More work needed to screen baby boomers at higher risk of hepatitis C

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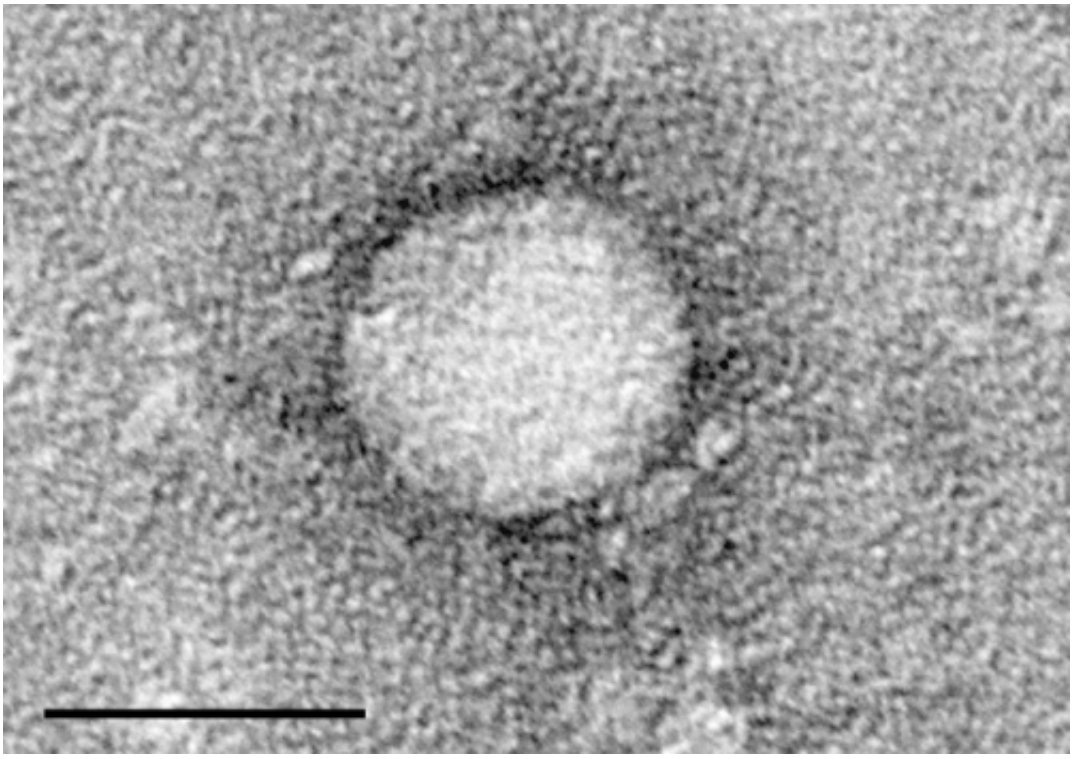

Electron micrographs of hepatitis C virus purified from cell culture. Scale bar is 50 nanometers. Credit: Center for the Study of Hepatitis C, The Rockefeller University.

In mass media and popular culture, medical research is often framed as a race to overcome a complex, seemingly insurmountable challenge, with lives hanging in the balance.

Enter the team of scientists in white lab coats, working around the clock to cure HIV, eradicate cancers or make Alzheimer's a thing of the past. This sort of narrative is dramatic, hopeful and in line with what some expect of science, but the reality is that progress is far more incremental.

Michael Houghton's "race" started 35 years ago in a San Francisco-area lab where he was part of the team that first identified hepatitis C. In those days, the early 1980s, scientists knew the virus existed—patients were getting sick because of blood transfusions—but it was labelled for what it wasn't: "non-A" or "non-B" hepatitis.

"It ended up taking seven years—a lot of false leads, a lot of frustration," remembers Houghton, now Canada Excellence Research Chair in Virology at the University of Alberta.

When Houghton's team did manage to discover the hepatitis C virus (HCV) in 1989, it was a watershed moment among virologists and immunologists—the first step toward eradicating an infectious disease that affects 170 million people worldwide. Spread largely through unsafe handling of blood and dirty needles, hep C in its chronic form can result in serious damage to the liver, including organ failure.

