the top diagnoses requiring hospitalization. This was the most common diagnosis among travelers who visited friends and relatives, most of whom traveled to South Central Asia. A high proportion of enteric fever in North America is consistently reported among travelers who visit friends and relatives in South Asia, which has among the highest incidence of the disease.<sup>8,14,15</sup> Population-based estimates of the medical costs of enteric fever in Ontario highlight the substantial avoidable health care spending required for diagnosing and treating these infections.<sup>16</sup> The World Health Organization has proposed a policy on the programmatic use of oral live-attenuated Ty21a typhoid and parenteral unconjugated Vi polysaccharide in endemic countries. Despite countries having limited vaccine uptake in routine immunization programs, the global incidence rates of enteric fever have decreased.<sup>15,17</sup> The newer generation typhoid conjugate vaccines have the potential to effectively reduce the global burden of enteric fever.<sup>18</sup> Until the programmatic use of the newer generation typhoid conjugate vaccines is established in endemic countries, British Columbians are at risk of acquiring enteric fever when traveling to those countries. Typhoid immunization with an appropriate vaccine that is available in Canada, which has shown moderate effectiveness in travelers, is recommended for travelers to South Asia.<sup>19,20</sup> However, pretravel consultation to facilitate vaccination is infrequently sought by travelers who visit friends and relatives in high-burden regions.<sup>21,22</sup> The reasons for not seeking travel health advice are multifactorial; thus, the approach to identifying British Columbians at risk for enteric fever and the tailoring of prevention strategies is critical.

### Study limitations

This analysis is representative only of BC international travelers who were assessed at referral-based CanTravNet sites in BC. For example, although sexually transmitted infections

are commonly acquired during travel, only 1% of travelers in this data set had a diagnosis of sexually transmitted infection. Thus, the severity and frequency of illness among returning travelers in BC is underestimated. With a lack of denominator data (i.e., the total number of travelers), travel-related disease rates and risks cannot be determined, and the proportion of hospitalized patients is likely overrepresented. However, the descriptive analysis specific to BC travelers does highlight the utility of travelers being assessed at a BC CanTravNet site

**Fever in returning travelers is a medical emergency, but chemoprophylaxis, vaccines, or other prevention strategies are available for many of the serious travel-related infections reported in this analysis.**

after travel, as this information can be used to tailor strategies for improving pretravel and posttravel health care. Previous Canadian GeoSentinel studies have shown that low numbers of travelers receive pretravel consultation, which is consistent with international GeoSentinel reporting. While limited data preclude definitive reporting of British Columbia pretravel practices, our data indicate that similarly low numbers of travelers received pretravel consultation. Public health strategies for encouraging pretravel and posttravel assessments could help reduce rates of potentially communicable travel-related illness and morbidity in BC.

### Conclusions

This analysis highlights the effect of travel-related illness on British Columbians. The detailed data on travelers may contribute to provincial public health strategies for increasing tailored pretravel health advice and posttravel assessment in order to prevent, control, and manage travel-related infectious diseases.

Broader and more accessible information on travel-related illness could benefit those at high risk of acquiring infectious diseases. This may further benefit British Columbians by reducing travel-related illness and morbidity, and potentially reducing costs to the health care system. As British Columbia's public health policies related to COVID-19 shift and international travel increases, referrals for prompt specialized posttravel assessment at a CanTravNet site in order to differentiate travel-related illness may facilitate improved patient outcomes. Further, a CanTravNet collaboration with BC public health promoting assessment at the dedicated posttravel clinics within the CanTravNet network (located in Vancouver, Surrey, and Victoria) may enhance the ability of the existing sentinel system to prospectively detect trends, monitor the burden of disease, and identify outbreaks among traveling British Columbians.

### Summary

In response to the COVID-19 pandemic, global public health networks have demonstrated the value of using and sharing public health surveillance data. Further, the pandemic highlights the significant public health effects of travel-acquired illness. There is a paucity of research on travel-related illness among British Columbians. Fever in returning travelers is a medical emergency, but chemoprophylaxis, vaccines, or other prevention strategies are available for many of the serious travel-related infections reported in this analysis. This highlights the opportunity to prevent illnesses acquired during travel by promoting pretravel health advice and to reduce morbidity by conducting rapid posttravel assessment by specialists in tropical medicine. Proactive and prompt posttravel assessment of British Columbians traveling to endemic areas is beneficial at both an individual level and a population level by detecting communicable diseases and reducing costs to the health care system, and may further facilitate global surveillance of travel-related infectious diseases. ■

### Acknowledgments

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co-director (WG), and Tracey Hooper for reviewing and copy editing this manuscript.

### Competing interests

None declared.

