

→ Global pestilence as harbinger of hope

Title as paradox

Joshua Lederberg

Sackler Foundation and The Rockefeller University, New York

The idea that we inhabit a single planet is one of the main lessons, by teaching and by technical accomplishment, of 20th Century Science.

The view of earth from space, the single globe with earth brown and green; with blue seas and white clouds, is a leading ikon of our time. For now all the mess of human artefacts and pollution is a detail beyond its resolution. The Internet spans the world, by wire, by optical fiber, by microwave from earth stations and in the sky. It has also captured the imagination of millions in personal discourse, idle chatter, commerce, entertainment and serious information-seeking through "the World Wide Web".

That unity is both confinement and opportunity: ^{are bounded by single} we ~~share a common~~ environment, physical, chemical and biological. The seas are a common reservoir for fisheries, recreation, transportation. A single ozono- sphere shields us from excess solar ultraviolet light; and excess CO2 production anywhere adds to the common burden of the greenhouse effect. Above all, we share common biological competitors in the form of predatory bacteria, fungi, protozoa, viruses, and we discover once again that health cannot be fragmented into sovereignties. The communicable diseases that break out in one territory are all too easily transmissible to others, in an age when a million travellers daily cross national boundaries ^{by air}. To counter that, health science is a common good: when new knowledge can be garnered anywhere, it is rapidly shared; though its application may be uneven when resources and educational insight are limited. Communicable disease, emerging infections in particular, will be my main theme.

For a time, the accepted wisdom was that we had ^{at least in economically advanced countries,} already conquered infection. Beginning about a hundred years ago with the pioneering scientific studies of Louis Pasteur in France, and Robert Koch in Germany, we saw a concerted attack on the etiological agents of infection. Knowledge rapidly accumulated about many of the most important infections: tuberculosis, cholera, dysenteries, scarlet fever, malaria, ... the list goes on

and on. For many viruses, vaccines were developed, with outstanding results for polio. Jenner's empirical remedy of vaccination -- the use of a cowpox to fend smallpox -- came under scientific scrutiny and global application, leading to the eradication of this disease, formally certified on December 9, 1979 by the Global Commission at WHO. This was a unique accomplishment in the history of medicine and of international cooperation.

As to bacterial infections, it is difficult to know how much to credit improvements in sanitation, water and food supply, and personal hygiene, and how much to the development of antibiotics in the last half-century. Together, these have transformed our outlook to the point that victory had been proclaimed about 25 years ago, that health professionals could turn their attention to chronic constitutional afflictions like heart disease, cancer and psychiatric disorder.

This illusion was shattered by the AIDS epidemic, which reached global notice barely 15 years ago, and of course continues its aggravated spread 'round the world. This has sensitized us to other communicable diseases, and we have headlines almost monthly of new outbreaks, the deadliest perhaps Ebola in Zaire. But there is a long list of other contenders: at this instant the most recent threat is evidently Venezuelan Equine Encephalitis, which has every opportunity to spread through North America, where mosquitoes competent for its spread abound. To make my point, I have to bore you with a much longer list: hantavirus, Lassa fever, Cholera 0139, Plague, Morbillivirus, E. coli O157, invasive streptococci, Lyme, I do have to stop. Equally ominous is a list of bacterial infections of more familiar genre -- tuberculosis, pneumonia, staphylococcus, gonorrhea which had for a time succumbed to modern antibiotics, but which have now evolved multiple drug resistance to the point of serious obstruction to treatment.

I have to make a special point of influenza, which tends to be underrated in the public mind, partly as it is confused with the common cold. The flu' and the cold viruses share an inexorable power to spread; but influenza accounts for substantial mortality in older people. Furthermore, as in 1918, there are episodic variants of influenza that sweep through the world with much higher lethality: the 1918 episode claimed at least 20 Million victims --

(included)

comparable to the casualties of military operations in World War I. We do have vaccines against standard 'flu strains. The question is whether existing technology would allow appropriate vaccines to be developed rapidly enough to stem a re-emergent 1918-like variant.

None of this would pass for newsworthy in the developing world, in the poorest countries, where baseline communicable disease accounts for almost half of mortality, in contrast to less than 10% in the developed world. The toll, year in, year out, of tuberculosis, malaria, diarrheal disease, far exceeds what would be labelled in the north as a shattering pandemic. "Emergence" is in fact *regression*, a return to the standard that prevailed universally in the previous century. It is the deviation from the accomplishments of the 1950's through 80's that we now assess a current crisis. And we arrive at the realization that --just as applied to smallpox -- world health is indivisible, that we cannot satisfy our most parochial needs without attending to the miseries of all the globe. *selfish and*

We stand at the summit of the food chain, with only the microspecies -- the littler fleas that Swift poetized -- as competitors. Other speakers will focus on how we deal with one another, within the human species. How do we cope with them?

One mode of accommodation is by genetic evolution: we see relics of prior history in the accumulation of genes for resistance to malaria in tribal areas where this disease is rampant. But, whereas rapid evolution is the hallmark of biological success for the microbe, for the human, it is intolerably costly in wasted lives, in those that natural selection would discard. We cannot wage a war of attrition against a foe which can crowd billions of microbes in a single test tube. Against their genes, rapidly evolving, we must pit our wits. And that calls for a social intelligence, as much as for individual genius.

While the competition cannot be swept aside, some may deplore the military metaphor: would it not be better to stress the harmony of nature, and look to a symbiotic detente with the microbial world? Whether or not "Nature" is inherently benign is already beside the point for our own uniquely

"manmade" species, a world population that since the Neolithic has expanded a hundred or thousandfold over its primitive bounds in a Rousseau-mythical State of Nature. Many aspects of emerging infection can be viewed as diseases of civilization, if we ^{scale} understand that ^{Civilization} embraces the invention of agriculture and then of urban life: the hubris that we could multiply indefinitely by the force of our tools of production. The lesson should not be lost that we often take too narrow a definition of the sources of disease being solely the etiological agents and their insect or other vectors, if that ignores the broader social, behavioral and cultural contexts which often tip the balance. Lacking, to this point, any means of direct attack on the HIV, these are the main approaches left to us for trying to deal with AIDS. *(behavior)* *with success, not as you know*

Where is there hope to be sought here? Some straightforward measures of scientific, technical and public health cooperation are self-evident:

1. Concerted global surveillance and diagnosis of disease outbreaks and endemic occurrence.
2. Vector management and provision for safe water and food supplies; and assurance of adequate nutrition.
3. Public and professional education.
4. Scientific research on causes of disease, pathogenic mechanisms, bodily defenses, vaccines and antibiotics.
5. Sharing and provision of the technical fruits of such research.

The WHO, UNICEF, World Bank, and a host of other intergovernmental and nongovernmental agencies have addressed these measures, with many notable successes, the most historic perhaps the eradication of smallpox just 19 years ago this week. We also know that the level of investment, and of escape from political entanglements, are far short of the needs even to assure health security within affluent nations, much less globally; and there are many distractions from other domestic and international claims for attention. The hope is in the widening understanding of these priorities, as a common cause.

But I cannot close without a reference to despair: that there are nations

who, in clear violation of established treaties have undertaken the development of the most ghastly weapons, which would use the same scientific and medical knowledge as agents of death, namely biological warfare. The most flagrant and exposed example has been Iraq -- perhaps there is also hope in the arousal of world conscientiousness ^{recognized by the United Nations} that exposure has generated, and which may help assure that no state or group which transgresses these bounds can go unpunished. *Better than deterrence would be the universal internalization of these norms, so that the use of germs as weapons would indeed be unthinkable.*