3 win Nobel medicine prize for discovering hepatitis C virus

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In this undated photo provided by the National Institutes of Health, Harvey J. Alter, left, talks to a patient hooked up to a Kaneka-fuchi Co. Liposorber MA-01, at the National Institutes of Health in Bethesda, Md. Alter and fellow American Charles M. Rice and British-born scientist Michael Houghton jointly won the Nobel Prize for medicine on Monday, Oct. 5, 2020, for their discovery of the hepatitis C virus, a major source of liver disease that affects millions

worldwide. (Rhoda Baer/Office of National Institutes of Health History and Stetten Museum via AP)

Three scientists won the Nobel Prize in medicine Monday for discovering the liver-ravaging hepatitis C virus, a breakthrough that led to cures for the deadly disease and tests to keep the scourge out of the blood supply.

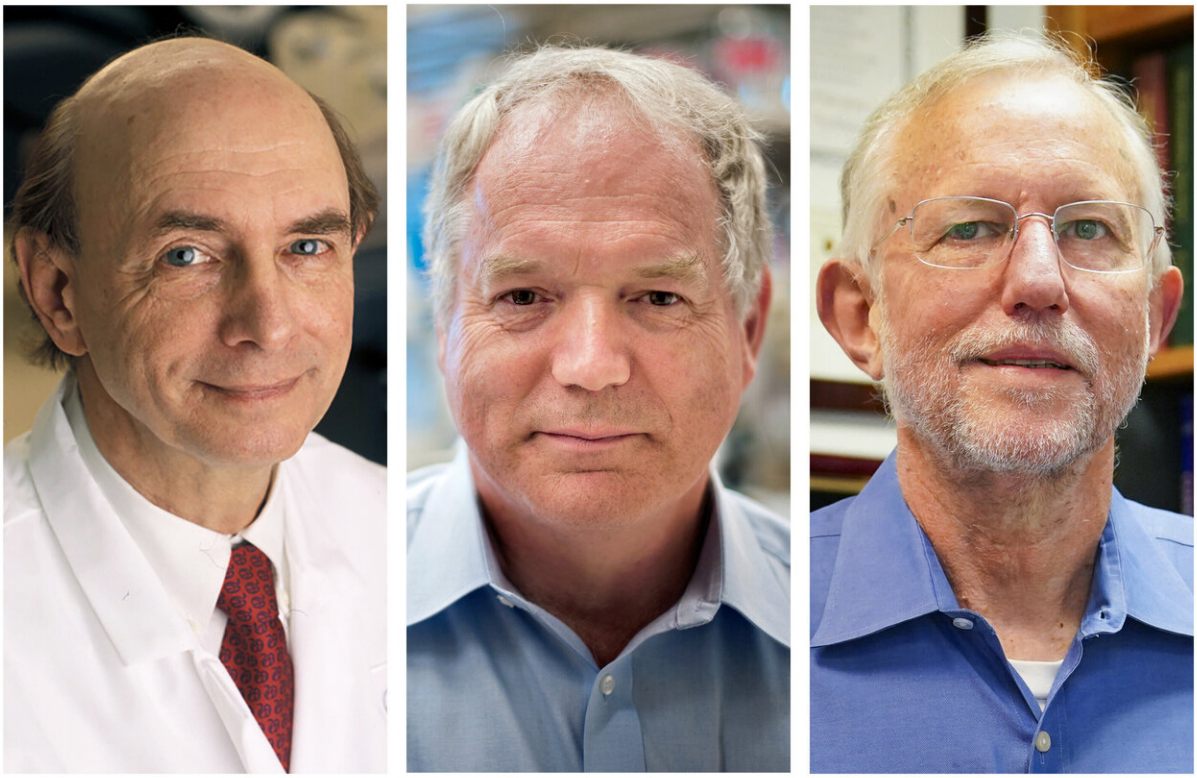
Americans Harvey J. Alter and Charles M. Rice and British-born scientist Michael Houghton were honored for their work over several decades on an illness that still plagues more than 70 million worldwide and kills over 400,000 each year.

"For the first time in history, the disease can now be cured, raising hopes of eradicating hepatitis C virus from the world," the Nobel Committee said in announcing the prize in Stockholm.

The challenge now is to make these still-expensive drugs more widely available and to stem the spread of the disease among drug users, whose sharing of needles has led to spikes in cases.

"What we need is the political will to eradicate it" and to make the drugs affordable enough to do it, Alter said.

