

Tales from a plague pit

Archeology and genetics combine to reveal what caused the Black Death.

Image courtesy of Spooky Pooka, Medscape Images



By Kirsten Bos

The Black Death is without a doubt one of the most famous infectious diseases in history. Sweeping across Asia and Europe during the mid-fourteenth century, it reduced European populations by as much as 50 % in urban centres, in the space of just five years (1347–1351)^{w1}. This huge death toll had a long-lasting effect on European culture: large declines in the peasant class destabilised the feudal system, paving the way for more favourable economic systems. Soon citizens could own their own land and cultivate their own crops.

Many historical records document the path of the Black Death across

- ✓ Biology
- ✓ Biochemistry
- ✓ History of medicine
- ✓ Ages 12-17

This article is appropriate for learning in an interdisciplinary way. Science teachers could use this article as a basis for projects in subjects such as molecular biology, biochemistry of DNA or microbiology, and even link in elements of bioinformatics.

The article could be used with students for a discussion about the transmission, diffusion and evolution of some infectious diseases such as the Black Death. Students will understand the active research underway about the biology of *Y. pestis* and the extent of infections of this bacterium each year in Europe and throughout the world, and can compare this information with the history of the Black Death.

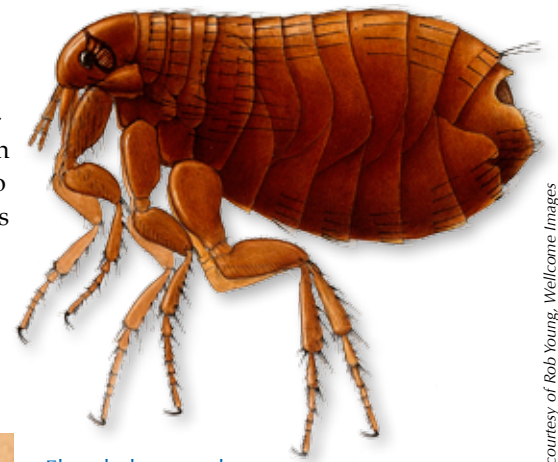
The article could also be used to start a project analysing the structure of the human tooth and how it is used for DNA extraction, as well as the techniques used to compare modern and ancient fragments of *Y. pestis* DNA and other bacteria with human DNA. A more intriguing activity is to ask students to hypothesise about the future of this research and, particularly, about its utility in helping us to understand changes in some of our genes.

Marina Minoli, Didactic expert at Agora University Active Science, Italy

REVIEW

medieval Europe, and some even include graphic descriptions of the disease's gruesome symptoms. The hallmark feature of the 'pestilence', as it was called at the time, was the presence of a single egg-sized swelling somewhere on the body. Based on this feature, medical historians today assume the disease was an unusu-

ally aggressive outbreak of bubonic plague, caused by the bacterium *Yersinia pestis*. Plague is normally found in rodents, which transmit the disease to each other through flea bites. Humans are one of about 200 mammalian species that are susceptible hosts to *Y. pestis* infections, and under certain conditions that we don't fully under-



Fleas help spread the disease

Image courtesy of Rob Young, Wellcome Images

stand yet, the disease can pass from rodents to humans. Today we still see about 2000 *Y. pestis* infections per year in the world, but they're nothing of the scale of the Black Death^{w2}.

The question of why humans succumbed to the Black Death is still unsolved. After all, a quick stroll through a subway station of any major city will tell you that we're not exactly free of rats. So was it that humans were living under conditions more conducive to bacterial infections in the past? Were medieval people simply more vulnerable to the disease, perhaps due to something in their genes? Or was the bacterium itself different in some special way that made it more virulent? An answer might come from the skeletons of people who were buried in plague pits in the city of London, England, during the height of the Black Death.

Digging down

Have you ever been to Tower Hill tube station in London? If so, you were right across the road from an ancient burial ground for plague victims. From 1986 to 1988, archaeologists at the Museum of London excavated this medieval plague pit and recovered the skeletons of 600 people (and there are still about 2000 more in the ground!)^{w3}.

I am part of a research team that took teeth from these skeletons to screen them for tiny pieces of *Y. pestis*



A physician wearing a plague preventive costume, people thought the disease was spread by foul air

Images courtesy of the Museum of London Archaeology



The excavation of the plague pit

DNA that might have survived being buried in the soil for almost 700 years. Teeth are the best part of the skeleton to use because the hard outer enamel works like a shell, protecting the DNA in the interior of the tooth for centuries.

You can think of this combination of archaeology and molecular biology as our lens to look into the past. Thanks to scientific developments in the past few years, we can now catch tiny

pieces of DNA from ancient diseases and look for clues about how their genes have changed over time. We can then use these differences to figure out how pathogens evolve.

