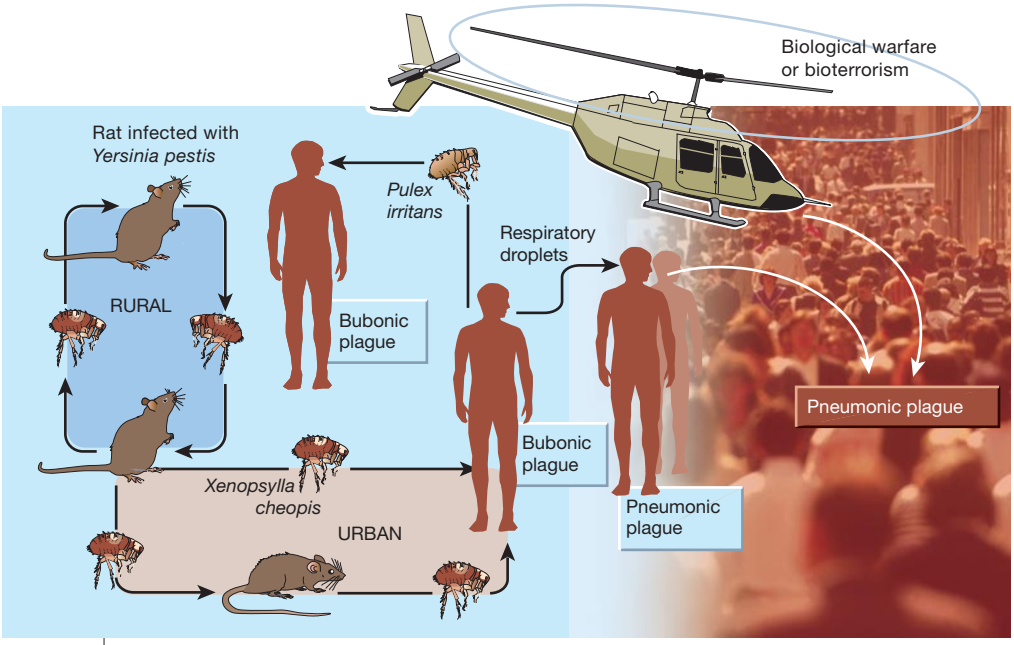

Figure 1 **How the plague is transmitted. The causative organism, the bacterium *Yersinia pestis*, has a rodent reservoir. The rodents' fleas, such as the oriental rat flea, *Xenopsylla cheopis*, acquire *Y. pestis* from a meal of infected blood, and transmit the bacterium primarily to other rodents or to humans, causing bubonic plague in people. Human-to-human transmission can also take place, through the human flea *Pulex irritans*. Pneumonic plague is less frequent but even more severe; it is transmitted from person to person through respiratory droplets, or even by artificially generated aerosols, containing *Y. pestis*.**

ing to bubonic plague. If the lymphatic system becomes overwhelmed, widespread dissemination and rapidly fatal blood poisoning result, with the bacterium spreading to all the main organs including the lungs. The disease then spreads in the air in droplets, culminating in highly contagious pneumonic plague, which can bring death in under three days. These properties make *Y. pestis* one of the most feared agents of biological warfare or bioterrorism.

Yersinia pestis is what's known as a bacillus — it is rod-shaped — and it belongs to a group of bacteria called the Enterobacteriaceae. Most of these bacteria are associated with animals and humans, and many are harmless. So what made *Y. pestis* such an aggressive pathogen and how, uniquely for this group, did it adapt to life in a blood-sucking insect? Parkhill *et al.*'s analysis[1] of the complete genome sequence of C092 — a *Y. pestis* strain isolated recently from a person who died of pneumonic plague — provides some fascinating answers.

The genome comprises a chromosome of 4.65 million base pairs, as well as three plasmids (circular DNA molecules) of some 96, 70 and 9.6 kilobases. As Parkhill *et al.* discover, this genome displays unusual fluidity: there is compelling evidence for the inversion of chromosomal segments and for gene acquisition and decay. Repeated sequences are abundant (making up about 3.7% of the total) and, as in the leprosy bacillus, these serve as sites for 'homologous recombination' events, which remodel the genome[3].

By investigating the bias towards guanosine and cytosine nucleotides (the G/C skew)[4] in different parts of the genome — a genomic parameter that highlights compositional irregularities — the authors detected three unusually large segments that had inverted or translocated. Analysis of the inversion endpoints indicated that both possible orientations could be found, in unequal proportions, in C092 samples, as well as in other strains, implying that several different chromosomal configurations can exist within the same population. As the expression of bacterial genes is influenced by their orientation with respect to the direction of DNA replication[5], this raises the possibility that differences in strain virulence could stem from differences in genome arrangement.

Using the G/C skew and other bioinformatics tools, Parkhill *et al.* also identified 21 regions of the chromosome that show characteristics of pathogenicity or adaptation islands, probably acquired from other organisms through horizontal transfer. These islands reflect the twin hosts of *Y. pestis*. They code not only for molecules implicated in infecting mammalian cells — such as adhesin proteins, two new siderophores (iron chelators), and secretion systems — but also for functions that might enable *Y. pestis* to colonize, and transit through, fleas. For example, several genes encode potential insecticides, and a baculoviral-like enhancin protein, that could damage the insect midgut. As in gastrointestinal pathogens, genes that code for factors involved in virulence are either chromoso-

ROBERT HARDING

100 YEARS AGO

There is only one class of zoologist that I would wish to blot out, and that is the class whose reckless naming of new "species" and "varieties" serves only to extend the work and the tables of the conscientious synonymy hunter. Other than this all classes will contribute to the advancement of the science. No doubt there are unlabled [*sic*] species and no doubt they must, as things are, be named. And no doubt genera and families must be "revised" and some groups split up and others lumped. So welcome to the old-fashioned systematist, though his day be short, and may he treat established genera gently. No doubt there are types of animals of whose structure we are woefully ignorant; no doubt we need to know their internal anatomy in great details. So welcome to the zootomist in this new century, and may he invent fewer long names for new organs. No doubt there are groups of whose relationships we know little, and which have been buffeted about from one class to another in a bewildering way. We need to have their places fixed. So welcome to the comparative anatomist and the embryologist, and may their judgment as to the relative value of the criteria of homology grow clearer. No doubt our knowledge of inheritance and development will be immensely advanced by the further study of centrosomes, asters and chromosomes. Welcome, therefore, to the cytologist, and may he learn to distinguish coagulation products and plasmolytic changes from natural structures. All these subjects have victories in store for them in the new century. To neglect them is to neglect the foundations of zoology.
From *Nature* 3 October 1901.

50 YEARS AGO

No scientific survey, however, would be complete without a visit to Sprotborough, near Doncaster, for here was Sprotborough Hall, the home of Sir Godfrey Copley, Bart. (d. 1709), who by his will left £100 to the Royal Society for "improving natural knowledge"… His £100 was allowed to lie idle for some time, but awards were made in 1731, 1732 and 1736, and then the money was used to found the Copley Gold Medal, now the oldest and most famous of prizes in the world of science… In 1749 the Medal was given to John Harrison, a native of Wragby, near Wakefield, for his "Curious Instruments invented and made by him for the exact Mensuration of Time".
From *Nature* 6 October 1951.