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**Proactive and prompt posttravel assessment of British Columbians traveling to endemic areas is beneficial at both an individual level and a population level by detecting communicable diseases and reducing costs on the health care system, and may further facilitate global surveillance of travel-related infectious diseases.**

# Where to find health statistics for BC

**H**ealth statistics are integral to making the best decisions for health care, whether at the individual or community level. Here are a few places to start your search for health statistics [Box].

The BC Centre for Disease Control offers data on many diseases, including several dashboards that allow interaction with data on such things as chronic diseases and reportable diseases, displayed by several criteria (over time, by gender, by health area). This is where you want to go if you're wondering about the measles infection rate for Southern Vancouver Island.

BC health authorities may offer statistics such as education levels, overall population health, provider availability in the community, or prevalence of certain conditions. The Provincial Health Services Authority supplies access to the BC Community Health Atlas. The atlas allows for investigation and manipulation of data, such as the number of incident cases of hypertension by local health area.

Topic-specific research and advocacy organizations and centres often collect data at a highly detailed level for particular health conditions or populations. The British Columbia Centre on Substance Use offers data and clinical advice from its various research projects, such as analyses of risk-mitigation services in the context of COVID-19 and the opioid epidemic. The Health Equity Collaborative's report contains valuable information about health barriers for sexual- and gender-diverse people.

Health statistics are also hiding among other data at BC Statistics, including rates and causes of fatalities. Beyond BC, provincial data can often be found in national reports, such as those from Statistics Canada and the Canadian Institute for Health Information. Happy hunting! ■

—Chris Vriesema-Magnuson  
Librarian

*This article is the opinion of the Library of the College of Physicians and Surgeons of BC and has not been peer reviewed by the BCMJ Editorial Board.*

## Where to find health statistics for BC

- BC Centre for Disease Control: [www.bccdc.ca/health-professionals/data-reports](http://www.bccdc.ca/health-professionals/data-reports)
- BC Community Health Atlas: <http://communityhealth.phsa.ca/Home/HealthAtlas>
- BC Statistics: [www2.gov.bc.ca/gov/content/data/statistics](http://www2.gov.bc.ca/gov/content/data/statistics)
- British Columbia Centre on Substance Use: [www.bccsu.ca](http://www.bccsu.ca)
- Preliminary Results from an Evaluation of Risk Mitigation Services amidst the Dual Crises of COVID-19 and Overdose among People Who Use Opioids in Vancouver, BC: [www.bccsu.ca/wp-content/uploads/2021/10/Preliminary-Results-Evaluation-of-Risk-Mitigation-Services-Amidst-the-Dual-Crises-of-COVID-19-and-Overdose-Among-People-Who-Use-Opioids-in-Vancouver-BC.pdf](http://www.bccsu.ca/wp-content/uploads/2021/10/Preliminary-Results-Evaluation-of-Risk-Mitigation-Services-Amidst-the-Dual-Crises-of-COVID-19-and-Overdose-Among-People-Who-Use-Opioids-in-Vancouver-BC.pdf)
- Canadian Institute for Health Information: [www.cihi.ca](http://www.cihi.ca)
- Health Equity Collaborative, Believe Me: Identifying Barriers to Health Equity for Sexual and Gender Diverse Communities in British Columbia: <http://peernetbc.com/wp-content/uploads/2021/01/HEC-Final-Report-WEB.pdf>
- Statistics Canada: [www.statcan.gc.ca](http://www.statcan.gc.ca)

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# Family medicine resident rotations at WorkSafeBC

When a worker gets injured, their family doctor plays a key role in their recovery. Every year, WorkSafeBC offers a unique opportunity to 20 to 30 family medicine residents in their second year of residency at the University of British Columbia. The year-2 family medicine residents complete a 1- to 4-day rotation with WorkSafeBC that introduces them to the claims process and services, offers practical sessions with rehabilitation programs, and presents them with the basics of primary care occupational medicine. It is a just-in-time opportunity to reach family medicine residents before they graduate and start practising.

Work injuries and work illnesses are an important part of what physicians deal with in family practice. The focus of the WorkSafeBC rotation is on providing evidence-informed care for workers, demonstrating the importance of the relationship between work and health, and encouraging a safe and timely return to meaningful work when it is appropriate.

The family medicine occupational medicine rotation is supervised and taught by a group of physicians who are medical advisors at WorkSafeBC. These advisors review practical topics, such as approaching a patient with a work disability and how to effectively communicate using WorkSafeBC forms (Form 8 and Form 11).

Other staff at WorkSafeBC participate in the rotation, introducing the concepts of case management at WorkSafeBC. Residents meet case managers (claim owners) and vocational rehabilitation consultants, as well as physicians, at the Mental Health Claims Unit, Occupational Disease Services, and Health Care Programs. They are also introduced to WorkSafeBC occupational hygiene officers from Prevention Field

Services and learn about billing from Payment Services staff.

