Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.
In this ongoing pandemic, we have science on our side, lending support that could almost appear miraculous and thereby helping to prevent many deaths. We can test ourselves for the presence of SARS-CoV-2, we can get vaccinated against it, and the authorities can monitor the spread of the disease based on wastewater analytics and spot outbreaks even before patients report to hospitals with serious symptoms (Curr. Biol. (2021) 31, R267–R269).

The tragic outcome that more than six million people have died from this new disease within its first 30 months and many more are left with long-term consequences is largely a failure of translating this groundbreaking science into public health policy and behaviour at the population level. Advance warnings were available, but the “let’s see how bad it gets” school of thinking prevailed especially among populist leaders and populations cherishing individualism, and measures were only taken at the last moment, when they became inescapable in order to prevent the collapse of health provision.

We have all the science we need to fight or even prevent global pandemics like COVID-19, but the forces of anti-science are severely hindering the efforts. In the history of human disease, this is a novelty. Previous pandemics struck people who had no way of knowing what was going on or how they might protect themselves. Only now, with the molecular toolkits for ancient DNA studies and the extra motivation provided by the current health crisis, are scientists beginning to understand the major pandemics of the past.

1918 Flu
The flu pandemic at the end of World War I ravaged countries already weakened by war and food shortages. Even though it killed an estimated 50 million people and proved surprisingly deadly to those aged 20 to 40, it was soon swept under the rug along with other unpleasant memories of war and suffering.

At the time, it was called the Spanish flu, but we now know that it definitely didn’t originate in Spain. Contemporary science wasn’t much clearer about the causes either. Although medical science had a phenomenological concept of influenza, the causative agent remained elusive. In a previous pandemic, the bacterial species Haemophilus influenzae was blamed for and named after influenza but turned out to be innocent. Only in the 1930s was it identified to be a virus, and only in the 1990s was the connection to avian influenza established. Now we know that it was an H1N1 strain of influenza A virus that caused the 1918 pandemic. The strains are categorised by their specific types of haemagglutinin (H) and neuraminidase (N) genes. We also know to look out for new variants of bird flu that might cross over and acquire the ability to spread between humans. Quite what caused the 1918 pandemic to become so deadly, however, has remained unknown.

In an effort to find out more about the 1918 pandemic virus, Livia Patrono from the Robert Koch Institute in Berlin, Germany, and colleagues analysed 13 formalin-fixed lung specimens dated between 1900 and 1931 from museum collections held in Berlin and Vienna. They identified influenza A virus in three of the specimens and produced one complete and two partial genome sequences of the virus (Nat. Commun. (2022) 13, 2314). Previously, only two complete sequences were known, both from victims in the USA, along with additional genetic data concerning the haemagglutinin gene. Suitably preserved samples from victims of the pandemic are very rare and hard to find, as the authors explain.

Comparing the new genomes to the known data from different places and times of the pandemic, Patrono and colleagues identified mutations that may be related to the virus adapting to the human host in the course of the outbreak, which may be linked to the observation that the second wave was deadlier than the first. They were also able to confirm that the H1N1 strains still circulating as seasonal flu are descendants of the pandemic strain.

Heart felt: The National COVID-19 memorial in London commemorates the 200,000 who died with the disease in the UK. (Photo: Geoff Henso/Flickr (CC BY-ND 2.0).)
Black Death
Considering the difficulty of finding samples relevant to the flu pandemic that occurred only a century ago, the research into medieval plague is flourishing remarkably. The notorious Black Death was the first wave of the second recognised plague pandemic. It swept across Europe from 1347 to 1352 CE killing up to half of the population in some areas. Subsequent waves of the second pandemic kept coming until the early 19th century but caused fewer casualties (pandemic kept coming until the early areas. Subsequent waves of the second killing up to half of the population in some recognised plague pandemic. It swept was the first wave of the second remarkably. The notorious Black Death into medieval plague is flourishing occurred only a century ago, the research samples relevant to the flu pandemic that (Curr. Biol. (2016) 26, R219–R221).

The Black Death was long assumed to have originated in Central or East Asia, as its progress from the coasts of the Black Sea towards the Mediterranean ports is well documented historically. One archaeological find that had been discussed as potentially relevant is a pair of burial sites near Lake Issyk Kul, in what is now Kyrgyzstan. Excavations in the 19th century revealed tombstones dating from 1338 to 1339 with inscriptions in the Syriac language citing a mysterious “pestilence” as the cause of death.

Marya Spirou from the University of Tübingen, Germany, and an international team have now used ancient DNA technology to analyse human remains from these burials and have successfully identified the plague pathogen, *Yersinia pestis*, in graves dated to 1338 (Nature (2022) 606, 718–724).

