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EDITORIAL

Year's comments for 2001

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In December 2000, our year's comments focused mainly on advances in genomics, and these have kept pace also throughout 2001. In early 2001, news related to microbiology were frequent in the media, especially in Europe: both bovine spongiform encephalopathy and foot-and-mouth disease (known also as aphthous fever) spread over the continent. It was especially after the events of September 11, however, that microbiology became one of the hottest issues in the mass media around the world. This was so not because of scientific achievements nor because of infectious natural outbreaks, but rather for political reasons.

Biological weapons are indeed a threat that cannot be overlooked. Nevertheless, they are not new in human history and surely they are not more threatening than most modern conventional weapons. Anthrax, the infectious disease caused by *Bacillus anthracis* and chosen by bioterrorists mainly in the United States, is not a new disease. In several countries, peoples involved in agriculture and animal husbandry have been acquainted with anthrax since remote times. *Carbunculus* was already mentioned in Saint Isidor's *Etymologiae* in the seventh century. (The current Spanish name for "anthrax" is *carbunco*, even if the mass media often call it *ántrax*. Curiously, in English there is also an illness called carbuncle, which is caused by *Staphylococcus aureus*. "Anthrax" means "coal" in Greek, and "carbunculus" is "small coal" in Latin.) Before the development of vaccines and antibiotics, anthrax was a threat to cattle, sheep, goats and horses, and for humans in contact with such animals. Nowadays, anthrax is still endemic in many regions in the world, and cases are recorded from time to time even in developed countries. Since *B. anthracis* endospores are viable in soil at least for several decades, eradication of the disease is very difficult. Direct human-to-human transmission is rare, and people usually become infected from close contact with infected animals or during the processing of animal products such as wool, hair, hides and bones. According to *Science* (Counterterrorism, 294: 761–763), in the United States, White House science adviser Jack Marburger gathered the Bush Administration's 19 top scientists on October 19 to discuss how their research programs could be coordinated to respond to bioterrorism. In addition, the National Academy of Sciences (NAS) and the National Science Foundation (NSF) have developed their own efforts to accommodate the government's plans regarding the new war situation. Experts in biological and chemical weapons from laboratories of the Department of Energy (DOE) are currently also working for intelligence and investigative agencies. In July 2001, the US Department of Defense (DOD) sent the Congress a report that highlighted the need for developing vaccines against potential bioweapons.

Bioterrorism, however, is not a threat that has arisen suddenly. Over the last few years experts have warned about the possibility of such a threat becoming real. The way in which the media have dealt with this topic may have resulted in public opinion being divided into those people that are scared of a possible pandemia, worse than the ones that have reduced human populations throughout history, and those people who think that the threat was an invention of the sensationalist media.

Genomics was the star scientific field in February. The International Human Genome Sequencing Consortium (made up by 20 groups from six countries) and Celera Genomics published simultaneously – the former in *Nature* (15 Februrary), the latter in *Science* (16 February) – their draft sequences of the human genome, which were generated from a physical map covering about 94% of it. The work published provided a global perspective of the human genome, revealing some surprising features such as the number of protein-coding genes, which turned out to be only about twice as many as in *Coenorhabditis* or *Drosophila*; the higher rate of mutations in males (about two-fold); and the much more frequent segment-duplication in humans than in yeast, fruitfly or worm. It was also surprising to learn that only 94 of 1,278 protein families in the human genome appear to be specific to vertebrates, and that some human genes might have come directly from bacteria. The sequencing

of microoganisms has continued, and those sequenced in 2001 include *Caulobacter crescentus*, *Escherichia coli* O157:H7, *Lactococcus lactis*, *Lysteria monocitogenes*, *L. innocua*, *Mycobacterium leprae*, *Mycoplasma pulmonis*, *Pasteurella multocida*, *Rickettsia conorii*, *Salmonella enterica* serovar Typhi CT18,*Streptococcus pneumoniae*, and *Sulfolobus solfataricus*.