Accompanied during worksite visits by occupational hygiene officers and a specialist with occupational disease expertise, the residents learn the role of WorkSafeBC's prevention arm in maintaining safety in the workplace. This firsthand experience allows for review and discussion of potential hazards or exposures experienced by workers in some occupations.

**Every year,  
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at the University of  
British Columbia.**

Residents report that the opportunity to be immersed in an unfamiliar occupational setting provides a unique lens into the working lives of patients.

During their rotation, residents attend a WorkSafeBC-contracted rehabilitation program in the community and spend time with medical and surgical specialists at the Visiting Specialist Clinic, a specialist clinic located at WorkSafeBC's head office in Richmond. The specialists see patients by referral and maintain the usual specialist-patient relationship with the worker. WorkSafeBC is able to expedite appointments with these specialists on behalf of their community physician or nurse practitioner.

In addition to the resident rotations, WorkSafeBC also offers academic sessions to family medicine residency programs. WorkSafeBC medical advisors provide annual guest lectures in many UBC family medicine training sites across the province.

The rotation is a mutual learning experience. At WorkSafeBC, we are provided with a great opportunity to learn about the needs of community physicians. For residents, we aim to build relationships between community physicians and WorkSafeBC medical advisors to support collegial conversations and to facilitate unique services that aim for the best clinical and vocational outcomes for injured workers.

Connecting with family medicine residents is part of a larger constellation of outreach initiatives that allow WorkSafeBC to reach physicians throughout their careers. If you are involved with a family medicine program and are interested in rotations for your residents, or if you are interested in an academic session, please contact a member of the supervising committee for the family medicine rotation:

- Dr Clare McGinness: 250 717-4321
- Dr Brian Ng: 604 244-6235
- Dr Alfredo Tura: 250 334-8783
- Dr Celina Dunn: 604 232-5825 ■

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



# Addressing the drivers of BC's overdose emergency

British Columbia has been in a public health crisis since 2016 due to escalating deaths from overdose, exacerbated during the COVID-19 pandemic, with an unprecedented six lives lost per day.<sup>1</sup> A better understanding of the root causes that contribute to overdose is key to orient harm-reduction strategies and offer sustainable prevention strategies. A recent comprehensive review of the literature identified the drivers of the overdose emergency. This work is an important addition to the efforts to expand downstream overdose prevention work, and both are necessary to halt the devastating loss of life.

Laws that criminalize people for simple possession of drugs and drug use create health and social harms. Criminalization can lead individuals to use higher-risk practices to avoid detection. It can contribute to stigma and negative attitudes in the public and among health providers that can block help-seeking activities and undermine an effective systemic response. Incarceration itself is a risk factor for overdose and poor health outcomes. Access to a safer supply of pharmaceutical alternatives is necessary to separate individuals from an increasingly toxic illegal drug supply. Doctors of BC has endorsed a policy advocating for both decriminalization and safer supply as key measures to save lives.<sup>2</sup>

Promoting family well-being is at the heart of overdose prevention. A 10% increase in overdose deaths parallels a 2% increase in child maltreatment and a 4% increase in child apprehension.<sup>3</sup> Child removal is associated with subsequent overdose for mothers, a risk that is increased twofold among Indigenous women.<sup>4</sup> Notably, losing a loved one to overdose during childhood is a marker of adversity with repercussions along the lifespan. Strengthening support

for parents and families, particularly for those experiencing stress (e.g., screening for adversity, nurturing supportive relationships and resiliency, providing alternatives to apprehension), is key to mitigating the reverberating impacts of overdose now and for future generations.

Overdose is strongly concentrated in social gradients. Socioeconomic marginalization, neighborhood poverty, food insecurity, unemployment, and housing instability are correlated with overdose, with structural racism identified as a root cause of the overdose epidemic. In one US study, overdose deaths among a White rural population were likely to be precipitated by an abrupt decline in circumstances (e.g., job loss, divorce), whereas overdose deaths among racialized communities were associated with intergenerational income immobility and deprivation.<sup>5</sup> Indigenous populations have used their collective strengths to buffer ongoing legacies of colonialism. Respecting Indigenous priorities and addressing stigma and racism will be key to addressing the unequal impacts of overdose on Indigenous people in BC and Canada.