Genome analyses showed that this was not just one of the many sites visited by the pandemic. The bacterial strain found matches the requirements for the common ancestor of the diversity that emerged during the Black Death, suggesting that the researchers have found the source population, complete with the historical place and time when it ravaged communities in Central Asia.

This remarkable discovery also enabled the researchers to investigate the likely animal source of the outbreak, as plague is known as a zoonotic disease that has permanent animal reservoirs and crosses into the human population occasionally.

“We found that modern strains most closely related to the ancient strain are today found in plague reservoirs around the Tian Shan mountains, so very close to where the ancient strain was found. This points to an origin of Black Death’s ancestor in Central Asia”, explains Johannes Krause from the Max Planck Institute for Evolutionary Anthropology (EVA) at Leipzig, Germany, a senior author of the study.

While the further progress of the Black Death can be traced across Europe, details of its impact can still be subject to debate. In a recent study Adam Izdebski from the Max Planck Institute for the Science of Human History at Leipzig and colleagues used a “big data palaeo-ecology” approach to investigate its impact (Nat. Ecol. Evol. (2022) 6, 297–306). The fundamental idea is that in pre-industrial times the land surface under cultivation was a direct function of the population available to work the fields. Thus, a population collapse of 50% or more should clearly lead to a reduction in crops being grown.

Studying pollen records from 261 radiocarbon-dated coring sites across Europe, Izdebski and colleagues found that the impact of the Black Death was as devastating as expected in many places, but that some regions, including Ireland, Iberia, and parts of Eastern Europe, appear to have had a lucky escape and carried on with their agricultural business as normal. While specific reasons for the dramatic differences in impact remain unknown, the authors suggest that local cultural, demographic, economic, environmental and societal contexts have shaped the different outcomes.

The take-home lesson also applies to present and future pandemics: “There is no single model of ‘the pandemic’ or a ‘plague outbreak’ that can be applied to any place at any time regardless of the context,” Izdebski said. “Pandemics are complex phenomena that have regional, local histories. We have seen this with COVID-19, now we have now shown it for the Black Death”.

Justinianic Plague
Before the Black Death, many ‘plagues’ have befallen early Eurasian civilisations that may or may not have been caused by *Y. pestis*. The Justinianic Plague, which in 541–542 AD hindered East Roman emperor Justinian’s attempts at restoring the empire’s unity and glory, is currently the earliest plague pandemic recorded by history and confirmed by DNA evidence. *Y. pestis* DNA from that period was first detected in victims in Bavaria, later also in France, Spain and England (Proc. Natl. Acad. Sci. USA (2019) 116, 12363–12373). The genomes revealed that this earlier pandemic strain is unrelated to the Black Death strains and both pandemics likely go back to separate zoonotic transfer events.

The discovery of multiple plague carriers in an Anglo-Saxon burial site at Edix Hill in Cambridgeshire may force a reconsideration of current ideas about the spread of the pandemic, as Peter Sarris from the University of Cambridge, UK, argues (Past & Present
DNA analyses of ancient burials have yielded valuable information on the spread and evolution of pandemics. This image shows a burial in Minoan Crete where the plague pathogen \textit{Yersinia pestis} was identified. (Photo: © Photini McGeorge https://doi.org/10.1016/j.cub.2022.06.094.)

The plagues to come

The impact of pandemics appears to be most dramatic when we can observe them derailing the machinery of a well-described civilisation, hence the European bias in the examples discussed. Death and disruption will have been similar, if less-well documented, in the Americas when the first Europeans arriving brought smallpox and other diseases to which the native population had no immunity. The scale of the depopulation of the Amazon and the resulting ecological changes are also the subject of ongoing research and debate (Curr. Biol. (2021) 31, R821–R824).

To better understand the dangers and long-term perspectives of the current pandemic and possible threats like monkeypox and new flu strains, it is most valuable to study these pandemics of the past with their detailed historical context and increasing amounts of molecular genetic details becoming available.

The 1918 flu pandemic has already provided warnings relevant to COVID-19, such as the effects of superspreader events. The way the H1N1 strain subsequently turned into seasonal flu also informs our thinking of what may happen to the current coronavirus in the long term.

The three plague pandemics provide a warning regarding the longevity of human diseases. The first two stretched out over several centuries, and the third, which started in the mid-19th century and spread \textit{Y. pestis} around the globe, was only cut short thanks to antibiotics. If and when a multidrug-resistant plague arises, we may find ourselves back to square one.

All these warnings from history are useful only to the extent that people are prepared to heed them. If COVID-19 is forgotten as quickly as the 1918 flu was and the anti-science mood of the era, may well become the era of even deadlier pandemics.

Michael Gross is a science writer based at Oxford. He can be contacted via his web page at www.michaelgross.co.uk