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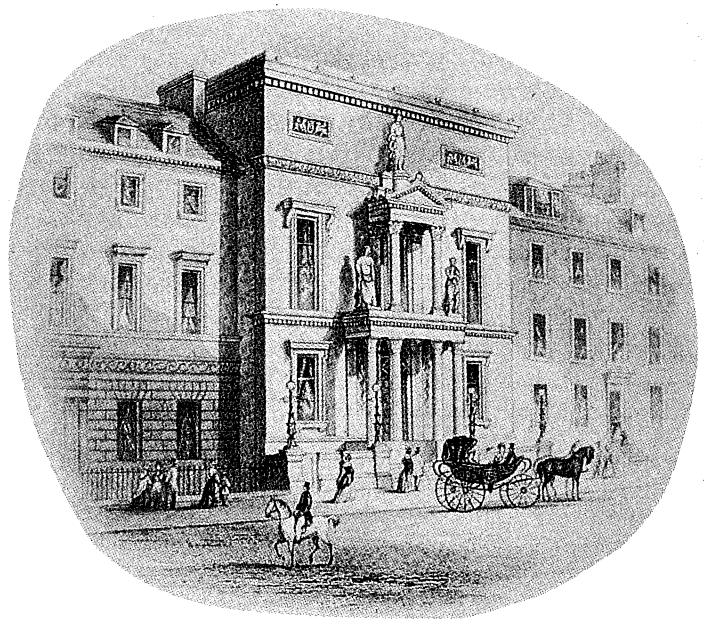

One hundred and fifty years ago: The Physician's Hall in Queen Street shortly after its opening on November 27, 1846.
Engraving by W. H. Lizars

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Book of the Quarter

THE COMING PLAGUE: NEWLY EMERGING DISEASES IN A WORLD OUT OF BALANCE

L. Garrett, Virago Press, 1995 pp 750 £20.00

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This book by a former fellow of the Harvard School of Public Health challenges the complacency of every politician and health professional. It is accepted that scientific progress over the last century has brought standards of material well-being unimagined in earlier times. Every dimension of life—health, physical security, economic and educational opportunity appears to have been transformed for the better, at least in Western societies. But things are not quite as we would like to believe. *The Coming Plague* in 622 pages of text and over 100 pages of detailed notes and references, is an attempt to identify emerging diseases in a world out of balance as a result of less successful aspects of our rapidly developing societies. It is both fascinating and terrifying. The thesis is that the world has become vulnerable to outbreaks and spread of both old and new infectious diseases and the author assesses the major factors that have contributed to this state.

Population movement
A major cause of the imbalance referred to in the title is the dramatic increase in worldwide movement of people, both refugees and tourists. Between 1980 and 1989 'the number of refugees fleeing from natural disasters, wars, famine, or oppression increased by 75 per cent every year'. According to the United Nations there were 17·5 million refugees by 1992, most of them living in squalor in the world's poorest countries. The author notes that 'millions of abandoned children roam the streets of the world's largest cities, injecting drugs, practising prostitution, and living on the most dangerous margins of society . . . . Studies demonstrate the rapid spread of disease among refugees and the emergence of antibiotic-resistant bacteria and drug-resistant parasites in such clusters of humanity'. Another indicator of population movement that can lead to the spread of infectious agents is illustrated by the dramatic increase in commercial air travel. Few areas of the globe remain isolated, and insects and infectious agents can be carried into previously unaffected environments. Between 1950 and 1990 the number of passengers aboard international commercial air flights has soared from 2 million to 280 million and the numbers are estimated to increase to around 600 million by the year 2000.