Scientists had long known of the hepatitis A and B viruses, spread largely through contaminated food or water and blood, respectively, but were "toiling in the wilderness" to try to explain many other cases of liver disease until the blood-borne hepatitis C virus was identified in 1989, said Dr. Raymond Chung, liver disease chief at Massachusetts General Hospital.



This combination of photos shows, from left, Harvey J. Alter, Charles M. Rice, and Michael Houghton who jointly won the Nobel Prize for medicine on Monday, Oct. 5, 2020, for their discovery of the hepatitis C virus. The major source of liver disease affects millions worldwide. (Rhoda Baer/National Institutes of Health, Richard Siemens/University of Alberta, AP Photo/John Minchillo)

Now, it's the only chronic viral infection that can be cured in almost all cases within a few months, using one of roughly half a dozen drugs, Chung said. Without such treatment, the virus can lead to permanent scarring of the liver, liver cancer or the need for a transplant.

In an interview with The Associated Press, Rice said he is most proud

that the group's work quickly led to a test to screen donors and make the blood supply safer.

"We take it for granted that if you get a transfusion, you're not going to get sick from that transfusion. That was not the case before but is certainly the case now," Rice said.

Dr. Jesse Goodman, a former blood safety expert at the U.S. Food and Drug Administration now at Georgetown University, said that before testing was available, about 1 in 10 blood transfusions carried the risk of passing the virus.

This undated photo provided by the National Institutes of Health shows Harvey J. Alter. Alter and fellow American Charles M. Rice and British-born scientist Michael Houghton jointly won the Nobel Prize for medicine on Monday, Oct. 5,

2020, for their discovery of the hepatitis C virus, a major source of liver disease that affects millions worldwide. (Rhoda Baer/National Institutes of Health via AP)

"Now it's 1 in a million," Goodman said.

Rice, 68, worked on hepatitis at Washington University in St. Louis and now is at Rockefeller University in New York. Alter, 85, worked for decades at the U.S. National Institutes of Health and remains active there. Houghton, 69, was born in Britain and worked on hepatitis at the Chiron Corp. in California before moving to the University of Alberta in Canada.

Alter first discovered that blood from patients who did not have hepatitis B could still cause liver inflammation and disease, but for years the cause was unknown. A breakthrough came in 1989, when Houghton and others at Chiron cloned the virus, making its genetic identity known and allowing further research on it, said Nobel Committee member Gunilla Karlsson-Hedestam.

Later, Rice developed lab tools and methods that confirmed the hepatitis C virus could cause liver disease in chimpanzees and humans, directly contributing knowledge that led to tests and treatments.

Michael Houghton smiles in a screen grab from a zoom meeting arranged by the University of Alberta on Monday, Oct. 5, 2020. The British-born scientist and Americans Harvey J. Alter and Charles M. Rice jointly won the Nobel Prize for medicine on Monday, Oct. 5, 2020, for their discovery of the hepatitis C virus, a major source of liver disease that affects millions worldwide. (University of Alberta/The Canadian Press via AP)

"We have not seen any more cases since 1997" of hepatitis from a transfusion, Alter said. "Currently we can cure virtually anybody who's identified. With that, it's possible to maybe even eradicate this disease over the next decade," as the World Health Organization hopes to do.

Nobel Committee member Patrik Ernfors drew a parallel between this year's prize and the rush by millions of scientists around the world to find a vaccine to combat the coronavirus pandemic.

"The first thing you need to do is to identify the causing virus," he said. "And once that has been done, that is, in itself, the starting point for development of drugs to treat the disease and also to develop vaccines against the disorder."

Alter and Rice are now working on coronavirus research, while Houghton is trying to develop a hepatitis C vaccine. Houghton said manufacturing delays have been a problem but he expects clinical trials to begin next year in many countries, including the U.S., Germany and Italy.

Charles M. Rice, professor of virology at Rockefeller University, poses for a portrait in his laboratory office, Monday, Oct. 5, 2020, in New York. Rice was awarded the Nobel Prize for Medicine or Physiology on Monday for the discovery of the hepatitis C virus along with fellow American Harvey J. Alter

and British-born scientist Michael Houghton. (AP Photo/John Minchillo)

