**Targeted drugs to tackle hepatitis C**

**But experts debate US screening recommendations.**

**BY BETH MOLE**

John strains to recall the gap between learning that he had hepatitis C and deciding to get treated: it was either four years or five. His thinking is clouded by the combination of three drugs that he is taking to clear the infection. After the treatments’ other side effects set in — severe flu-like symptoms, depression and exhaustion — he took leave from his job as a chef in New York. John, whose name has been changed to protect his privacy, was at high risk of catching the virus, having once been addicted to crystal methamphetamine. But as a 51-year-old, he is also a baby boomer — a member of the generation born between 1945 and 1965 — millions of whom will face the disease and its sometimes harrowing treatment.

Better drugs are on the way. But the possibility of improved treatment is intensifying a debate about whether to screen a broad swathe of the US population for hepatitis C.

Last month, the pharmaceutical company Gilead, based in Foster City, California, submitted its hepatitis-C drug sofosbuvir to the US Food and Drug Administration for approval, after phase II trials showed a 100% success rate in a few patient groups when it was used in combination with existing drugs. Last week, the first phase III results showed similarly promising results (E. Lawitz et al. N. Engl. J. Med. http://doi.org/mcc; 2013).

The drug is one of at least ten in phase III trials in the United States that promise to improve results or reduce side effects. The first of these drugs could reach the market as early as 2014, and a recommendation from the US Centers for Disease Control and Prevention (CDC) in Atlanta, Georgia, to screen an entire generation for the disease could create vast demand for them.

John is a part of a demographic time bomb. “The AquaBounty example has [made] the company very sceptical about how much investment to pour into the US regulatory process,” he says. Yet Stotish says that GM animal products will inevitably find their way to grocery stores. He points to heavy investment in the technology in China, where dozens of GM farm animals are in development. “I think we will end up eating genetically modified animals of a variety of species,” says Stotish. “But they’ll come from other countries.”

**AGAINST THE CURRENT**

The US Food and Drug Administration (FDA) has been slow to approve a genetically modified (GM) salmon made by AquaBounty of Maynard, Massachusetts. The fish would be the first GM animal authorized for human consumption.

**1989** Canadian researchers engineer wild Atlantic salmon to overexpress growth hormone.

**1995** AquaBounty files an Investigational New Animal Drug application with the FDA.

**2001** AquaBounty submits its first regulatory study to the FDA.

**2009** The FDA releases guidance for its evaluation of genetically engineered animals as veterinary drugs; AquaBounty completes its FDA submission.

**2010** The FDA says that GM salmon is safe to eat.

**2012** The FDA completes its draft environmental assessment in May, but does not release it to the public until December.

**2013** The public-comment period for the draft environmental assessment is extended by two months and concludes on 26 April.

**1950** Cirrhosis

**1990** John strains to recall the gap between learning that he had hepatitis C and deciding to get treated: it was either four years or five. His thinking is clouded by the combination of three drugs that he is taking to clear the infection. After the treatments’ other side effects set in — severe flu-like symptoms, depression and exhaustion — he took leave from his job as a chef in New York. John, whose name has been changed to protect his privacy, was at high risk of catching the virus, having once been addicted to crystal methamphetamine. But as a 51-year-old, he is also a baby boomer — a member of the generation born between 1945 and 1965 — millions of whom will face the disease and its sometimes harrowing treatment.

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**AN APPROACHING BURDEN**

The high number of hepatitis-C infections in the United States is expected to lead to a peak in cases of cirrhosis, or liver scarring, by around 2020.
That means that doctors should consider birth year when deciding whether to offer screening, but should take other factors into account. The mediocre grade could discourage many health-care providers — including Medicaid, the provider for people with low incomes — from pushing screenings.

As with its controversial recommendations in 2009 and 2012 to limit screening for breast and prostate cancer, the USPSTF has tried to balance the benefits of screening against the risk of unnecessary treatment. The combination therapies used to combat hepatitis C can cost US$1,100 per week and last for up to a year, with severe side effects. Other treatments cost $4,100 per week. (Gilead declined to comment on the future price of sofosbuvir-based treatments.)

Roger Chou, an internal-medicine specialist at Oregon Health and Science University in Portland and a scientific reviewer for the USPSTF, adds that in most patients, the disease is imperceptible: only 20% of people develop liver scarring in the first 20 years of infection, according to the CDC. Of the few baby boomers that might be caught through additional screening, says Chou, some will not need to be treated.