Urbanisation
Urbanisation has provided a setting, particularly in the poorer countries, in which poor hygiene and overcrowding give easy opportunities for infectious agents to spread from person to person. Once microbes reach new locales, increasing human population and urbanisation ensures that even relatively poorly transmiss-

ible microbes are more likely to be spread from person to person. Accounts going back 2,000 to 4,000 years tell of scourges carried by lice, fleas and ticks—all diseases that the writers noted were abundant in the dense housing conditions of cities. On the basis of historical accounts from Greece, Rome, Europe and the pre-Columbian Americas, twentieth century scholars have tried to interpret which diseases affected ancient urban centres. During the Peloponnesian War of 430 B.C. a devastating epidemic killed up to half the population of Athens. The disease, later thought to have been the plague, typhus or smallpox was probably imported by returning soldiers. Thucydides said of it, 'no scourge so destructive of human life is anywhere on record. The physicians had to treat it without knowing its nature, and it was among them that the greatest mortality occurred'.

The world has experienced at least two great panedmics of bubonic/pneumonic plague in the last millenium. *Yersinia pestis* carried by rat fleas enters the human bloodstream after flea or rat bites or by inhalation of the microbe. When it enters the lymphatic system it kills massive numbers of cells, giving rise to grotesque buboes and pus-filled boils. The book documents the spread of the bacteria to various organs including the brain. During the Middle Ages, the demented behaviour of these patients was interpreted as intervention by Satan. Chinese records dating back to 243 B.C. also noted massive epidemics claiming millions of lives. The Black Death was believed to be responsible for reducing the Chinese population from 123 million in 1200 A.D. to 65 million in 1393. As the plague made its way to India, Europe and North Africa, each city anticipated its arrival and tried to protect itself. Travellers were barred entry, drawbridges were raised. Great purges and outright slaughter of tens of thousands of Jews and alleged devil worshippers were staged. The death rates were staggering in cities throughout Europe. London with a pre-plague population of 60,000 lost 35,000 of its inhabitants. Another oubreak occurred in London in 1665, when a *Yersinia* epidemic claimed 100,000 lives within a year.

According to the World Bank, African cities were increasing in size by 10 per cent a year throughout the 1970s and 1980s, constituting the most rapid proportional urbanisation in world history. By the year 2000 urban growth is predicted to increase to a population of 3·1 billion crammed into 24 megacities, most of them located in the world's poorest countries. By the mid-1980s, 100 million homeless adults were reduced to roam the streets of developing-world cities. Half the city dwellers of developing countries who are not classified as homeless lived in shantytowns and slums that lacked safe drinking water; 40 per cent were without public sanitation or sewage and a third without garbage or solid waste collection.

Carriage of dangerous viruses between continents

A dramatic example is the 1967 outbreak of Marburg virus infection in a vaccine-producing subsidiary of Hoechst AG in Marburg, Germany. 'The thirty one cases struck terror in European research circles because of the ferocity of the disease and its spread from patients to their health care providers. Nobody knew what caused the ailment, how it was spread, what treatments might be effective, and/or how many more people might eventually be stricken'. The disease started with flu-like symptoms then enlarged spleens, leucopenia and clotting defects occured. By day 6, patients were covered with a sensitive red rash and had sore throats and diarrhoea. By day 8, capillary networks were blocked and the red blood cells

immobilised giving the patients a crimson glow; and by the tenth day patients were vomiting blood. At three weeks, the skin peeled off as oxygen and nutrient starved cells died by the millions. The patients were soon bleeding to death with blood pouring from all orifices.

All the original cases in Germany and Yugoslavia involved men who had worked with monkeys that had originated from Uganda and had been transported from there to Belgrade and then onto Marburg and Frankfurt. Despite intensive investigations over a number of years, no disease reservoir was found. Experimental infection of Old World primates proved invariably fatal, yet it was clear that many, if not most, monkeys that were infected in the wild survived. All that could be concluded was that the Marburg outbreak arose from monkey cells and that the virus originated somewhere in the geographic space spanning thousands of miles from Nairobi to Cape Town. It seemed inconceivable that late twentieth century medical science was incapable of solving this mystery but we still have no answer.