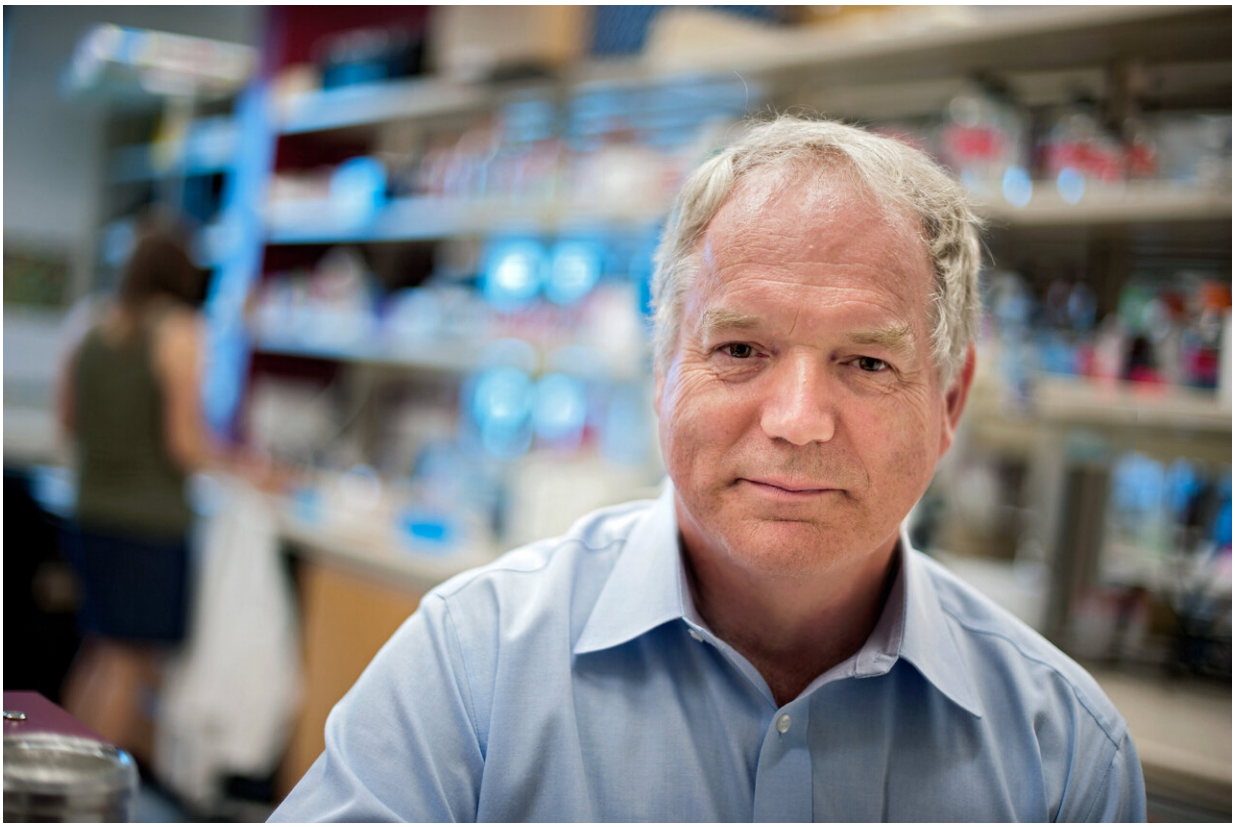
"To control an epidemic, you need to have a vaccine," Houghton said. For "diseases like gonorrhea, syphilis, chlamydia, we've had cheap drugs available for decades, and yet we still have big epidemics of those diseases."

John McLauchlan, a professor of viral hepatitis at the University of Glasgow, said the three laureates' discovery has made the global elimination of the disease possible—"the first time we might possibly control a viral infection using only drugs."

Hepatitis C drugs were around $40,000 when they first came out less than a decade ago. They have come down to roughly a quarter of that but are still out of reach for much of the world.

India, Eastern Europe, Egypt and parts of Asia, including Mongolia, remain the areas hardest hit.

Monday's medicine award is the first of six prizes this year being announced through Oct. 12. The others are for work in physics, chemistry, literature, peace and economics.



In this undated photo provided by the University of Alberta, Dr. Michael Houghton poses in his lab at Li Ka Shing Institute of Virology - University of Alberta, in Edmonton, Alberta, Canada. The British-born scientist and Americans Harvey J. Alter and Charles M. Rice jointly won the Nobel Prize for medicine on Monday, Oct. 5, 2020, for their discovery of the hepatitis C virus, a major source of liver disease that affects millions worldwide. (Richard Siemens/University of Alberta via AP)

Thomas Perlmann, far right, Secretary of the Nobel Assembly announces the 2020 Nobel laureates in Physiology or Medicine during a news conference at the Karolinska Institute in Stockholm, Sweden, Monday Oct. 5, 2020. The prize has been awarded jointly to Harvey J. Alter, left on screen, Michael Houghton, center, and Charles M. Rice for the discovery of the Hepatitis C virus. (Claudio Bresciani/TT via AP)

The Nobel Committee often recognizes basic science that laid the foundations for practical applications in common use today.