Tooth extraction

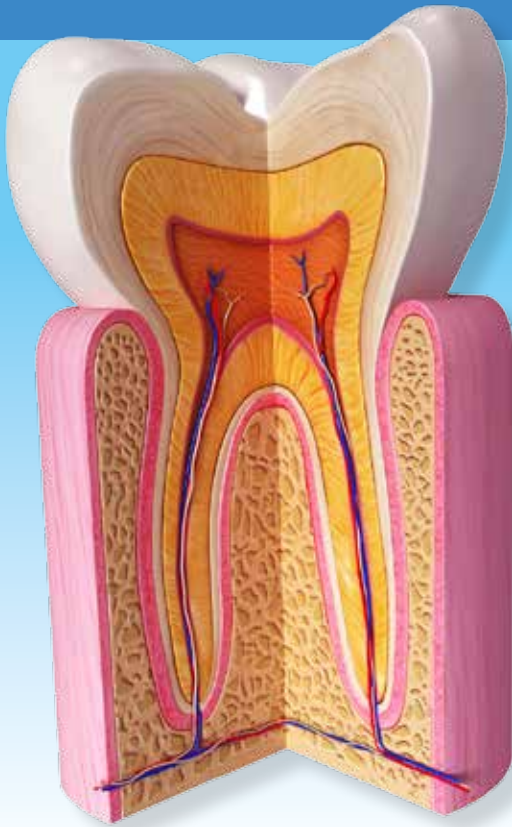
After collecting the teeth, we take them through a chemical process to isolate the DNA molecules from the cells that we've recovered. Unfortunately this process indiscriminately



takes DNA from all sources – plant, human, soil, bacteria – and somewhere in this giant molecular haystack are the tiny pieces of ancient pathogen DNA. The problem is finding them.

We use something called DNA capture to get these specific pieces of DNA. It's kind of like fishing, only rather than catching fish, we catch molecules. We design baits that match parts of the genetic code of the *Y. pestis* target we are looking for

Biology



Structure of the tooth. The hard enamel shell of teeth can protect DNA in the pulp for years

and go fishing in our giant molecular haystack, pulling out fragments that match. The whole process takes about a week, and at the end we have a raindrop-sized amount of liquid that hopefully contains pieces of the genetic code of the ancient pathogen that have survived for hundreds of years inside the tooth.

We don't end up with one long string of DNA coding for *Y. Pestis*. Instead, we have a whole bunch of tiny fragments of DNA. We can then use a computer (and a computer specialist!) to put the puzzle back together, giving us the reconstructed ancient genome of the disease. But don't worry – it's just a file on a computer, it's not in our lab!

With the reconstructed genome on file, we can compare the ancient disease to the versions of *Y. pestis* that circulate today, to see if it has changed over time. Interestingly, we found that the ancient plague was almost identical to the *Y. pestis* bacteria that is

around today, which was something we weren't expecting.

This means that the ancient disease was probably no more virulent than the one we see today. So perhaps, rather than the disease changing, humans themselves have changed. We could simply be living under conditions that prevent large-scale infections like the one that plagued medieval Europe, but a more intriguing possibility is that *our* genes may have changed to make us better able to deal with this particular infectious disease. The next step will be to look at ancient humans to see if their genes are different from ours. Clearly there are more secrets in ancient bones, and now we have the knowledge and expertise to do our detective work!

Web references

w1 – An interactive map shows how the Black Death spread across Europe in a few short years. See: <http://tinyurl.com/o4hjh56>

w2 – The Education Portal discusses the microbiology of *Yersinia pestis*, including videos and quizzes. See: <http://tinyurl.com/p558467>

w3 – For more information from the Museum of London about plague in the city, visit <http://tinyurl.com/ngy8au4>

Resources

The game Plague Inc., developed in association with the Wellcome Trust, is a mix of strategy and realistic simulation available for mobiles and PCs. As a pathogen, you must continually evolve to become a global plague. See: www.ndemiccreations.com/en/22-plague-inc

Plague is a zoonotic infection, passed from animals to humans. You can find out more about how infectious agents can make the leap in issue 27 of *Science in School*.

Heymann J (2012) Evolving threats: Investigating new zoonotic infections. *Science in School* 27: 12-16.

www.scienceinschool.org/2013/issue27/zoonosis

If you enjoyed this article, you may like to browse the other biology-related articles in *Science in School*. See: www.scienceinschool/biology

Dr Kirsten Bos is a postdoctoral researcher at the University of Tübingen's Institute for Biological Archeology, where she researches the genetics of ancient diseases. Kirsten received her PhD from McMaster University in Canada for her work on investigating the genetics of the Black Death.



Image courtesy of Wellcome Library, London



A physician wearing a plague preventive costume



To learn how to use this code, see page 57.