

## Massimo Galli

Massimo Galli had thought that retirement was going to arrive quietly within a couple of years. In January, 2020, Galli, who is head of the Infectious Diseases Unit at the University of Milan-affiliated Luigi Sacco Hospital in Milan, Italy, had just recovered from a pulmonary thromboembolism. But the next few months would be the most challenging of his career as the COVID-19 pandemic exploded in Italy.

He has spent his entire career in Milan, working between the Sacco Hospital and the University of Milan where he is a full professor of infectious diseases. "When I was a young doctor, I wanted to go to America and study immunology", Galli tells *The Lancet Infectious Diseases*. "This was the early 1980s, and then the HIV epidemic arrived. My boss told, Massimo, you should stay here. This will need to be your America now".

Having studied medicine at the University of Milan, he specialised in clinical immunology and allergology and later in infectious diseases and internal medicine. His earliest research interest, in 1976, had been on cryoglobulinaemia, a condition in which cold sensitive antibodies precipitate from the blood. For some years this condition had been thought to be driven by hepatitis B virus, but Galli's studies in the early eighties helped to downsize the role of that virus, and in the 1990s he helped identify hepatitis C virus as a predominant cause of this disorder.

As HIV tightened its deadly grip in the 1980s, Galli researched clinical epidemiology, therapeutics, prevention, focusing in particular on the epidemic among the key risk group of heroin users in Italy. He was an expert on the toxic effects of antiretroviral therapy, and his group was among the first to highlight the lipotropic effects of nucleoside reverse transcriptase inhibitors. This work led to his position on the Italian National Commission on HIV and AIDS, a role he held from more than 10 years. He also contributed to Italy's latest national plan for the fight against HIV/AIDS, launched in 2017. And in the 1990s and 2000s, Galli coordinated various programmes to combat AIDS in Africa, Latin America, and eastern Europe, promoted by the Italian National Association for the Fight Against AIDS (ANLAIDS), of which he is one of the founders.

As President of the Italian Society of Infectious and Tropical Diseases from 2017 to 2019, he passed a resolution endorsing the HIV undetectable=untransmittable concept. "One of my main concerns is that young Italians today do not sufficiently recognise HIV or its effects. And that PrEP is not yet widely available in Italy", he says. He also advocated for mass testing for hepatitis C so that Italy can eliminate its remaining cases, having successfully treated some 200 000 so far.

Since 2000, Galli has been a full professor at the University of Milan, and in 2018 he became director of the University's Department of Biomedical and Clinical Science L. Sacco, overseeing some 70 medical professors. He also teaches and still works in the hospital clinic. He will step down from his directorship in November 2020, and do another year of research before retiring completely in 2021. "I already have many investigations into COVID-19 in progress. But I also want to return to other projects I have left in the desk drawer!", he says.

Dealing with the severe acute respiratory syndrome coronavirus 2 outbreak has been an enormous challenge for all doctors in Italy. Galli's hospital is the reference centre for epidemic emergencies and bioterrorism in northern Italy, so his team is all fully trained in the use of personal protective equipment and the use of negative pressure rooms to stop transmission. They have also tripled their ICU capacity. "While no colleagues in my hospital have been infected, others across Italy have sadly lost their lives", he says.

His team has quickly produced several research papers on the coronavirus outbreak, including a phylogenetic analysis of the origin of the Italian epidemic published in the *Journal of Medical Virology*, showing Italy's index case to have travelled from Munich in late January. "It's very clear that the virus arrived in Italy in January and spread for 3 or 4 weeks undetected", explains Galli. At the time of writing, daily deaths from COVID-19 in Italy are declining from their peak. While we finish our interview, Galli takes a call from a member of Italian Government to discuss how to ease their lockdown.

After he retires, Galli will pursue his interest in much older pandemics, including the plague. "I am analysing the register of deaths in Milan that goes from as far back as 1452 to early 19th century, and using it to establish the cause of death. The quality of information in this register is amazing, despite its age", he says.

"Beyond any professional achievement Massimo is one of the few remaining men in the world with a true encyclopaedic knowledge. One of his preferred dinner questions is to ask around if any of the guests know who were the six wives of Henry VIII!" says Giovanni Di Perri, Professor of Infectious Diseases at the University of Torino, Italy. "In this recent COVID-19 outbreak he played as a giant the role of the independent as well as brilliant spokesman on behalf of all doctors and nurses involved in the epidemic. I would like to have him as the next Prime Minister of Italy!"