The movement of viruses between species has become an increasing cause for concern. Examples of this which have emerged in various parts of the world are described in dramatic detail: Ebola in Africa; PVD-2; Muchupo; Lassa and swine flu virus infections. Viruses of the Herpes group found in spider monkeys harmlessly infecting virtually 100 per cent of the host species were found to be potent cancer-causing viruses in other monkey species, infecting cells of the immune system causing lymphomas and leukaemias with approaching 100 per cent lethality. Experimental infection of rabbits was lethal, and the viruses were found to be transmitted by the airborne route. Laboratory analysis of one of these viruses (*Herpes saimiri*) revealed such an astonishing rate of mutation and gene swapping, that it was impossible to recover the original strain from infected cells. A herpes virus, designated B virus, infects about 10 per cent of all imported rhesus monkeys. From the time of its discovery in 1975 until 1989, twenty-eight animal handlers had contracted B virus infection and 25 developed encephalitis. Only five humans have ever survived B virus infection.

Environmental changes

In 1992 WHO reviewed the available data on the expected health effects of global warming and pollution and the results were not what one might want to hear. There was compelling evidence of increased human susceptibility to infectious diseases due to radiation damage to the immune system and pollutant impacts on the lungs and immune system. The agency was similarly concerned with estimates of current and projected changes in the ecology of disease vectors, particularly insects. Arbovirus researchers at Yale predicted that global warming would allow mosquito species to spread northwards, invading population centres such as Tokyo, Rome and New York. The Asian tiger mosquito could carry the dengue virus, and other mosquitos both dengue and yellow fever. British experts thought that global warming would greatly expand the territory and infectivity ratio of the East African tsetse fly carrying the trypanosomes responsible for sleeping sickness. The same conclusion could also be drawn for malaria. A WHO task group in 1990 suggested that even a 1 degree C temperature increase due to altered wind patterns, changes in levels of relative humidity and rainfall would alter the ecology of microbes carried by insects and animals such as monkeys, rats, mice and bats, and would bring these vectors closer to man.

Mutation of microorganisms

The book contains detailed examples of problems relating to viral and bacterial mutation. The human immunodeficiency virus (HIV), an RNA virus, was estimated to make a significant mutational change in one out of every 1000 viral replications, so that the essentially labile nature of the virus made its future incalculable. RNA viruses evolve extremely rapidly and it is probably more correct to refer to them as 'consensus sequences' rather than species. Such rates of mutation are so high that RNA virus populations are pools of genetic concoctions, some particular form of which might dominate at any particular time.

Mutations are most likely among infectious microbes inside severely infected individuals whose immune system is unable to control their replication. As populations swell, there are greater opportunities for both viral spread and mutation. Many microorganisms evade the immune response by changing the antigens on their surface. HIV, influenza, polio, schistosomes, *Plasmodium falciparum* and staphylococci all have hypervariable mutation sites that code for such surface proteins.

Such is the mutability of these viruses that the question posed by Fields of Harvard is of more than academic interest. He asks why have viruses not wiped out all life on earth: he points out that the answer lies in the difference between studying viruses in test tubes and studying them in animals or humans. In the real world, those mutants still had to deliver their genetic payloads to the proper types of cells inside an animal or person and that necessary leap proves too great an obstacle for most mutant microbes. Laboratory evidence, nevertheless, continues to provide a more worrying picture. Researchers have found that many extremely divergent microbial species shared genetic signalling sites (operons), that with very minor mutation, conferred multiple antibiotic resistance on the organism. For example, seven Gram negative species (*Escherichia, Salmonella, Shigella, Klebsiella, Citrobacter, Hafnia* and *Enterobacter*) shared an operon (mar RAB) which, with a single point mutation, made the organisms resistant to tetracycline, chloramphenicol, norfloxacin, ampicillin and quinolones. Experiments showed that genetic recombination and resultant adaptive mutation could occur in the absence of bacterial reproduction. In other words, bacteria altered themselves not just through a process of random mutation, error prone reproduction that eventually yielded a surviving strain—the classic Darwinian view.