"It takes time before it's fully apparent how beneficial a discovery is," said Thomas Perlmann, secretary-general of the Nobel Committee.

The Nobel comes with a gold medal and 10 million Swedish kronor

(over $1.1 million), courtesy of a bequest left 124 years ago by the prize's creator, Swedish inventor Alfred Nobel.

The Nobel Foundation announcement:

The Nobel Assembly at Karolinska Institutet

has today decided to award

the 2020 Nobel Prize in Physiology or Medicine

jointly to

Harvey J. Alter, Michael Houghton and Charles M. Rice

for the discovery of Hepatitis C virus

SUMMARY

This year's Nobel Prize is awarded to three scientists who have made a decisive contribution to the fight against blood-borne hepatitis, a major global health problem that causes cirrhosis and liver cancer in people around the world.

Harvey J. Alter, Michael Houghton and Charles M. Rice made seminal discoveries that led to the identification of a novel virus, Hepatitis C virus. Prior to their work, the discovery of the Hepatitis A and B viruses had been critical steps forward, but the majority of blood-borne hepatitis cases remained unexplained. The discovery of Hepatitis C virus revealed the cause of the remaining cases of chronic hepatitis and made possible blood tests and new medicines that have saved millions of lives.

Hepatitis – a global threat to human health

Liver inflammation, or hepatitis, a combination of the Greek words for liver and inflammation, is mainly caused by viral infections, although alcohol abuse, environmental toxins and autoimmune disease are also important causes. In the 1940's, it became clear that there are two main types of infectious hepatitis. The first, named hepatitis A, is transmitted by polluted water or food and generally has little long-term impact on the patient. The second type is transmitted through blood and bodily fluids and represents a much more serious threat since it can lead to a chronic condition, with the development of cirrhosis and liver cancer. This form of hepatitis is insidious, as otherwise healthy individuals can be silently infected for many years before serious complications arise. Blood-borne hepatitis is associated with significant morbidity and mortality, and causes more than a million deaths per year world-wide, thus making it a global health concern on a scale comparable to HIV-infection and tuberculosis.

An unknown infectious agent

The key to successful intervention against infectious diseases is to identify the causative agent. In the 1960's, Baruch Blumberg determined that one form of blood-borne hepatitis was caused by a virus that became known as Hepatitis B virus, and the discovery led to the development of diagnostic tests and an effective vaccine. Blumberg was awarded the Nobel Prize in Physiology or Medicine in 1976 for this discovery.

At that time, Harvey J. Alter at the US National Institutes of Health was studying the occurrence of hepatitis in patients who had received blood transfusions. Although blood tests for the newly-discovered Hepatitis B virus reduced the number of cases of transfusion-related hepatitis, Alter

and colleagues worryingly demonstrated that a large number of cases remained. Tests for Hepatitis A virus infection were also developed around this time, and it became clear that Hepatitis A was not the cause of these unexplained cases.

It was a great source of concern that a significant number of those receiving blood transfusions developed chronic hepatitis due to an unknown infectious agent. Alter and his colleagues showed that blood from these hepatitis patients could transmit the disease to chimpanzees, the only susceptible host besides humans. Subsequent studies also demonstrated that the unknown infectious agent had the characteristics of a virus. Alter's methodical investigations had in this way defined a new, distinct form of chronic viral hepatitis. The mysterious illness became known as "non-A, non-B" hepatitis.

Identification of Hepatitis C virus

Identification of the novel virus was now a high priority. All the traditional techniques for virus hunting were put to use but, in spite of this, the virus eluded isolation for over a decade. Michael Houghton, working for the pharmaceutical firm Chiron, undertook the arduous work needed to isolate the genetic sequence of the virus. Houghton and his co-workers created a collection of DNA fragments from nucleic acids found in the blood of an infected chimpanzee. The majority of these fragments came from the genome of the chimpanzee itself, but the researchers predicted that some would be derived from the unknown virus. On the assumption that antibodies against the virus would be present in blood taken from hepatitis patients, the investigators used patient sera to identify cloned viral DNA fragments encoding viral proteins. Following a comprehensive search, one positive clone was found. Further work showed that this clone was derived from a novel RNA virus belonging to the Flavivirus family and it was named Hepatitis C virus. The presence of antibodies in chronic hepatitis patients strongly

implicated this virus as the missing agent.