Addressing comorbidities and maximizing health care interactions is essential. The likelihood of overdose increases fivefold when a substance-use disorder is present and close to fourfold when a mental illness is present, and it is highest yet for those with a dual diagnosis.<sup>6</sup> A 2016 BC Coroners Service review found that one-third of youth and young adults who died by overdose in BC had a mental illness diagnosis.<sup>7</sup> Transitions to or from an abstinence-based context, such as incarceration or substance-use treatment, are vulnerable periods for overdose, while access to harm-reduction services (such as supervised consumption sites) and family physicians is protective. Proactive screening and follow-up at key health care access points (e.g., primary care, mental health, emergency services) is fundamental to preventing overdose deaths.

We have to do better. Engaging people with lived and living experience is necessary

to contextualize the literature and share what is needed. Interventions such as safer supply and decriminalization are imperative to provide alternatives to the toxic drug supply now. Timely access to robust, integrated population data specific to BC, encompassing rural and remote communities, is essential to focus proactive and equitable overdose response efforts throughout the health system and beyond. And elucidating pathways that may lead to overdose, including the role of adversity and social disadvantage, is critical to better supporting individuals, families, and communities in overdose prevention across the lifespan. ■

—BCCDC Overdose Drivers Knowledge Translation Group

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# Obituaries

We welcome original tributes of less than 300 words; we may edit them for clarity and length. Obituaries may be emailed to [journal@doctorsofbc.ca](mailto:journal@doctorsofbc.ca). Include birth and death dates, full name and name deceased was best known by, key hospital and professional affiliations, relevant biographical data, and a high resolution head-and-shoulders photo.



## Dr Archibald Douglas Young 1926–2021

With great sadness, we announce the passing of Dr Archie Young on 13 November 2021, in Chilliwack.

Archie was born on a farm in Keir Village, Dumfriesshire, Scotland, in 1926, the sixth of eight children of John Young, a dairy farmer, and his wife Mary, a schoolteacher.

When Archie was three, the family, along with a herd of 24 Ayrshire dairy cows and one bull, immigrated to Vancouver, where John was to manage the farm on the new Point Grey campus of the University of British Columbia. Two years later, the world economic crash forced massive cuts to the university's budget, and John's job was terminated. However, John convinced the university to let him run the farm as a working farm, and with a concession to deliver milk on the University Endowment Lands, the family made a life there for 20 years. When his older brothers left to fight in World War II, 14-year-old Archie rose each day at 5:30 a.m. to deliver milk and then rushed off to University Hill School, where he was known to fall asleep in class. Until the end of his life, he would reminisce fondly about growing up on the farm at UBC.

Archie received a Bachelor of Science degree from UBC in 1947, and later that year he began medical school at McGill University after a 5-day bus ride from Vancouver to Montreal. He interned at Montreal General Hospital, and it was there, while laid up in hospital for a short time, he was cared for by a young nurse, Beatrice Clarke. They were married on Boxing Day 1951 and soon moved to Vancouver, where Archie did a year of postgraduate training at Shaughnessy Hospital. In 1953 he began general practice in Hope, BC, as one of only two doctors in the town, later moving down the road to Chilliwack. In 1962, to his eternal gratification, Archie partnered in his medical practice with his younger brother Drew, and they practised in the same clinic together until Archie's retirement in 1997.

To fully describe and do justice to Archie's professional life in this space is simply not possible. He was a beloved family doctor for the community of Chilliwack for 45 years. With a strong foundation of training, an enquiring mind, a humble demeanor, and a caring and understanding nature, Archie possessed a full breadth of tools that made for an exemplary medical career. His memory for events throughout his career (and life) was tremendous. As a strong patient advocate, he could put patients at ease and make them feel better with just a visit, no matter what their ailment was. Archie's outstanding community service of 45 years of medical practice was recognized by the Canadian Medical Association with a Senior Membership Award in 1996.

Archie is survived by his four children, Doug (Leonie), Claire (Tom), Stuart (Cynthia), and Ross (Tannis); seven grandchildren; three great-grandchildren; and his youngest sister, Jean Smith.

—Young Family



## Dr Gail Verlaine Dickinson 1944–2022

Gail and I became fast friends during our first year of UBC Medical School in 1966. We were both from small towns, from out of the province, she from Saskatchewan and I from New Brunswick. The UBC program at that time had a quota system for women, and we called ourselves "the token 10." Gail's ambition to become a doctor started at age 7 when she noticed that her local doctor had a house with a tennis court, which he used regularly. It was not wealth that got her attention, but the way her doctor was enjoying life to the fullest. That's what she wanted.

Gail did a 2-year residency in New Zealand and loved the country so much she stayed another 3 years. She sailed the South Seas on her 38-foot sailboat, *Coruba*, and as captain, she had an all-woman crew. On returning to Canada, she bought a little cabin in Rossland to be close to the ski hills (she was a champion downhill racer) and worked as a GP in Trail.