Garrett lists a number of the questions posed by the scientific community; what are the odds against a new pathogenic organism emerging, either as the result of recombination among other microbes or of large scale mutation? Is it likely that old well-understood microbes might mutate into more dangerous forms? She concludes that the number of unknowns involved in computing answers to these questions were 'so enormous that they prevented conclusive analysis'.

Virulence

The traditional view that all pathogenic microbes seek a state of moderate virulence, so that they did not kill off their hosts too rapidly, has been challenged by the contrast between two viral 'cousins'. HIV-2 in West Africa became markedly less virulent between 1981 and 1993, infecting fewer people and possibly causing less severe disease. HIV-1 seemed to be more transmissible over the same period and to cause a more rapidly developing disease. In 1994, HIV-1

was spreading at an extraordinary pace, and strains of the virus had recently emerged that seemed to be especially adapted to rapid spread by heterosexual transmission or intravenous injection. New thinking on virulence began to emerge suggesting that microbes would be extremely virulent if long term survival of the host was not important for the spread and survival of the microbial species. If population density increased, the microbes could afford to become more virulent as they were guaranteed greater exposure to secondary and tertiary victims. This theoretical view was supported by experimental work on studies of fig tree wasps and minute round worms that parasitized these insects. Virulence appeared to be related to wasp population size. A researcher at Harvard who had developed techniques for studying virulence genes concluded that many microbes stored virulence factors, just as they did resistance genes, on plasmids and transposons and expressed them when the time was ripe.

A major source of pressure influencing such gene expression is the host immune system. Microbes had to evolve escape mechanisms and so escape destruction, for example by disguising themselves by changing their surface antigens, hiding inside cells and manipulating chemicals of the immune system to set off false alarms. Immunocompromised individuals and those suffering from chronic malnutrition provide a potential breeding site for new or mutated microbes. Herd immunity resulting from successful vaccination programmes can result in an immune individual acting as a carrier, travelling to a geographic area where herd immunity is low or non-existent. In this new population an organism of relatively low virulence can cause an epidemic.

Diagnosis and containment

In 1989 the American Society of Tropical Medicine staged a war games scenario for some 800 experts gathered in Honolulu. The objective was to test the ability of the public health emergency system to respond to an emerging pandemic due to a mysterious microbe that appeared to be airborne, 100 per cent lethal and probably of viral origin. The scenario involved three mythical equatorial African countries in which an ethnically divided civil war was in progress, similar to that that developed later Rwanda. An epidemic developed among the refugees and before it was noticed, ailing individuals infected with a mysterious microbe similar to Ebola virus had travelled to the US, the Philippines, Thailand, Germany and neighbouring African countries. As readers no doubt have predicted the war game revealed an appalling state of non-readiness. There were no prepacked infectious disease hospitals anywhere in the United States or at WHO in Geneva that were ready to be airlifted into an epidemic area. Virtually no civilian hospitals in the US were equipped to handle a highly contagious, lethal microbe, either in patients or inside their laboratories and there was only one permanent maximum-containment facility inside the US Public Heath Service system. The military had no available expertise and only a limited supply of tropical disease vaccines, medicines and diagnostic equipment. It was pointed out that the WHO's infectious disease control efforts were running on a shoestring budget. In 1993 the WHO emergency fund to deal with outbreaks was $25,000, less than the cost of a secretary's salary.

Of the 1,000 members of the American Society of Tropical Medicine, the majority were retired or approaching retirement age. Neither America nor

Europe offered the required training in tropical medicine and epidemiology, and no ambitious junior scientist saw any future in the area.

It seems that little has been learned from this exercise as 7 years later there were continuing limitations in the mobilisation of control measures for infectious disease which can be reliably monitored and for which there are effective vaccines. The recent epidemic of meningococcal disease in northern Nigeria, reported to claim 3,500 lives, provides a striking example of the inability of community and international health services to deal with an emergency.