In the years since discovering the virus, the U.K.-born Houghton has led efforts at the U of A's Li Ka Shing Institute of Virology to create the world's first vaccine capable of protecting the body from all strains of HCV. There are seven major genotypes of the virus, each with hundreds of different subtypes, making it genetically more variable than HIV and thus that much harder to treat. If their phase 1 clinical trial succeeds, the vaccine will prevent 500,000 new infections estimated to happen every year.

This race should be over, but it isn't

And while his U of A team focuses on the long game of vaccination, several pharmaceutical companies have developed new antiviral drugs that effectively cure hep C.

This race is all but over. At least it would be, if the new antivirals did not cost upward of $1,000 per pill, putting a cure out of reach of thousands of infected Canadians. At the same time, Canada lacks a concrete national strategy for hepatitis C that focuses on eliminating the disease through improved co-ordination, prevention and management of the disease, particularly among those at higher risk of infection, such as intravenous drug users. In early March, Action Hepatitis Canada—a group representing 35 member organizations that include the Canadian Liver Foundation, Canadian Treatment Action Council and Canadian AIDS Society—called on Ottawa to develop such a strategy.

"It's very frustrating, for me and the whole field, when we can cure hepatitis C but what's restricting us in the U.S. and in Canada is just the price of the drug," says Houghton, a professor in the Faculty of Medicine & Dentistry.

Houghton isn't out to blame Big Pharma. He did, after all, spend a considerable portion of his career in the private sector and understands the cost realities associated with the research and development of drug therapies.

But there are also hard realities for Canadians and our provincially run health-care systems. With drugs that cost on the order of $60,000 to $150,000 per patient for a 12-week treatment, curing every Canadian infected with HCV would cost on the order of tens of billions of dollars, Houghton estimates.

But failing to act, he adds, would be even more costly given the potential risks associated with hep C. Three-quarters of people infected with the

virus develop chronic hepatitis, and a quarter of those develop problems such as cirrhosis, liver failure or liver cancer.

One of the major challenges with hepatitis C is many people don't know they are carriers for years—sometimes decades—after becoming infected, often learning of their diagnosis after showing symptoms of liver damage. The new antivirals are so expensive that in many cases provincial pharmacare programs only cover patients with more pronounced symptoms.

"It's almost like we're going to wait until you get very sick before we treat you. That's never ideal," says Houghton. "The treatment cures hep C, not liver cancer, and that's a very real risk when you delay treatment."

Hepatitis C survivor "one of the lucky ones"

Edmontonian Jack McClure knows he's one of the lucky ones—and this coming from a guy who fought through liver cancer and underwent a transplant with complications so severe his second liver nearly failed.

"I was real sick," he remembers. "I struggled—one foot on a banana peel and the other on a grave for one year, but I pulled through on that one."

McClure, 64, isn't sure when he was infected with HCV, but suspects it happened in the 1980s when he experimented with cocaine, a less common but possible method of transmission. He was diagnosed roughly 15 years ago when he applied for work as a garbageman and underwent a physical. He didn't take the job, but the blood test he was given confirmed his infection.

"I didn't know anything about hepatitis," he says, something he would soon learn mirrored much of society at the time—even some physicians. "The first doctor I went to, at a medical centre, told me it was caused by

sex. So I looked it up and thought, 'You're an idiot, that's hep B.' Generally, hep C isn't passed along through sex…. Eventually society learned more about hepatitis, that you can get it in various ways, but at first you're kind of ostracized."

A year ago, McClure qualified for a clinical trial for hep C patients who have received liver transplants. He was treated with Sovaldi in combination with another drug. Unlike older-generation drugs like interferon, which is also used in chemotherapy, there were no side-effects. Through the course of the six-month trial, his blood gradually showed smaller and smaller concentrations of the virus until it was gone.

McClure, now retired from hauling roof trusses and jobs like door-to-door milk delivery, only wishes every patient with hep C could have free and timely access to the same medicines, including friends and family who have been "pulled down" from delayed treatment.