Still, the world was calling her. She took a job in Saudi Arabia as an ER physician because it afforded her access to travel the globe. There she met her husband of 30 years, Naren Simone, and alongside work, they enjoyed skiing, snorkeling, diving, kayaking, and hiking.

But their real love was international travel. In all, she visited 128 countries.

Gail had amazing resilience. She survived cancer four times. First it was breast cancer on one side, then the other. While in remission from that she was diagnosed with leukemia, which was successfully treated, but it reoccurred. I saw her in the oncology ward at Vancouver General Hospital. She told me there was a 15% chance of survival and that she would be part of that 15%. She was right. After recovering in India she went back to work in the Middle East.

When Gail retired in 2008, she and Naren moved to Sidney, BC, but they were continually on the move. Winters were spent oil painting in Indio, California, and skiing in Rossland, and summers in Sidney and Rossland. She loved her flower garden in Rossland and was a regular at Butchart Gardens. She was a very accomplished and prolific painter, a skill she learned in Abu Dhabi.

When she learned that she had lower motor neuron disease, she had already faced death many times. We spent the last year telling each other funny stories.

Gail was a brilliant doctor and a great friend, and she had an extraordinary zest for life. She always looked for the good in people, made friends easily, and was full of cheer and good spirit. She insisted on celebrating her life while she was still alive, and when the final moment came, she said adieu to this world while sipping Dom Pérignon. She died at home in Sidney on 13 January 2022. She is survived by her husband, Naren Simone; her sister, Marilyn; and two brothers, Gary and Barry.

—Mary Conley, MD  
Victoria

**BCCDC**

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7. BC Coroners Service Child Death Review Panel. Preventing death after overdose: A review of overdose deaths in youth and young adults 2009–2013 [report to the chief coroner of British Columbia]. January 2016. Accessed 29 April 2022. [www2.gov.bc.ca/assets/gov/birth-adoption-death-marriage-and-divorce/deaths/coroners-service/child-death-review-unit/reports-publications/overdose-death-youth-young-adult.pdf](http://www2.gov.bc.ca/assets/gov/birth-adoption-death-marriage-and-divorce/deaths/coroners-service/child-death-review-unit/reports-publications/overdose-death-youth-young-adult.pdf).

# CME calendar

**Rates:** \$75 for up to 1000 characters

(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. **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. **Planning your CME listing:** We suggest that your ad be posted 2 to 4 months prior to the event. **Ordering:** Place your ad at [www.bcmj.org/cme-advertising](http://www.bcmj.org/cme-advertising). Payment is accepted by Visa or Mastercard on our secure online payment site.

## PSYCHOLOGICAL PPE, PEER SUPPORT BEYOND COVID-19

**Online (every 2nd and 4th Wednesday)**

In response to physician feedback, the Physician Health Program's drop-in online peer-support sessions, established in April 2020, are permanently scheduled for every second and fourth Wednesday at noon. The weekly sessions are cofacilitated by psychiatrist Dr Jennifer Russel and manager of clinical services Roxanne Joyce, and are drop-in with no commitment required. The focus is peer support, not psychiatric care. All participants have the option to join anonymously. To learn more about the sessions and the program, visit [www.physicianhealth.com/how-we-can-help/peer-support](http://www.physicianhealth.com/how-we-can-help/peer-support). Email [peer.support@physicianhealth.com](mailto:peer.support@physicianhealth.com) for the link to join by phone or video.

## ANATOMY-BASED BOTULINUM TOXIN TRAINING

**Online and Vancouver UBC campus (Now–30 Dec 2022)**

Expand your practice with injectables. Learn both the therapeutic (migraines/headaches) and aesthetic (fine facial lines and wrinkles) applications. PTIFA offers anatomy-based training (20+ hours) and training recognized by the highest standard of practice in Canada. Receive the most clinically based training, including the opportunity to inject eight-plus patients. Courses held monthly on UBC Campus in Vancouver. Start today with the online Level 1 – Advanced Anatomy course (20 CME). Save \$500. Use code “BCMJonline” before 30 June 2022. Register now at [PTIFA.com](http://PTIFA.com).

## GP IN ONCOLOGY EDUCATION

**Online (12–23 Sept and 3–17 Oct 2022)**

BC Cancer's Family Practice Oncology Network offers an 8-week General Practitioner in Oncology education program beginning with a 4-week virtual introductory session every spring and fall at BC Cancer–Vancouver. This program provides an opportunity for rural family physicians, with the support of their community, to strengthen their oncology skills so that they can provide enhanced care for local cancer patients and their families. Following the introductory session, participants complete a further 30 days of clinic experience at the cancer centre where their patients are referred. These are 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](http://www.fpon.ca) or contact Dilraj Mahil at [dilraj.mahil@bccancer.bc.ca](mailto:dilraj.mahil@bccancer.bc.ca).