Later studies described by Garrett showed that there were serious weaknesses in the United States Centers for Disease Control (CDC) disease surveillance system, both national and international. Even diseases that were legally obliged to be reported by state authorities were going unreported. AIDS surveillance, in 1990 the best funded of CDC programmes, was under reported by a minimum of 20 per cent. In 1992 a survey of 23 state health department laboratories found that all but one had a hiring freeze, and in a dozen states, there was no qualified scientist on staff to monitor food safety. The situation outside the United States was even worse with major deficiencies in laboratory skills and equipment. Half of the laboratories could not diagnose yellow fever, 53 per cent could not diagnose Japanese encephalitis, 56 per cent could not identify hantaviruses, 59 per cent failed to diagnose Rift Valley fever, and 82 per cent missed California encephalitis. Virtually no laboratories had the necessary reagents to deal with Ebola, Marburg, Lassa or Machupo viruses. A former director of the CDC, Dr William Foege, pointed out that one trillion dollars are spent annually on weapons and that it would take two and a half billion dollars to save the lives of nine million of the fourteen million children who died in 1989. This is the amount spent each year in the US on cigarette advertising.

D. A. Henderson who led the successful campaign to eradicate smallpox said at a WHO meeting in Geneva in 1993 'there is a growing belief that mankind's well-being, and perhaps even our survival as a species, will depend on our ability to detect emerging diseases... . Where would we be today if HIV were to become an airborne pathogen? And what is there to say that a comparable infection might not do so in the future?' Other concerns, raised by researchers in the field, regarding the ease with which dangerous pathogens could be generated for use in germ warfare came to the forefront during the Gulf war.

Garrett also assesses the political problems involved in control of infection. The UN Charter proscribes it from doing anything that might be viewed as disrespecting national sovereignty. It cannot deploy a team of physicians to investigate an unusual disease in Rwanda any more easily than in Los Angeles or Paris. In the absence of global supervision, some governments have felt free to slaughter their own people, exterminate rival minorities and take away all social and medical facilities from them, and to deny the existence of disease. The global thinking that is perceived as essential to keep track of ecological disturbances and the emergence of dangerous microbes appeared to be of little interest to federal health bureaucracies in Washington, Paris or London.

Bureaucracy has been correctly defined as an administrative system in which the need or inclination to follow complex procedures impedes effective action. A comment of the UN secretary general, Boutros Boutros-Ghali, reflects the engendered disillusion 'The lesson I learned in Cairo still applies. The only way to deal with bureaucracies is with stealth and sudden violence'. Garrett concludes

that the human race seems equally complacent about blazing a path into a rain forest with bulldozers and arson or using an antibiotic scorched earth policy to deal with unwanted microbes. In both macro- and micro-ecology, human beings appear in the words of Harvard's Dick Levine, to be 'utterly incapable of embracing complexity'.

New developments in surveillance

The Gulf war has had the effect of concentrating the attention of governments on biological warfare and has made them more receptive to the concerns of those setting up surveillance systems and epidemiological studies of dangerous pathogens. The author lists a number of issues that need to be addressed: research in the world's urban centres to determine which aspects of city life are responsible for amplifying the spread of microbes and the rodent population; the role of air pollution in enhancing susceptibility to respiratory disease; the role of open water containers in promoting the growth of mosquito populations; studies on overcrowding and population growth; development of vaccination programmes.

Problems and solutions—the way ahead

There has at least been a little progress. Zambia became the first developing country to become linked to data bases in medical libraries in the US and Canada. By the middle of 1993, eleven developing countries were connected to medical data bases with six more in the advanced stages of planning. For the first time their physicians could consult colleagues in neighbouring nations or medical libraries and data banks to help solve puzzling cases and alert one another to disease outbreaks. Genetic data bases and PCR techniques have begun to transform the ability of researchers worldwide to screen for viruses and bacteria found in their patients and to compare the strains with those already in the data bank.