Canada's uneven response to hep C

Taking new medicines such as the hepatitis C antivirals Solvadi or Harvoni from the lab to a patient's bedside is a complicated process in Canada. Pharmaceutical companies must first prove a new drug is safe and effective for a specific treatment purpose through lengthy and expensive clinical trials before Health Canada decides whether the product can be sold, though it makes no determination on the actual cost.

Once a drug is approved by Health Canada, another federal agency examines the evidence on the drug and what a manufacturer wants to charge before determining whether the medicine should be listed by provincial, territorial and federal formularies. It's then up to those jurisdictions to determine whether a drug will be covered by their respective pharmacare programs. This can lead to an uneven response between provinces, with some, such as Quebec, typically quicker to

cover new drug costs.

"It's expensive to respond, to put these drugs on the formulas. However, treatment might be expensive but disease might be more expensive," explains Lorne Tyrrell, a close colleague of Houghton's and director of the Li Ka Shing Institute of Virology.

Tyrrell, too, is one of the world's leading authorities on viral hepatitis. He co-developed the first oral antiviral treatment for hepatitis B, lamivudine, now used in more than 200 countries around the world. His accomplishments in the field have landed the former dean of medicine in the Canadian Medical Hall of Fame and last year saw him honoured with a Killam Prize.

Tyrrell says Alberta is generally in the middle of the pack in Canada in terms of its response to hep C, though when the first protease inhibitors were licensed in November 2011, it took a full year before they were covered in this province. Part of the problem, he says, is the people making the recommendations for Alberta's drug benefit formulas are not experts in the field, which can delay decisions.

Any delay can have long-term health implications for those infected with HCV. There are four stages of infection, from stage 0 where there is no evidence of inflammation or fibrosis in the liver to stage 4, which is full-blown cirrhosis. Across Canada, patients must show signs of stage 2 before their medication is covered by provincial pharmacare. That's also the standard for Blue Cross, though some private insurers do cover earlier stages, Tyrrell explains.

"We do scans on our patients, and if they don't meet the criteria, they don't get the treatment. We have patients that have earlier hepatitis C—stage 1 fibrosis—and they know it will progress but can't get access to therapy."

Living in fear of hepatitis C

Cynthia Robson did not quality for the antiviral Harvoni until her fibrosis advanced to stage 2. The Sherwood Park resident was infected in 1985 when she received a transfusion after giving birth to her son. She's among the estimated 60,000 Canadians infected with HCV between 1960 and 1992 from tainted blood transfusions and blood products, a public health scandal that gave rise to the Krever Inquiry into the country's blood system.

Robson says she's lived in fear of hepatitis C since being diagnosed in 2001—fear that she would accidentally spread the disease, fear that it would ultimately take her life before her time. After twice undergoing exhausting and unsuccessful 48- and 30-week treatments with interferon and ribavirin, she resigned herself to a bleak fate.

"I figured I would just end up getting liver cancer, that's all there was to it," she says.

The first time Robson heard of a curative drug for HCV, Harvoni, was when celebrity Pamela Anderson posted an Instagram photo announcing to the world she was free of the disease after nearly 15 years. Robson, who also suffers from osteoarthritis and fibromyalgia and receives AISH because she can't work, says at one point she contemplated approaching Harvoni's maker, Gilead Sciences, to see whether she would qualify to receive the drug as a research patient because she had no way of paying $150,000 for the 12-week treatment.

It was around the same time she learned that her specialist, Tyrrell, had already applied for her to receive the drug, and was fully covered by AISH. When she sat down in Tyrrell's office this past January to go over her latest blood work results, the virus was gone.

"I started crying, I just couldn't believe it. I kept saying, 'I never cry like this,'" she remembers.

And though she's relieved and happy for herself, Robson recognizes her story could have been drastically different if AISH hadn't fully covered her treatment. A friend of the family recently lost his father due to hep C complications, and she fears working Canadians without employer-provided or private health insurance will fall through the cracks.