But new drugs, however expensive, could change the calculus for doctors and patients, says Mark Eckman, a physician at the University of Cincinnati in Ohio, who has calculated that even screening the entire US population would be cost effective given the financial and personal burdens of living with liver diseases (M. H. Eckman et al. Clin. Infect. Dis. 56, 1382–1393; 2013).

For example, sofosbuvir, which is one of a set of new antiviral drugs that specifically target hepatitis C rather than viruses in general, can achieve success rates above 90% in combination treatments of just three months. The drug inhibits the virus’s RNA polymerase, preventing viral replication. It is also being tested without interferon, which boosts the immune system but causes harsh side effects.

The USPSTF is still reviewing its draft recommendations, but it is likely to make a final decision in the next few months, well before approval of sofosbuvir or other new drugs could alter the calculations.

That is too bad, says David Thomas, a viral-hepatitis specialist at Johns Hopkins University in Baltimore, Maryland, who argues that the next generation of drugs helps to justify wide-scale screening. “It makes a pretty easy case for doing something different,” he says. ■

**BIOMEDICINE**

Clinician to head Wellcome Trust

Jeremy Farrar to lead one of world’s largest research charities.

BY RICHARD VAN NOORDEN

From his base in Vietnam, Jeremy Farrar has spent the past 17 years on the front line of the battle with infectious diseases, from dengue and typhoid to severe acute respiratory syndrome (SARS) and now H7N9 avian influenza. The British clinician has led the Oxford University Clinical Research Unit in Ho Chi Minh City as it has grown from a dozen people to around 200 researchers supporting public-health efforts in Vietnam, Nepal and Indonesia.

Now, Farrar is stepping up to lead the UK institution that paid for much of his work: the Wellcome Trust, one of the world’s largest charities funding biomedical research. Colleagues and public-health leaders say that the trust, which last year spent £746 million (US$1.15 billion), has made an excellent choice — and wonder whether it signals an even greater focus on funding research in developing countries.

“He’s massively driven, and a great visionary. He’s invested his career in doing the research where the problem lies; he believes tropical medicine should be done in the tropics,” says Bob Snow, one of Farrar’s collaborators, who works on malaria and public health in Nairobi.

Farrar moved to Vietnam in 1996, when the Wellcome Trust was boosting investment in disease-ridden countries in Africa and southeast Asia. He saw the SARS outbreak in 2003 at close quarters — his friend, Carlo Urbani, died of the virus while working for the World Health Organization (WHO) in Hanoi. Then came a surge in H5N1 avian flu, which hit Vietnam hard. “It was a tense time for everyone,” says Cameron Simmons, a dengue expert who works with Farrar; clinicians were treating patients and trying to explain the crisis. Through all of this, Farrar’s leadership and ability to build trust between people was evident, says Simmons.

“Jeremy’s very much a shrewd team player,” says Colin Blakemore, a neuroscientist who works at the University of Oxford, UK, and former head of Britain’s Medical Research Council. Farrar has brokered funding from several sources, and his centre’s work on flu required negotiations with countries such as China to obtain samples. Those skills will serve him well when he moves to the Wellcome Trust in October.

For the past decade, Farrar has been migrating to a more strategic role, Snow says, serving on WHO advisory boards and pushing for a greater focus on flu surveillance and on capacity-building in the developing world.

“I believe that we have to bring some of the huge investment by the developed world in genom- ics, technology and training to affected countries in Asia and elsewhere,” Farrar wrote last year (Nature 483, 534–535; 2012).

Farrar would not divulge whether his vision of international public-health strategy would affect the trust’s priorities: “I have too much to do on H7N9 and hand, foot and mouth disease to talk about that,” he says. But Snow says that researchers are hopeful. Since 2008, the charity — under its previous director Mark Walport, now the UK government’s chief scientific adviser — has increased its spending outside the United Kingdom from 14% to 22%, expanding support for programmes in India and sub-Saharan Africa in particular. It has also doubled the share of its cash it gives to translational research, from 6% to 12%. David Heymann, chairman of the advisory board for Public Health England, says that Farrar is likely to encourage those trends.

“It wasn’t an easy decision for him to give up the science,” says epidemiologist Simon Hay, a collaborator at the University of Oxford, “but there’s a responsibility for people that have been advocating in public health to step up when these positions come up.” Moreover, the Vietnam unit can now operate without Farrar.

“There will be tears from our end and from our Vietnamese partners. The trust is very lucky to be getting Jeremy — he’s a remarkable leader,” says Simmons. ■

Additional reporting by Ewen Callaway and David Cyranoski.

**CORRECTION**

The News Feature ‘The gun fighter’ (Nature 496, 412–415; 2013) did not cite the sources for the graphs. These have now been added online.