In contrast to the small amount of progress the downside is overwhelming. As a result of the world economic depression of the 1990's no funds were available to develop health infrastructures in Armenia, Romania, Albania, Burma, or the Dominican Republic. Pharmaceutical companies saw no profits in making vaccines intended for use by poor people and by 1990 more than half of all vaccine manufacturers had pulled out of the business. The misuse of antibiotics has resulted in the emergence of resistance in many of the important human pathogens so that medical science is rapidly running out of options. A report by the charity 'Save The Children' confirms the continuing breakdown of primary health provision in many African countries.

The emergence of multiple drug resistant tuberculosis should be a warning of the problems ahead; 1995 was a record year for tuberculosis, killing more than three million people according to David Newnham (The Guardian 27th April 1996). In the 19th century the white plague was killing 7 million people every year and was so rampant that some believed that it might extinguish European civilisation. WHO has calculated that between five and six million people in the world are infected with both HIV and tubercle bacilli, and it is predicted that tuberculosis will be the leading cause of death among HIV infected people. Crofton's master-strategy for wiping out the disease proved very effective in the 1960s, at least in the developed countries. But his warning that the safety of all depended on the safety of the few, was conveniently forgotten and research funding moved away from tuberculosis into other areas. He recently pointed out

that the UK had even refused to pay the paltry £35,000 subscription to the International Union against Tuberculosis. It seems that Crofton's course of action proposed in 1961 still shows few signs of becoming more than a pious hope because of those who hold the world's purse strings.

Medical science needs to develop new strategies for infectious diseases. An encouraging approach that depends on the prevention of adhesion of micro-organisms to their target cells and thus colonising host tissues, was the topic of a recent symposium in Israel. As most microorganisms must first adhere to a mucosal surface to establish infection, prevention of this initial step might abort the disease. The emphasis was on the development of oligosaccharides as anti-adhesion agents. The success of this approach depends on a better understanding of carbohydrate chemistry and microbial adhesion mechanisms. Perhaps future antimicrobial therapy will depend on successful application of this approach to problems of multiple antibiotic resistant bacteria such as *Staphylococcus aureus*.

The real problem is that the academic/medical/political powers simply do not realise the urgency of problems related to infectious diseases and are not directing adequate funds in that direction. Most university departments have been unable to fill vacancies for more than a decade. Researchers with the necessary expertise are thin on the ground and desperately trying to satisfy the increased demands of increasing numbers of students and of bureaucratic demands now associated with academic life. Public Health Service laboratories are struggling to survive in the face of reducing budgets. The recent BSE hysteria illustrates all too dramatically how a previously unknown disease can suddenly emerge leaving the scientists with insufficient background knowledge to provide satisfactory answers. How well prepared are we to deal with an emerging devastating infectious agent that could spread rapidly in the community? Even diseases that are of considerable public concern such as meningitis are currently being dealt with by reference laboratories with annually decreasing staff and resources. The information set out in *The Coming Plague* should be a warning of future trends, but sadly it is likely to be ignored until the next crisis arises. National priorities appear to be determined more by short term economic considerations and 'crisis management' than by the dangers posed by our 'invisible' microbial neighbours. It is in the interests of the rich nations as pointed out in the Economist (25th–31st May 1996) to encourage economic development in the developing countries so that with increased prosperity they can provide the crucial requirements underlying freedom from infection—clean water and sewage disposal.

The lack of scientific knowledge among our politicians is illustrated by the absence until recently of a House of Commons Select Committee dealing with science. This was only set up after representations from the scientific establishment in the late 1980s. Even now, how many government ministers, supposedly representing the nation's science, have any background in science? Politicians are readily influenced by powerful business interests such as the agricultural industry, but the science lobby consisting of mainly academic scientists, appears to have little influence. Politicians supposedly reflect the needs and interests of society, and one can only assume that the voters are themselves insufficiently well informed of scientific issues. One of the major reasons for this is described in the Economist (20th–26th January 1996), 'the prevailing assumption in Whitehall is not that the public have a right to information, but that the government has every right to decide what it discloses, and what form such disclosure should