The discovery of Hepatitis C virus was decisive; but one essential piece of the puzzle was missing: could the virus alone cause hepatitis? To answer this question the scientists had to investigate if the cloned virus was able to replicate and cause disease. Charles M. Rice, a researcher at Washington University in St. Louis, along with other groups working with RNA viruses, noted a previously uncharacterized region in the end of the Hepatitis C virus genome that they suspected could be important for virus replication. Rice also observed genetic variations in isolated virus samples and hypothesized that some of them might hinder virus replication. Through genetic engineering, Rice generated an RNA variant of Hepatitis C virus that included the newly defined region of the viral genome and was devoid of the inactivating genetic variations. When this RNA was injected into the liver of chimpanzees, virus was detected in the blood and pathological changes resembling those seen in humans with the chronic disease were observed. This was the final proof that Hepatitis C virus alone could cause the unexplained cases of transfusion-mediated hepatitis.

Significance of this Nobel Prize-awarded discovery

The Nobel Laureates' discovery of Hepatitis C virus is a landmark achievement in the ongoing battle against viral diseases. Thanks to their discovery, highly sensitive blood tests for the virus are now available and these have essentially eliminated post-transfusion hepatitis in many parts of the world, greatly improving global health. Their discovery also allowed the rapid development of antiviral drugs directed at hepatitis C. For the first time in history, the disease can now be cured, raising hopes of eradicating Hepatitis C virus from the world population. To achieve this goal, international efforts facilitating blood testing and making antiviral drugs available across the globe will be required.

Key publications:

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Feinstone SM, Kapikian AZ, Purcell RH, Alter HJ, Holland PV. Transfusion-associated hepatitis not due to viral hepatitis type A or B. N Engl J Med. 1975; 292:767-770.

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Alter HJ, Purcell RH, Holland PV, Popper H. Transmissible agent in non-A, non-B hepatitis. Lancet. 1978; 1:459-463.

Choo QL, Kuo G, Weiner AJ, Overby LR, Bradley DW, Houghton M. Isolation of a cDNA clone derived from a blood-borne non-A, non-B viral hepatitis genome. Science. 1989; 244:359-362.

Kuo G., Choo QL, Alter HJ, Gitnick GL, Redeker AG, Purcell RH, Miyamura T, Dienstag JL, Alter CE, Stevens CE, Tegtmeier GE, Bonino F, Colombo M, Lee WS, Kuo C., Berger K, Shuster JR, Overby LR, Bradley DW, Houghton M. An assay for circulating antibodies to a major etiologic virus of human non-A, non-B hepatitis. Science. 1989; 244:362-364.

Kolykhalov AA, Agapov EV, Blight KJ, Mihalik K, Feinstone SM, Rice CM. Transmission of hepatitis C by intrahepatic inoculation with transcribed RNA. Science. 1997; 277:570-574.

Recent winners of the Nobel Medicine Prize

Here is a list of the winners of the Nobel Medicine Prize in the past 10 years following the announcement of the 2020 award on Monday:

2020: Americans Harvey Alter and Charles Rice, together with Briton Michael Houghton, for the discovery of the Hepatitis C virus, leading to the development of sensitive blood tests and antiviral drugs.

2019: William Kaelin and Gregg Semenza of the US and Britain's Peter Ratcliffe for establishing the basis of our understanding of how cells react and adapt to different oxygen levels.

2018: Immunologists James Allison of the US and Tasuku Honjo of Japan, for figuring out how to release the immune system's brakes to allow it to attack cancer cells more efficiently.

2017: US geneticists Jeffrey Hall, Michael Rosbash and Michael Young for their discoveries on the internal biological clock that governs the wake-sleep cycles of most living things.

2016: Yoshinori Ohsumi (Japan) for his work on autophagy—a process whereby cells "eat themselves"—which when disrupted can cause Parkinson's and diabetes.

2015: William Campbell (US citizen born in Ireland) and Satoshi Omura (Japan), Tu Youyou (China) for unlocking treatments for malaria and roundworm.

2014: John O'Keefe (Britain, US), Edvard I. Moser and May-Britt Moser (Norway) for discovering how the brain navigates with an "inner GPS".

2013: Thomas C. Suedhof (US citizen born in Germany), James E.

Rothman and Randy W. Schekman (US) for work on how the cell organises its transport system.

2012: Shinya Yamanaka (Japan) and John B. Gurdon (Britain) for discoveries showing how adult cells can be transformed back into stem cells.

2011: Bruce Beutler (US), Jules Hoffmann (French citizen born in Luxembourg) and Ralph Steinman (Canada) for work on the body's immune system.

More information: Scientific background: www.nobelprize.org/prizes/medi … dvanced-information/