

► *Medicine* on 2 October undercut a popular theory behind the outbreak — and underscored how far researchers still have to go to pinpoint its cause. (Y. M. Butt *et al.* *N. Engl. J. Med.* <http://doi.org/gf9f5c>; 2019).

Many of those who were made ill had vaped cartridges containing tetrahydrocannabinol (THC) — the active ingredient in marijuana — that had been diluted with oily chemicals.

Larsen's study is the largest analysis so far of lung tissue taken from affected vapers. The scientists searched for evidence of lipid pneumonia, a condition that arises when oil enters the lungs. It is marked by the presence of lipids in lung tissue and in cells called macrophages, which normally sweep up debris in the lungs. But Larsen and his colleagues did not find substantial lipid droplets in any of their samples from 17 patients. Instead, their findings point to general lung damage and inflammation caused by exposure to toxic chemicals.

There are reasons to be sceptical of those results, says Kevin Davidson, a pulmonologist at WakeMed, a hospital system based in Raleigh, North Carolina. Larsen looked for signs of disease that would be apparent only if someone had inhaled a large amount of oil all at once, he says, not small amounts over time.

#### DISEASE DETECTIVES

But Larsen's findings do align with mouse studies carried out by Farrah Kheradmand, a pulmonologist at Baylor College of Medicine in Houston, Texas (M. C. Madison *et al.* *J. Clin. Invest.* **129**, 4290–4304; 2019). Her team found lipids accumulating in the lung macrophages of mice exposed to e-cigarettes. The scientists traced the build-up to the breakdown of pulmonary surfactant, a lipid-rich compound

produced by the lungs. Kheradmand says this suggests that vaping damages cells that line airways and help to maintain surfactant levels.

She is now hoping to repeat her mouse studies using e-cigarette vapour that contains vitamin E acetate, an oily chemical that has been suggested as a cause of the vaping illness.

Other researchers are considering similar experiments. Steven Rowe, a pulmonologist at the University of Alabama, Birmingham, hopes to test suspected culprits using ferrets,

**“I could tell you something today and next week it could be totally wrong.”**

Health in Boston, Massachusetts, is planning an experiment to see which genes are switched on or off in lung cells taken from vapers. He hopes to get tissue samples from those who have become ill.

But Kheradmand cautions against hoping for quick answers: her initial mouse study took three and a half years to complete.

“Science will win at some point,” says Albert Rizzo, chief medical officer at the American Lung Association in Chicago, Illinois. “But I don’t think it’s going to be as soon as people would like.”

More immediately, researchers are scrambling to categorize the chemicals contained in e-cigarettes. That is no simple task when there are thousands of products available, and a culture of users modifying e-cigarettes and their contents to change characteristics such as flavour or amount of vapour produced. “This is a tough nut to crack, to be

honest,” says Larsen. “And that’s where the research really needs to go: figuring out what the contents are in all of these things.”

The range of chemicals that vapers are exposed to is dazzling, says Mignonne Guy, a biobehavioural researcher at Virginia Commonwealth University in Richmond. Her laboratory has studied YouTube videos and other online sources to learn more about how e-cigarette users are modifying their devices. They found that vapers are altering everything from how hot their e-cigarettes get to what chemicals are included in vaping cartridges — including, in at least one instance, liquid Viagra.

Online forums have pointed computational epidemiologist Yulin Hswen towards an early-2019 spike in posts about how to make e-cigarette cartridges. This was soon followed by an increase in posts from users warning about black-market cartridges being sold with branding that could mislead the purchaser into thinking they were made by a reputable company. Hswen, who works at the Harvard School of Public Health in Boston, Massachusetts, plans to look into this more closely to see whether this spike in homebrew cartridges could have contributed to the outbreak.

Ultimately, researchers might never be able to track down a single cause for the outbreak, says David Christiani, a pulmonologist at Harvard’s public-health school. But even just narrowing it down to a process — such as using oils to dilute THC — could help to squelch the current epidemic and save lives. “We have a very serious epidemic and we absolutely need to get that under control,” he says. “Then that will allow us to go back to focusing on chronic effects of vaping.” ■

#### ARCHAEOLOGY

# Bronze Age DNA hints at roots of social inequality

*Family trees gleaned from ancient human genomes are set to transform archaeology.*

BY EWEN CALLAWAY

In a first-of-its-kind study, scientists have used DNA to reconstruct the family trees of dozens of individuals who lived in a small German valley around 4,000 years ago.

The genealogies point to social inequality within individual households, which encompassed both high-status family members and unrelated, low-status individuals — possibly servants or even slaves — as well as mysterious foreign females related to no one else (A. Mittnik

*et al.* *Science* <http://doi.org/gf9rmr>; 2019).