take. Secrecy is deeply embedded in the system . . . . Britain's government is among the most secretive in the developed world. The extent of information hidden from the public is huge . . . . To give consent, to exercise any democratic right, citizens need to know what their government is doing, and why . . . . After all, the government is supposed to be their servant not their master'. The report further notes that a variety of delaying tactics and obstacles are placed in the way of an investigator seeking information, for example, 'an independent health researcher, who sought to find out which local health authorities had reported outbreaks of salmonella in eggs, was faced with a bill of £2,000 from the Public Health Laboratory'.

A proposal in a *Lancet* editorial (6th April 1996) dealing with the BSE issue is that an independent agency should be set up that reports to the public rather than to the policy makers. This would allow information and opinions to be debated publicly and subject to critical evaluation and perhaps to build foresight into political policy decisions. The existence of an informed public might even deter politicans from their usual mistake of equating absence of risk with evidence of little or no risk as exemplified in their recent pronouncements on bovine spongiform encephalopathy. As Alfred North Whitehead pointed out 'there are no whole truths, all truths are half-truths. It is trying to treat them as whole truths that plays the devil'.

Science and the media

Progress in any scientific research is not made in dramatic breakthroughs but by a careful series of steps that require more than the parsimonious funding provided by short term grants. 'There is no greater impediment to progress in the sciences than the desire to see it take place too quickly' (G. C. Lichtenberg, German physicist and philosopher, 1742–99). Scientists themselves must accept some responsibility for this state of affairs which must be in part due to the unwillingness of scientists to take the media into their confidence and discuss their concerns and predictions for the future. Few newspapers carry a science page, and when scientific issues are discussed, they are often dramatised, distorted and exaggerated to the embarrassment of the scientists involved. Public expectations that cannot be easily achieved are raised, so that disillusionment with science is the result. Unfortunately the culture of science is such that in order to retain credibility, a scientist cannot be seen to be wrong or to make exaggerated claims for his work. To 'cry wolf' too often is damaging to one's reputation, particularly in the case of a supposedly highly educated and informed member of the academic community. If the message set out in *The Coming Plague* is anywhere near the truth, science cannot affort to hide behind academic respectability, the alternative is too dangerous for the survival of our species. The historian A. J. P. Taylor pointed out that 'there is nothing more agreeable in life than to make peace with the Establishment—and nothing more corrupting'. John Stuart Mill wrote 'that so few dare to be eccentric, marks the chief danger of the time'.

An optimistic note appeared in The Independent (5th April 1996) in which a science correspondent reported that a new seriousness has recently appeared within the government about biotechnology. As a result of a report by a government panel on sustainable development, a conference will be set up within the next 12 months on possible biotechnological hazards. Perhaps the contemporary naïve belief in the 'quick fix, the magic bullet and the wonder drug' is at last

being challenged by a new awareness that living systems have been shown to be far more complex and interdependent than ever imagined.

Conclusions

The human world was optimistic on 12th September 1978, when the nations' representatives signed the Declaration of Alma Alta. It was a fundamental human right to be attained by the year 2000 that disease and infirmity be reduced so that a level of health was achieved enabling people to lead a socially and economically productive life. Governments were called upon to develop financially and geographically accessible primary health care facilities for all their people. Garrett, writing nearly 20 years later, concludes that 'as the world approaches the millennium, it seems, from the microbes' point of view, as if the entire planet, occupied by nearly 6 billion mostly impoverished *Homo sapiens* is like the city of Rome in 5 B.C.'. At that time only about one of every three of its citizens reached the age of thirty compared to 70 per cent of their rural counterparts many of whom reached the age of eighty. Recent figures provided by WHO estimate that 17 million people die each year (a third of the total deaths) from infectious diseases. As human population swells the opportunities for pathogenic microbes multiply. The rapid reproductive rate of microorganisms over that of their animal hosts provides them with an unassailable advantage to adapt to any preventive measures we may devise. If as some have predicted, 100 million people might become infected with HIV, 'microbes will have an enormous pool of walking immune-deficient Petri dishes in which to thrive, swap genes, and undergo endless evolutionary experiments'. Joshua Lederberg posed the question in 1994 'are we better off today than we were a century ago?', and concluded that 'in most respects, we are worse off. We have been neglectful of the microbes, and that is a recurring theme that is coming back to haunt us'.