Tony Kirby





## Larisa Rudenko



Born in 1943 during World War 2, Larisa Rudenko grew up in Zaporozh'ye, in southeast Ukraine. Having lost her father during the war, she was raised by her mother, a paediatrician, and spent many early days queuing for food rations. Later, things improved and they were able to take family holidays to Crimea. "I saw many unhappy children in wheelchairs there, and mother told me they had polio and there was no treatment", she tells *The Lancet Infectious Diseases*. "I wanted to help those children. My mother said that American and Russian scientists were working together on a vaccine to help prevent this horrible disease."

After high school she decided to enter medical school in Leningrad (today St Petersburg). She was thrilled to attend a lecture by the polio vaccine creator Anatoly Smorodintsev who was head of the virology department at the Institute of Experimental Medicine of the Russian Academy of Sciences. She asked him nervously if she could work there to learn basic virology. He said yes, and the rest is history. At that time (the 1970s) cold-adapted live influenza vaccines were being clinically tested at her institute. "These were amazing times, because many foreign scientists, including Hilary Koprowski and Robert Chanock visited our department, and we met them and attended their lectures", she recalls.

After graduation, Rudenko completed her PhD on the development of a live oral adenovirus vaccine, under the guidance of Smorodintsev. Then, together with Galina Alexandrova, she worked on a new generation of live attenuated influenza vaccines (LAIV) using the reassortment method for preparing vaccines. They also collaborated with the US Centers for Disease Control and Prevention (CDC) and their advanced technology to fully characterise the master donor strains.

Their team used the reassortment method to prepare the various vaccine strains, and coordinated 8 years of clinical trials including 120 000 children and later older and elderly adults. These studies established the safety, immunogenicity and effectiveness LAIV and the world's first LAIV was registered in the former USSR in 1987.

Although inactivated influenza vaccines have dominated US markets, American scientists showed interest in Russian LAIVs. Other trials of LAIVs were conducted in collaboration with CDC and the University of Michigan, including among schoolchildren in Novgorod and elderly in the Leningrad. These trials changed the opinions of American experts, since LAIV establish herd immunity among the non-vaccinated, whereas inactivated forms do not. Despite this, LAIV were only approved and registered in the USA in 2003. They remain in use in the USA and many European countries today.

While her research on LAIV continues, Rudenko's other major focus has been as an expert for WHO's Global Pandemic Preparedness Plan (GAP). LAIV was included in the GAP as a vaccine which, in the event of a pandemic, can be made much more quickly and in larger quantities compared with inactivated vaccines.

Over the past decade, Rudenko's team has developed all of WHO's recommended potentially pandemic influenza virus candidates of the H1, H2, H5N1, H7N3, H7N9 subtypes, which underwent preclinical testing and phase I clinical trials. Rudenko then worked with WHO to transfer the technology to LAIV producers in other countries, with licenses granted to companies in Thailand, India, and China.

Rudenko believes that the next influenza pandemic could be caused by the H2N2 type that spread through Singapore in 1957. "Most people alive today would have no immunity to this strain," she explains. "However, it is a human virus with a human receptor. It could be virulent again. Our institute has developed all the reassortants for this strain. If it appears, we will be ready."

On the COVID-19 crisis, Rudenko needs to see more evidence before deciding if it has escaped from a live animal market, a laboratory, or come from another source. "COVID-19 could come back every winter until we find a vaccine", she says. However, always keen to emphasize the positive, she says that "coronavirus has really focused the world's attention on the importance of vaccines and when a vaccine will arrive". Her own team has begun work on a nasally applied double vaccine to combat influenza and the novel coronavirus. She estimates 2-3 years are needed to establish if it is safe and efficacious.

In addition to her research, Rudenko has been the mentor for many young scientists at her institution, with the latest generation inspiring her with their knowledge of new techniques in biotechnology and molecular biology and helping develop LAIVs that are more broadly protective. Outside the laboratory, she loves to immerse herself in culture, including visiting the opera.

"I first met Larisa Rudenko at a meeting on influenza vaccines, at the beginning of the conceptualisation of WHO Global Action Plan", says Marie-Paule Kieny, director of research at Inserm, Paris, France, and former assistant director-general at WHO. "By bringing the discussion back to science, she convinced most experts and LAIV became WHO's vaccine of choice in case of a pandemic. Following this, Larisa also became a friend and a role model for me, for her strength, energy, determination, and dedication to science, public health, and her team."

Tony Kirby