"There are people who were in worse shape than I was and they could be cured. But they're not, and that's very unfortunate," she says.

McClure's assessment is far less forgiving. To him, there is no difference between the high cost of hepatitis C drugs and "that bastard in the States," Martin Shkreli, the former Turing Pharmaceuticals executive who became an international pariah after raising the price of the HIV drug Daraprim by 5,000 per cent.

"It's a crime, you know—you come up with a cure and then you make the cure and it's too expensive," McClure says. "They've got to get it together and let society get together and get their hands on [the medicines] without liquidating their assets."

Rising drug costs are a major concern for governments and health-care systems across Canada.

According to the Canadian Institute for Health Information, prescription drug spending reached an estimated $28.8 billion in 2014—representing 13.4 per cent of all health-care spending. The public sector paid 42 per cent of that total, or $12.1 billion, with another $16.7 billion covered by private insurers ($10.3 billion) and Canadian households ($6.4 billion).

Drug prices in Canada are determined by the Patented Medicine Prices

Review Board, which generally sets prices at the median of seven other countries—the United States, France, Germany, Italy, Sweden, Switzerland and the United Kingdom.

A major factor in the cost of hepatitis C antivirals is that they are so new to the market, they are still covered by patents. In Canada, drug patents extend 20 years from the date of filing, but the actual time a medicine is protected is typically less than half that, because of the years it takes for regulatory approvals.

"There's no such thing as cheap medications for hepatitis C. They're all quite expensive," says Tyrrell.

He notes that pharmaceutical companies invest significant dollars developing new drug therapies, often with a limited window to recapture their investment. In many cases, drugs are on the market for a short time because they didn't sell, had side-effects or were replaced by newer and better therapies, he says. In the case of hepatitis C drugs, this advance in therapies happened in a short window of just a few years.

Costs only come down when there are competitive alternatives or when a patent expires, giving rise to generic versions of a drug.

Another way to bring down costs is through bulk buying—provinces and territories joining forces to negotiate cheaper prices from pharmaceutical companies. The pan-Canadian Pharmaceutical Alliance was created in 2010 with just that in mind, though its impact in Alberta has so far been limited, says Dean Eurich, a clinical epidemiologist in the School of Public Health with a background in the pharmaceutical sciences.

Eurich was part of a team of scientists who studied the alliance's impact on drug access in Canada, looking at approvals three years before it was

created and the following three years. For some provinces, the alliance seems to be working and increasing access, though in Alberta it hasn't had a huge impact on drug listing decisions, explains Eurich.

As of March 2015, the alliance reports it has completed joint negotiations resulting in price reductions on 63 brand-name and 14 generic drugs—saving Canadians an estimated $490 million annually.

Eurich says one of the issues for researchers, clinicians and, ultimately, patients, is the lack of transparency in those negotiations—private contracts between government and pharmaceutical companies. When the alliance says it's saving money, the public has to take its word for it, without a true understanding of a drug's cost—something he thinks should change.

"If you're looking at a publicly funded formulary, then, yes, there should be disclosure," Eurich says, though he recognizes that clearly wouldn't sit well with private companies that wouldn't want to divulge that information.

Governments should invest in their own medicines, recommend screening

In addition to bulk buying, Houghton suggests there's an opportunity for international collaboration between governments and research universities to develop their own drugs and vaccines. The Helmholtz-Alberta Initiative between the U of A and the Helmholtz Association of German Research Centres is an example of a viable partnership with the expertise in research and development capable of taking a discovery from bench to bedside, he says.

The investment cost would be high initially, but health-care savings

would be in the billions, not just for hepatitis C drugs but also for medicines for cancer therapies, which can be even more expensive.

"The counter-argument is pharma know better how to do this than government, but many people now have that expertise. I came from the biotech sector to do this and we at the U of A are starting that discussion. We are at the start of a new era," Houghton says. "The cost is high initially, but in the long run, the country is going to save billions and billions."