The conclusions of Garrett's book are based on carefully researched data. It has been described by another reviewer as 'encylopaedic in detail, missionary in zeal and disturbing in its message'. Although some of the examples given are dramatic, the importance of the message justifies the style of presentation. Garrett in her role as an investigative journalist has attempted to bring a balanced view of the problems facing both developed and developing societies in relation to emerging infections. Its warning should be heeded by medical professionals, politicians and civil servants charged with development of health policies. Politicians must be reminded that scientific problems are not amenable to the solutions applied to political issues: that they will not go away with time, spindoctoring, kind words and a little money. Unfortunately Nature does not respond to that agenda. Garrett by describing the appalling consequences of neglect puts on record the reasons we need to reassess our priorities in disease surveillance and in the environmental changes brought about in the name of progress; and she is right.

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Letter from Australia

THE IMPORTANCE OF A-MAIL

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At first sight, hospitals and slime moulds may not seem to have much in common, but second sight often affords a better view. It's all to do with entelechy—the becoming actual of what was previously only potential, and with what happens when a group of individuals suddenly becomes an individual group.

Cellular slime moulds, officially known as acrasiomycetes, inhabit warm, dark damp, places such as the leaf litter of rain forests. For those with no local rain forest, a compost heap, or American bison dung are promising alternatives. These strange organisms cause classificatory consternation, as sometimes they look like animals, sometimes like plants. Botanists first claimed them as fungi, until a few distinctly carnivorous habits were observed. The fascinating feature of slime moulds, however, is their dual existence and their response to hard times. They are usually to be found as single amoeboid cells, stealthily slithering around the forest floor, frightening the neighbourhood bacteria, and eating any that look particularly tasty. When food is scarce, or the bacteria learn to duck and weave, a remarkable change occurs. Individual cells congregate in their thousands, and fuse into a highly organised multicellular organism, with a stalked front end, a sporing rump, and a bright orange coat. The invitation to join the party goes out not by e-mail, but a-mail; by the release of the chemical messenger, acrasin, a whiff of which says, in essence, 'Food's scarce chaps, let's stick together'. Analogies with football crowds or carnival congas are not really apt—this transformation is more akin to a bag of blood on a drip stand suddenly turning into a circulatory system and setting off down the ward in hunt of supper, a fight, or a little procreative sport. Perhaps the analogy with football crowds is apt after all. A wonderful example of entelechy—the whole suddenly becoming more than the sum total of the parts, and in the process, acquiring quite different behaviour. This is a characteristic also shown by swarming insects, and humans that live in other warm, dark, damp, places such as hospitals. A suitably nasty external threat is liable to transform an apparently harmless rabble into a mean machine, as Dr Andrew Refshauge recently learned to his discomfort.

A few weeks ago Dr Refshauge, the Minister for Health in the State of New South Wales, seemed to share with his counterparts around the world, the notion that large inner city teaching hospitals only have two problems—they are large, (and thus expensive) and they are in the inner city, (and thus removed from where most of the suburban voters choose to live). Let us leave aside for the moment the question of just what is the right size for a teaching hospital, and whether it makes more sense to move hospitals a few kilometres, or to improve public transport. Let us accept that Dr Refshauge was right to decide that St Vincent's Hospital, an old and venerable institution in the inner city of Sydney, should be transplanted to Kogarah in the outer city, the site of another, younger teaching hospital, St George. Perhaps the names should have been warning enough, in a country in which the underground rivers of the Protestant-Catholic