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## PRACTICES AVAILABLE

### BURNABY—FULL-TIME FAMILY PRACTICE AVAILABLE

Organized, well-established family practice available. MedAccess EMR; 12-year-old office building at PrimeCare Medical Centre with four other FT and six PT colleagues and support of walk-in and urgent-care clinics. Obstetrics/hospital optional. Willing to consider part-time. Income split or 100% less overhead. Enquiries to [ron.demarchi@primecaremed.ca](mailto:ron.demarchi@primecaremed.ca) or 604 520-3006.

### COQUITLAM—NEW TURNKEY SPACIOUS MEDICAL CENTRE FOR SALE

This 2200 sq. ft., fully furnished, eight-exam-room medical clinic is for sale. The recently renovated primary-care clinic is ready for a practice immediately. The clinic is turnkey and all equipment on site comes with the sale of the business. This includes \$200 000 of furnishings and equipment. Email [syuan@elicare.ca](mailto:syuan@elicare.ca).

### KAMLOOPS—SOLO PRACTICE AVAILABLE FOR FAMILY PHYSICIAN

Family physician with solo practice in Kamloops is looking to turn over a fully equipped practice to a physician able to provide longitudinal care for his patients. The clinic is centrally located and is set up with a well-managed and organized

EMR (Telus Med Access). Available December 2022. For further information contact Santie at 778 220-0848.

### VICTORIA—FP WALK-IN

Fee-for-service practice near downtown Victoria for 30 years with new and long-term patients of varied demographics. Looking to transfer ownership for retirement but will continue regular shifts for smooth transition. Oscar EMR, two exam rooms, equipped for minor procedures. Contact Dr Michael Greenwood at 250 388-9934 or [jbcentre@telus.net](mailto:jbcentre@telus.net).

## EMPLOYMENT

### ABBOTSFORD—FP FOR MULTIDISCIPLINARY MATERNITY OFFICE

Seeking family physician to join the Fraser Birth Collaborative in beautiful Abbotsford, BC. We are a team of physicians, midwives, counselors, nurses, physiotherapists, RMTs, etc., that provide full care for mothers and babies until 2 months after birth. We would like a physician to join us and provide family practice care inside the clinic to follow these babies after discharge from our care. Abbotsford is a community of 160 000 people, with a newer regional hospital, 1 hour from Vancouver. Contact [inbox@fraserbirth.ca](mailto:inbox@fraserbirth.ca).

### ACROSS CANADA—PHYSICIANS FOR YOU—MATCHING DOCTORS WITH CLINICS

Are you a physician looking for work or a medical facility requiring physicians? Our team works with independently licensed Canadian physicians, CFPC/RCPSC-eligible international medical graduates, and clinics across Canada. Check out our reviews and current job postings, and call Canada's trusted recruitment firm today! Visit [www.physiciansforyou.com](http://www.physiciansforyou.com).

### BC—CANABO MEDICAL SERVICES, PART-TIME, CHOOSE YOUR HOURS

Canabo Medical Clinic has a long-term mandate as being a leader in medical cannabis research. Physicians will enjoy the service of our professional team that takes care of all administrative, management, and billing needs to allow for complete focus on patients. Most patients come into our clinics with a diagnosis from their family physicians, making our physicians' jobs quite easy. We offer a very competitive split, part- or full-time schedules, and paid training with one of our leading expert physicians. We are fully compliant with CMPA and College of Physicians and Surgeons standards of practice as well as Health Canada guidelines. Please contact Natalie Davis at [ndavis@cmclinic.ca](mailto:ndavis@cmclinic.ca).

### BURNABY METROTOWN—FULLY FURNISHED, READY TO WORK, MEDICAL OFFICE SPACE FOR LEASE

Updated COVID-19-compliant, fully furnished, five-room medical clinic (970 sq. ft.). Street-level location and ample walk-by traffic. Free parking and within walking distance of Metrotown SkyTrain. Perfect for family practice, a walk-in clinic, and/or cosmetic medical. Incentives and attractive lease rates offered. If interested, please contact [drniou@gmail.com](mailto:drniou@gmail.com).

### NANAIMO—GP

The Caledonian Clinic has availability for a general practitioner (locum or permanent position). We are a well-established, very busy clinic with 23 general practitioners, one first-year resident, one second-year resident, a podiatrist, a geriatrician/internist, and an orthopaedic surgeon. Our EMR is Profile by Intrahealth. We are located in a modern new clinic in the Nanaimo North Town Centre. Lab and pharmacy services are on site within the centre. Contact Lisa Wall at 250 716-5360 or email [lisa.wall@caledonianclinic.ca](mailto:lisa.wall@caledonianclinic.ca). Visit our website at [www.caledonianclinic.ca](http://www.caledonianclinic.ca).

