Unsolved Mysteries

BERNARD DIXON

"The hand of the Lord was against the city with a very great destruction: and he smote the men of the city, both small and great, and they had emerods in their secret parts" (1 Samuel 5:9).

What on earth was going on here? An outbreak of hemorrhoids? Venereal disease? Biblical citations are not exactly thick on the ground at scientific meetings, but these were the quotes with which veteran microbiologist Chris Collins opened part of the Society for Applied Bacteriology's Summer Conference in Nottingham last month. The session ranged over several "old plagues," including several of disputed identity. It also prompted suggestions that the polymerase chain reaction (PCR), now widely famed for the fact and fantasy of amplifying human and other DNA from ancient bones, might also be used to retrieve microbial DNA and thus learn something about infections in the mists of history. After *Jurassic Park*, the Black Death?

There are certainly many epidemiological riddles to which it would be nice to have answers. Was the bubonic plague of history really what we believe it to have been—the well-defined condition caused by *Yersinia pestis*? Were Roland Rosquist and colleagues at the Swedish Defense Research Establishment, Umea, correct in arguing (*Nature* **334**:522, 1988) that single point mutations produced, from less virulent *Y. pestis*, the hypervirulent strains that triggered the great epidemics? What of Graham Twigg's theory, in his book *The Black Death—A Biological Reappraisal* (Schocken Books, 1985), that the Black Death was a major epidemic not of plague but of anthrax?

Then there is the puzzle of the Sweating Sickness or English Sweat. Affecting the rich rather than the poor, this first broke out around the time of the battle of Bosworth in the English midlands in 1485, spread quickly to London, and then caused further epidemics in 1508, 1517, and 1528 before making its last appearance in 1551. After that date, all references to the disease simply disappeared. Medical historians have suggested that the Sweating Sickness was in fact influenza, but this is hard to accept because while some symptoms can be recognized in common between the two conditions, the Sweating Sickness did not seem to affect the respiratory tract.

It has, of course, become successively easier, as the twentieth century has unfolded, to determine the real causes of earlier, hitherto unexplained outbreaks of disease. Thus the investigators of what became known as Legionnaires' disease at the Bellevue-Stratford Hotel, Philadelphia, in July 1976 were later able to test samples of blood preserved from the victims of Pontiac fever nine years earlier, and show that most of those patients had also developed rising levels of antibodies against *Legionella pneumophila*.

But what are the prospects of applying PCR to the study of pathogens from previous centuries? As with animal cells, the question hinges largely on finding microbial DNA that has not been denatured and which therefore still contains meaningful coding sequences. It's a fanciful idea at first, but on reflection the possibility of retrieving such material seems more plausible than might be imagined.

Viruses can be maintained indefinitely, like chemicals, on a laboratory shelf. There seems every reason to suppose, therefore, that some viruses of past times may have persisted in, for example, permafrost or desiccated burial vaults. The prospect of viable organisms being released from such sites was taken very seriously by the World Health Organization during the smallpox eradication campaign of the 1970s, when Peter Razzell of Bedford College, London, writing in *New Scientist* (**71**:35, 1976), drew attention to an eighteenth century smallpox outbreak apparently triggered by the disinterring of a smallpox victim buried 30 years earlier.

Writing in *The Lancet* (**2**:1454, 1984), Arie Zuckerman of the London School of Hygiene and Tropical Medicine argued that the risk of smallpox reappearing in this way was small, as was the danger for archeologists handling incompletely decomposed bodies. But the remote possibility remains, while Peter Lewin of the Hospital for Sick Children, Toronto, has drawn attention (*JAMA* **253**:3095, 1985) to the likelihood that viable smallpox virus and other pathogens have been preserved in the graves of people buried in the Arctic over the past 150 years.

Sporing bacteria too are notoriously hardy, as illustrated by the survival of *Bacillus anthracis* in the soil of Gruinard, off the west coast of Scotland, decades after the organism was released there in biological warfare experiments during 1942-43, until the island was decontaminated a few years ago. A variety of other organisms, including *Mycobacterium tuberculosis*, with its lipid-rich cell wall, can survive for long periods even in nonideal conditions. Finally, there are prion and related diseases whose coded information is integrated into human and other animal genomes. Their agents, or fragments of them, may have survived in bones that are already being examined using PCR.

Retrieving valuable microbes, or even whole genomes, preserved over centuries is an undertaking as remote as that of cloning *Tyrannosaurus rex*. But I'll bet there is sufficient ancient microbial DNA around to use to learn *some* things about the plagues and pestilences of times past. ///