Plague– which was first known as the Great Pestilence and later as the Black Death– is one of the four horsemen of the apocalypse, along with hunger, death and war. For centuries humans feared this disease, and this fear was indeed justified: the three known plague pandemics killed a total of more than 200 million people. During the pandemic that spread from southern China in 1894, Alexander Yersin discovered the causative agent of plague, the gram-negative bacterium *Yersinia pestis*. Later, its life cycle, which involves a mammalian reservoir and an insect vector, was also described. Nowadays plague is no longer a threat for humans; however, in contrast to other infectious diseases, its almost complete disappearance cannot be attributed only to antibiotics. In fact, before the discovery of antibiotics, this disease seemed to have already lost its extreme virulence. Thus, one may wonder if deciphering the genome of *Y. pestis* is worthy of the efforts of a team of more than 30 researchers (Parkill et al. *Nature* 413:523–527). The discovery of *Y. pestis* strains resistant to multiple drugs and the bacterium's easy dissemination in the air in droplets that can produce a highly contagious– and fatal in most cases– pneumonic plague make it a feared potential biological weapon. In addition, *Y. pestis* is a member of the Enterobacteriaceae, a group of bacteria associated with humans and other animals. As most Enterobacteriaceae are harmless, the knowledge of *Y. pestis* genome provides some clues as to its pathogenicity.

Salmonella enterica (*S. typhi*) Typhi CT18 is a multi-drug-resistant serovar of the causal agent of typhoid fever, a serious human disease that still kills around 600,000 people annually. More than 200 pseudogenes have been identified, of which several correspond to genes that are known to contribute to virulence in *Salmonella typhimurium*. In addition, serovar CT18 hosts a multi-drug-resistant plasmid, and another plasmid which shows some relationship with a virulence plasmid of *Y. pestis*.

The threat of biological war and bioterrorism has cast a shadow over other scientific news, even the announcement of the Nobel awards, which this year celebrated their first centenary. Microorganisms were the subject of the Nobel Prize for Physiology or Medicine. On October 8, the Nobel Foundation announced that Leland H. Hartwell, R. Timothy Hunt and Paul M. Nurse were the recipients of the award for their discoveries of "the regulators of the cell cycle." Leland Hartwell, discoverer of a specific class of genes that control the cell cycle in eukaryotes, used *Saccharomyces cerevisiae* as a model for his studies. It all started when he assigned a new project to his undergraduate student, Brian Reid, in his laboratory at the University of Washington, Seattle. Hartwell had found mutant yeast strains that, when grown at high temperatures, formed very odd shapes. The reason for such strange shapes were mutations that disrupted the cell cycle. By 1970–1971, his team had identified more than 100 genes that were implicated in the control of the cell cycle. These genes are known as *cdc* (cell division cycle) genes. Hartwell also studied the sensitivity of yeast cells to irradiation and defined the checkpoint phenomenon, which is the pausing of the cell cycle when DNA is damaged, so that it can be repaired before the cell cycle proceeds to the next step. In the meantime, Paul Nurse, who was a young researcher completing his undergraduate studies in the United Kingdom, read Hartwell's papers and became interested in this subject. As a young postdoctoral assistant at the University of Edinburgh, he carried out research in *Schizosaccharomyces pombe*, in which, in addition to characterizing other *cdc* genes, he identified so-called wee mutations which both promoted early mitosis and turned out to be the cause of malformation in affected yeast strains. When Nurse identified one of those *wee* genes as being a *cdc* mutant he had isolated previously– *cdc2* – it became clear that it must be involved in the control of the beginning of mitosis. In pursuing this research, Nurse and his team discovered that the *cdc2* gene was almost identical to the *cdc28* gene identified by Hartwell in *S. cerevisiae* and that it codes for a kinase.

Today, scientific developments have become part of people's general interests because of a growing awareness of the implications that science has for their everyday lives. This is especially the case for issues pertaining to human/animal health and the environment, which will continue to be important in the years to come. Therefore, it is the responsibility of both those who are involved in the advancement of science (scientists) and those whose job it is to disseminate science-related information (scientists and journalists) to contribute to a better, clearer, and deeper understanding of scientific work.

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