The cost of the new hepatitis C antivirals is just one area of disappointment for researchers in the field. Three years ago, the U.S. Centers for Disease Control adopted guidelines recommending blood screening for HCV among all baby boomers—a demographic at higher risk of infection as a result of casual drug use in the 1970s. The Public Health Agency of Canada has failed to act, which has been a "huge disappointment," says Houghton.

Tyrrell says Canada could learn from countries such as Australia and Scotland, which have excellent hepatitis C strategies with guidelines covering screening, prevention, treatment and monitoring. Provincially, Alberta finds itself "in the middle of the pack," Tyrrell adds, with British Columbia leading the way in documenting and identifying HCV carriers and co-ordinating a response.

"Screening becomes more important when you have good therapy. Then you can offer patients a real alternative to get rid of it and clear the virus," he says.

Supervised injection facilities key to reducing infection rates

Beyond screening, governments at every level have an opportunity to reduce the spread of infection among the most vulnerable and at-risk populations. That is precisely the goal of Access to Medically Supervised Injection Services Edmonton, a group representing 25 organizations interested in creating a supervised injection service in the city.

Elaine Hyshka, an incoming assistant professor in the School of Public Health who has studied inner-city drug use and health needs in Edmonton, says intravenous drug use appears to be on the rise in the city and the vast majority of the people she has studied say they have contracted hepatitis C.

Hyshka and a research assistant spent five months conducted 320 hour-long interviews with inner-city Edmontonians to learn more about their health and factors negatively influencing their health such as drug abuse.

Some 91 per cent reported injecting drugs intravenously, with 80 per cent saying they'd used in public and 26 per cent confirming they'd borrowed or shared needles. The researchers were not equipped to test participants' blood, but through self-reporting found that about 70 per cent of men and women had previously tested positive for HCV.

One of the problems with existing needle exchange programs, Hyshka says, is they aren't open 24 hours a day. Her group would like to see a 24/7 supervised injection service added to an existing Edmonton facility, one stocked with clean needles and supervised by nurses.

"It is fundamental," she says of such a facility's role in harm reduction and curbing the spread of diseases like hep C. "It provides a safe, sterile environment to inject drugs and access to other health services."

Access to Medically Supervised Injection Services Edmonton is finalizing its proposed service model, which it plans to take to

stakeholders for consultation in addition to seeking the federal exemption needed to operate.

Though supervised injection sites such as Insite in Vancouver have been politically nebulous in the past, Hyshka and her peers are buoyed by leaders at all three levels of government who have shown signs of support for harm reduction and protecting society's most vulnerable citizens.

"It's important to know that these services have been implemented in almost 60 cities worldwide and there's no evidence to support that they increase crime or substance abuse," Hyshka says.

Designing the "ultimate" hep C vaccine

Just as he's done for 35 years, Houghton continues his research into manufacturing what he calls "the ultimate vaccine" for HCV. Unlike another HCV vaccine in development, his lab is developing one that uses the body's immune response to produce antibodies that neutralize the virus.

Initial testing has shown the vaccine effective against all seven genotypes of HCV. It will be tested in healthy, uninfected people by the end of 2017, part of a phase 1 clinical trial. If the trial is a success and the vaccine is approved, potentially toward the end of 2018, it will be given to Canadian patients considered at high risk such as intravenous drug users, paramedics, police officers and health professionals exposed to blood. The vaccine would be administered more broadly in developing countries where disposable needles are not used in medical practice.

The ultimate goal is to perfect the dosage and land on a vaccine that is affordable, at a cost of about $50, that can be used anywhere in the world.

"Getting a vaccine out there that's affordable to Canada and to the United States and developing countries is an important goal for all of us," Houghton says. "And in terms of a national plan for Canada for protecting the community from hep C, this is a major plank in the plan."

For survivors like Robson, life after hep C is transformative. She will be around to see her grandchildren grow up—granddaughter Eva was born last April and she's crossing her fingers for a few more additions to the family.

Suddenly, her 65th birthday this August is no longer a gloomy prospect.

"I'll be having a big party this year. Instead of a fateful party, I'll be having a real celebration."

Provided by University of Alberta