



MICROBIOLOGY

Microbe outbreak panics Europe

Spread of rare Escherichia coli strain raises questions over surveillance of infectious diseases.

BY MARIAN TURNER IN MUNICH

Confronted with what has become one of the world's most severe outbreaks of *Escherichia coli*, physicians and scientists in Germany say that the country's fractured health-management system has failed to handle the crisis properly. They are calling for major reforms so that outbreaks are reported sooner and more modern technology is used to help identify their source, in order to bring health emergencies under control more quickly.

During the past month, a strain of enterohaemorrhagic *E. coli* (EHEC) has infected more than 2,400 people in 13 countries across Europe, killing 23 (see 'A killer strain'). Public-health experts — scattered across many state and federal ministries for health, agriculture and consumer protection — are still trying to pin down where the bacterium came from and why it causes such severe symptoms.

Hospitals recorded the first cases on 1 May, according to the Robert Koch Institute (RKI), the German federal agency for disease surveillance in Berlin. Yet it was not until 22 May that

the first report of an unusual number of EHEC infections in Germany arrived at the European Centre for Disease Prevention and Control in Stockholm. This was unusually long — it typically takes 14 days to detect an outbreak, says Angelika Fruth from the RKI.

Several factors conspired to cause the delay. EHEC infections are not common in adults — so physicians might have initially diagnosed a *Salmonella* or viral infection. The microbe also behaves differently to typical EHEC strains when cultured for diagnosis, which hampered scientists trying to identify it. And under the German health system, local authorities only report such infections weekly to state governments — which then have another week to tell the RKI. It was not until 25 May that the rare *E. coli* strain O104:H4 was named as the culprit.

The strain produces proteins that help it stick to food, and to the human gut. This might explain why symptoms seem more severe than in previous *E. coli* outbreaks, including bloody diarrhoea and, in almost one-third of patients, haemolytic uraemic syndrome (HUS), which can cause kidney failure, neurological

complications and death. Indeed, so many patients have developed HUS that German physicians have treated more than 200 people with the antibody eculizumab, which had previously only been used to treat three infection-related cases of the syndrome.

Despite all the obstacles, the outbreak could have been identified earlier, says Flemming Scheutz, head of the World Health Organization Collaborative Centre for Reference and Research on *Escherichia* and *Klebsiella* in Copenhagen. The polymerase chain reaction (PCR) could have been used to amplify the microbe's genes, he says, enabling scientists to identify it in hours rather than the days it took to culture and test bacteria from patients' stool samples. "PCR testing for bacteria is already in routine use in livestock and food, and hospitals already have the technical platforms to do PCR," says Scheutz, "but these tests just aren't used regularly in people."

Fruth agrees that a PCR protocol would be highly desirable. However, even though it is as cheap as culture-based techniques, it is not funded as a standard test for cases of diarrhoea by the German health-care system, she notes.

Faster reporting would also help next time there is an outbreak. The US Centers for Disease Control and Prevention (CDC) in Atlanta, Georgia, introduced a rapid-surveillance platform called PulseNet following an outbreak of a different EHEC strain, called O157:H7, in 1993. The system rapidly compares the molecular fingerprints of suspected bacterial infections in food or humans with those of known pathogens. The results are uploaded to a national database, which allows real-time tracking of the infection clusters in an outbreak.

Epidemiologist Christopher Braden from the CDC says that the number of recognized US outbreaks has now doubled thanks to PulseNet, often leading to earlier identification of problems in food production. Europe does not have a similar real-time tracking system, although Denis Coulombier of the European Centre for Disease Prevention and Control says that the existing European surveillance system has worked reasonably well during this outbreak. Moreover, PulseNet might have overlooked the unusual O104:H4 strain, because there is no definitive list of the *E. coli* strains that represent a threat to human health. "We need a constellation of genes, including those for strain markers and toxins, that could be used to identify dangerous bacteria," says Glenn Morris, director of the Emerging Pathogens Institute at the University of Florida in Gainesville.

Comparing the genome of O104:H4 with that of other pathogenic *E. coli* strains should reveal similarities and differences that will be useful in diagnosing future infections. Alexander Kekulé, a microbiologist at the Martin Luther University of Halle-Wittenburg in Halle, Germany, hopes politicians will learn from the outbreak too, and establish a long-overdue national authority for controlling outbreaks. ■