### NISGA'A VALLEY—FAMILY MEDICINE LOCUMS AND FTES

Family physicians needed to provide primary and urgent care for a population of 3500 in four

communities across the traditional Nisga'a Territory, easily accessed by flights into Terrace. A supportive team of three to four physicians work together to provide full-scope services (excluding obstetrics). The health centres are staffed with full-time RNs who take the first call after hours. Soaring mountains, dramatic lava beds, natural hot springs, mountain-biking trails, and thriving salmon-filled rivers offer outstanding recreation year-round. Excellent remuneration, average more than \$11 000 per week. Contact Dr Jeremy Penner at md@nisgahealth.bc.ca.

#### **NORTH VAN—FP LOCUM**

Flexible hours and vacation time with no call. In-office and telehealth options available with great MOA support staff and a new competitive split; 100% to doctors for optional hospital visits, nursing home visits, medical-legal letters, etc., or sessional work. For further information contact Kim at 604 987-0918 or kimgraffi@hotmail.com.

#### **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. Phone: 604 485-3927, email: clinic@tmca-pr.ca, website: powellrivermedicalclinic.ca.

#### **SOUTH 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 (BEAR CREEK AND NEWTON)—FAMILY PRACTICE**

We are looking for part-time/full-time physicians for walk-ins/family practice to work on flexible shifts between 9 a.m. and 6 p.m.; option to work 7 or 5 days per week. Clinic with eight exam rooms, two physio rooms, and pharmacy on site. Competitive split. For more information, please contact Anand at wecaremedicalclinic2021@gmail.com or 778 888-7588.

#### **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.

#### **SURREY (SCOTT ROAD)— FT/PT GPS FOR SUPPORTIVE, ESTABLISHED, PHYSICIAN-OWNED CLINIC**

Arista Medical Centre is seeking FT/PT GPs for a busy family practice. Flexible schedule. Brand-new, modern, multidisciplinary, multiphysician clinic with a very collegial atmosphere and physician-focused MOA support with seven exam rooms. Free parking. Highly competitive split. Please contact Manni at

info@aristamedical.ca or 604 572-1000.

#### **VANCOUVER—FP/ GYNECOLOGIST/PEDIATRICIAN/ SPECIALIST, AND RMT**

Cross Roads Clinics: Opportunity to join our large multidisciplinary clinic with excellent support focusing on family health, preventive health, and the care of women and children. Virtual care, extended flexible hours/scheduling, and vacation friendly. Modern 9000 sq. ft. facility with 34 patient rooms and gymnasium. Physiotherapy, massage therapy, naturopathic medicine, acupuncture, dermatology, minor surgery, pediatrics, women's health, infertility, contraception, menopause, and incontinence clinic on site. No need to build your practice as we have patients immediately available to you. Potential service contract for family medicine. Great opportunity to focus on patient care, whether new to practice or semi-retiring; allow us to manage the rest. Please contact admin@crossroadsclinics.com.

#### **VANCOUVER/RICHMOND— FP/SPECIALIST**

We welcome all physicians, from new graduates to semi-retired, part-time or full-time. Walk-in or full-service family medicine and all specialties. Excellent splits 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.

#### **VICTORIA—FAMILY PHYSICIANS, URGENT AND PRIMARY CARE CENTRES**

Island Health has exciting opportunities for family practitioners to work at new UPCCs.

Join a team of primary care providers and other allied health staff to collectively deliver integrated team-based care. The UPCCs are bright new clinics offering turnkey operation with no overhead costs and a group clinical service contract with competitive rates. Patient visits consist of scheduled LC and unscheduled UC or same-day primary care. For further information or to discuss these opportunities directly with our medical director, please contact our recruitment team at medstaffrecruitment@islandhealth.ca.

#### **VICTORIA—HOSPITALISTS**

Hospitalists in Victoria provide comprehensive 24-hour care to a wide variety of patients at both Victoria General Hospital and Royal Jubilee Hospital. We are involved in undergraduate and resident teaching through UBC. Experience engaging and rewarding medicine in one of Canada's most beautiful cities! Email recruiting@si-hi.ca.

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#### **MEDICAL OFFICE SPACE**

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#### **SURREY—SELF-CONTAINED SPACE ACROSS FROM SURREY MEMORIAL HOSPITAL**

Medical office space at City Centre 2. Two physician offices, 990 sq. ft. waiting area, four exam rooms. Space for two MOAs. One private bathroom. Parking space available for rental at additional cost. Utilities included. Available starting February 2022. Email: Carla at frasergeneralsurgerygroup@gmail.com. Phone: 604 416-0084. Turnkey options also available.