Such insights could never have been made without using ancient DNA, says Philipp Stockhammer, an archaeologist at the Ludwig Maximilian University of Munich in Germany, who co-led the study. “For me, this is the future of archaeology,” he says. “We are now forced to see social inequality and complexity on a completely different scale, that we haven’t taken into account for the deep past.”

During the Bronze Age, the Lech River Valley in southern Bavaria was packed with

small farmsteads, each with its own cemetery. Archaeological excavations in the 1980s and 1990s uncovered dozens of skeletons dating to between about 2800 and 1700 BC.

Grave goods from these burials, such as daggers, arrowheads and ornaments, suggest that many Lech Valley inhabitants were well off, although the region lacks the mound-like ‘princely graves’ found elsewhere in Bronze Age Europe. Those often contain huge gold artefacts and show evidence of a social elite, archaeologists say.

K. MASSY

To better understand the social structure of the Lech Valley, Stockhammer and Johannes Krause, at the Max Planck Institute for the Science of Human History (MPI-SHH) in Jena, Germany, and their team sequenced DNA from 104 individuals from 13 farmstead cemeteries. They constructed six family trees, which encompassed as many as five generations.

Nearly all first- and second-degree relationships the team uncovered were between individuals from the same farmstead; a few, more distant relations were found in different hamlets. These close family members, either male or female, tended to be buried alongside ample stashes of grave goods, suggesting high status was inherited. Cemeteries contained two other groups of individuals who were unrelated to any family members: people with poorly furnished graves, and high-status females.

It is impossible to say whether the low-status individuals represent servants, farm workers or slaves, according to the authors. But the social structures of the Lech Valley are reminiscent of those in ancient Greece and Rome, where slaves were considered members of the family unit.

The role of the high-status females is even more enigmatic. These women, who were buried with ornaments and jewellery similar to those of the female family members, grew up hundreds of kilometres away, Stockhammer says: the levels of strontium isotopes in their teeth, which vary with local geochemistry, are unlike those present in southern Germany. These women showed levels more similar to those found in eastern Germany and the Czech Republic.

But no children of theirs were found in the Lech Valley graves. One possibility is that females travelled hundreds of kilometres to the Lech Valley as part of alliances between wealthy families, and that any children were then returned to their mothers' native lands. The grave goods of some of the foreign



This ornate pin from the grave of a woman in Königsbrunn, Germany, suggests she had high social status.

females resemble those of the Únětice culture in the Czech Republic, Eastern Germany and Poland from around the same time.

#### WHO'S WHO

"It's a really, really beautiful paper," says Kristian Kristiansen, an archaeologist at the University of Gothenburg, Sweden. "I know we'll see more of this." In unpublished work, Kristiansen and his colleagues sequenced DNA from more than 100 individuals from southern Germany and built family trees from the data.

"It does get to the heart of what archaeologists have been trying to do. They spend a lot of time working out who's related to who in cemeteries," says evolutionary geneticist Krishna Veeramah at Stony Brook University in New York. But he notes that few archaeologists

will have access to the approach until sequencing costs come down.

The study marks a shift in how ancient genomics has been applied to archaeology, say Kristiansen and others. Many earlier studies — especially of Bronze Age Europe — sampled large numbers of unrelated individuals spread across dozens of sites in multiple countries. Many studies went on to document profound shifts in the genetic make-up of a region's inhabitants, to the chagrin of many archaeologists who tend to focus on local change and the lives of individuals.

"Instead of talking about a spread of an ancestry, we're really getting deep into the living history of these people," says Alissa Mittnik, a geneticist at MPI-SHH and Harvard Medical School in Boston, Massachusetts, who co-led the *Science* study. She hopes that shifts identified in earlier studies can be explained in more depth. For instance, her team reports that nearly all the women in the Lech Valley had moved away from their families — potentially spreading new cultural practices.

And as the number of sequenced ancient human genomes swells into the thousands, researchers will be able to build even bigger ancient family trees and identify distant relatives, just as customers of consumer-genetics firms such as 23andMe and Ancestry.com do today. Some of the individuals studied by Stockhammer, Mittnik and their collaborators turned out to be related to two other Lech Valley inhabitants whose genomes were sequenced as part of a 2015 study of 101 ancient humans (M. E. Allentoft *et al.* *Nature* **522**, 167–172; 2015). They were from a nearby burial, but, with luck, more distant connections will emerge, Mittnik says. "One day we'll find where these foreign women in the Lech Valley came from. That would be amazing." ■

ABK SÜD



Isotopic analysis revealed that this woman found near Kleinaitingen, Germany, grew up in a distant land.