#### **VANCOUVER—MEDICAL CO-WORKING SPACE**

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## Pr DAYVIGO™ lemborexant tablets

### INDICATION AND CLINICAL USE:

*Sleep disturbance may be the presenting manifestation of a physical and/or psychiatric disorder. Consequently, a decision to initiate symptomatic treatment of insomnia should only be made after the patient has been carefully evaluated.*

DAYVIGO™ (lemborexant) is indicated for the treatment of insomnia, characterized by difficulties with sleep onset and/or sleep maintenance. DAYVIGO is not recommended for patients under the age of 18 years. DAYVIGO is not recommended in patients with severe hepatic impairment.

### CONTRAINDICATIONS:

- Hypersensitivity to this drug or to any ingredient in the formulation, including any non-medical ingredient, or component of the container.
- Patients with narcolepsy.

### RELEVANT WARNINGS AND PRECAUTIONS:

- Abnormal thinking and behavioural changes
- CNS depressant effects (including alcohol) and daytime impairment and risk of falls
- Complex sleep behaviours
- Sleep paralysis, hypnagogic/hypnopompic hallucinations, and cataplexy-like symptoms
- Worsening of depression/suicidal ideation
- Co-morbid diagnoses
- Drug interactions - inhibitors and inducers of CYP3A
- Patients with galactose intolerance
- Driving and operating machinery
- Patients with dependence/tolerance and abuse liability
- Rebound insomnia
- Patients with hepatic impairment
- Patients with compromised respiratory function
- Pregnant or breastfeeding women

### FOR MORE INFORMATION:

Please see the Product Monograph at <https://ca.eisai.com/en-CA/our-products> for important information on adverse reactions, drug interactions, and dosing not discussed in this piece. The Product Monograph is also available by calling 1-877-873-4724.

† Based on a 1-month global, randomized, double-blind, parallel-group, placebo- and active-controlled, phase 3 study (SUNRISE 1) in 743 participants with insomnia disorder (age ≥55 years). Participants received placebo (N=208) or DAYVIGO 5 mg (N=266) or 10 mg (N=269) at bedtime. Latency to persistent sleep baselines: placebo, 44 mins; DAYVIGO 5 mg, 45 mins; DAYVIGO 10 mg, 45 mins. Wake after sleep onset baselines: placebo, 112 mins; DAYVIGO 5 mg, 113 mins; DAYVIGO 10 mg, 115 mins.<sup>2</sup>

### REFERENCES:

1. DAYVIGO Product Monograph, Eisai Limited, November 3, 2020.
2. Rosenberg R, Murphy P, Zammit G, et al. Comparison of Lemborexant With Placebo and Zolpidem Tartrate Extended Release for the Treatment of Older Adults With Insomnia Disorder: A Phase 3 Randomized Clinical Trial. *JAMA Network Open*. 2019;2(12):e1918254.

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# INSOMNIA TREATMENT: WHEN DAY TURNS TO NIGHT CONSIDER

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DAYVIGO<sup>TM</sup> is indicated in adults for the treatment of insomnia, characterized by difficulties with sleep onset and/or sleep maintenance.

Symptomatic treatment of insomnia should only be initiated after the patient has been carefully evaluated to rule out a physical and/or psychiatric disorder.

## Demonstrated efficacy<sup>1</sup>

- At Days 1/2, DAYVIGO 5 mg reduced sleep onset time (LPS) from baseline by 17 minutes vs. 6 minutes with placebo ( $p < 0.01$ ).<sup>1†</sup>  
The primary efficacy endpoint was the mean change in latency to persistent sleep (LPS) from baseline to end of treatment, as measured by polysomnography. LPS was defined as the number of minutes from lights off to the first 10 consecutive minutes of non-wakefulness.
- At Days 1/2, DAYVIGO 5 mg improved sleep maintenance (WASO) from baseline by 51 minutes vs. 18 minutes with placebo (secondary endpoint) ( $p < 0.001$ ).<sup>1†</sup>  
The secondary efficacy endpoint was the mean change from baseline to end of treatment in wake after sleep onset (WASO) measured by polysomnography. WASO was defined as the minutes of wake from the onset of sleep until wake time.

## A proven safety profile<sup>1</sup>

- DAYVIGO was generally well tolerated.
- Most common adverse events were headache (5 mg: 6%, 10 mg: 4.6%), somnolence (5 mg: 5%, 10 mg: 8.4%), nasopharyngitis (5 mg: 2.8%, 10 mg: 1.7%), fatigue (5 mg: 2.1%, 10 mg: 1.5%), urinary tract infection (5 mg: 0.7%, 10 mg: 2.1%).<sup>1</sup>

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\*Comparative clinical significance unknown.

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