emergency threats of emerging infections in the future. For example, scientists can perform relevant research and can warn; agencies can inform and advise top government officials; presidents can initiate emergency responses; Congress can carry out emergency legislation; industry can produce vaccines in substantive amounts, if given 6 or more months' notice; state and local health organizations can deliver vaccines; and the public can be informed. These essential elements can potentially be accomplished successfully in case of an emergency, since they were achieved in 1976.

But, what went wrong? The judgments of 1995 can benefit from the clarities of hindsight (Figure). The principal reality, perhaps, is that a hard core of well-intentioned scientists and agency personnel, working with theory and limited data, exercised substantial clout to establish and maintain a changeless agenda for vaccination without meaningful periodic review and reevaluation. This reality was despite an early and increasing disenchantment in the larger scientific community with the idea that there was a real threat of pandemic influenza. No one could reasonably fault the initial concerns and actions of February and March 1976, even though built on a dubious concept that an antigenic difference alone would suffice to drive an animal influenza virus through a human population with pandemic force. The swine virus was zoonotic of origin and was of limited communicability in humans since there was no evidence for spread beyond Fort Dix. The centrist determination for immunization prevailed even though there was reason to question the initiative by June and certainly to end the program in September before the October immunization campaign began.

The lessons of 1976 will provide valuable guidelines for decisions and handling of future threats from emerging disease. Such planning will benefit by obtaining a broad scientific and technical consensus and by conduct of periodic review and reevaluation that was not part of the 1976 initiative.

Maurice R. Hillman, PhD, DSc

Editorials

Editorials represent the opinions of the authors and THE JOURNAL and not those of the American Medical Association.

Infection Emergent

The depredations of the global HIV pandemic have been a humbling experience for the scientific infectious disease community and the public health authorities. This can hardly be compared with the human suffering induced by this alien surprise, and what may still lie ahead. However, it may yet have some salutary effect if it alerts us to still further hazards that we face as a species in our competition with microbial competitors, who crowd us at the summit of the terrestrial food chain.

This month, JAMA and 35 other journals worldwide will document the occurrence, causes, and consequences of emerging and reemerging infections. This resurgence of scientific interest has been marked in popular media, in the pages of newspapers, newspaper headlines, best-selling books, TV shows, and movies like Outbreak. Tangible responses by governments in the form of budgetary or staffing commitments remain negligible, and political debates about health have focused on billions of dollars for health care insurance while state and local health organizations can deliver vaccines; and the public can be informed. These essential elements can potentially be accomplished successfully in case of an emergency, since they were achieved in 1976.

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This resurgence of scientific interest has been matched in popular media, in the pages of high profile journals. From Rockefeller University, New York, NY, where Dr Lederberg is the Raymond and Beverly Sackler Foundation Scholar.


Reprint requests to Rockefeller University, 1320 York Ave, New York, NY 10021-6398 (Dr Lederberg).


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modifiers in response to malarial infection; many others are
sure to be discovered. Whether they will also be such mixed
blessings as hemoglobin S, thalassemia, or erythrocyte G6PD
deficiency remains to be seen. Arguably, cystic fibrosis might
fall in this category as a prophylaxis against cholera.2

At any rate, human genomic change is not the answer for the
foreseeable future. Most of human culture transcends the bio-
logical, with transmission through learning, artefactual tech-
nology, and social institutions. In that sense, as I believe was
said by the anthropologist Alfred Kroeber, “man is a manmade
species,” for better or worse out of nature, and with many
penalties in store for that hubris. In purely biological terms, we
face a war of attrition against a foe that can crowd billions of
microbes into a single test tube. While some may deplore the
military metaphor, preferring the harmony of nature and a
symbiotic détente with the microbial world, whether “Nature”
is inherently benign is already beside the point for a world
population that since the Neolithic has expanded a hundred-
fold from its Paleolithic numbers. Many aspects of emerging infection
can be viewed as diseases of civilization, if we understand what
embraces the invention of agriculture and then of urban life.
To turn back the clock, to return to the Garden of Eden, would also
be to dispose of most of now-living humanity.

We come then to social intelligence as our remaining option
to counter the evolutionary drives of the microbial world. That
intelligence must include a profound respect for the ecological
factors that enhance our vulnerability. Many have commented
about the disturbance of natural environments and the lash-
back of arthropod vectors and zoonotic parasites; and the
consequences of global warming are mainly unpredictable
(hence, probably harmful).4 Nevertheless, the preponderant
changes are the sheer expansion of our species, with high
population densities, and much the worse, egregiously stratifi-
ced by standards of economics, nutrition, housing, and public
health. At the same time, we have unprecedented mixing of
people: a million passengers a day cross national boundaries by
air, not to mention the movements of armies, refugees, and
road transport as well-documented vehicles for the rapid spread
of disease. One could hardly have concocted a better-calculated
recipe for a tinderbox, as AIDS already harshly teaches. From
this perspective, we have never been more vulnerable; this
vulnerability must be matched against the extraordinary so-
phistication of the science and technology that we are, in prin-
ciple, able to pit against the threats.

Doubtless, much of the “emergence” is that of reassessment
of the ongoing situation. Lyme and legionnaires’ diseases and
Hantavirus infection were surely with us for many years before
modern diagnostic technology enabled their more precise deline-
ation. Most peptic ulcer disease will now be correctly re-
classified as a Helicobacter infection. These included, many of our
concerns would hardly pass for newsworthy in the developing
world, in the poorest countries, where baseline communicable
disease accounts for almost half of mortality, as a primary cause
of death. This is in contrast to less than 10% in the developed
world, according to traditional scorekeeping. The toll, year in,
year out, of tuberculosis, malaria, and diarrheal disease far ex-
cceeds in the developing world what would be labeled elsewhere
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 our accomplishments of the
1950s through the 1980s that we now assess as a current crisis. And

we arrive at the realization that world health is indivisible, that
we cannot satisfy our most parochial needs without attending
to the health conditions of all the globe.

One line of social thought would argue that the only answer
is a fundamental convergence on population and poverty.
Even were the will to do so to exist, and that will needs every
encouragement, the history of social experiment in the 20th
century would leave one in despair. Health is also a precondition
to economic development, so that more modest and selfishly motivated measures can be a great beneficence to the
overall human condition.

The current situation in the United States is surveyed
throughout this issue of JAMA. Infectious disease remains a ter-
tiary category for mortality, still far behind heart disease and
cancer.5 But it is rising, in important measure from AIDS, but
also in a range of other categories. Outbreaks of new, or newly
recognized, diseases have been seen throughout the world, some
regionally grievous—eg, cholera O139—or in even more fero-
cious but thus far mostly localized style—Ebola in Zaire. The
United States has had its own examples: Hantavirus, Esche-
richia coli O157, Cryptosporidium, which, because of their
smaller numbers, have not shown up in overall vital statistics. On
a substantially larger scale, the genomic innovations of antibiotic
resistance are becoming increasingly troublesome, especially for
nosocomial infections and for multidrug-resistant tuberculosis.
We do not as yet have a quantitative measure of their impact on
mortality through treatment failure, but a potential collapse of
medical management of some bacterial infections is in sight.

Likewise, we have had several cycles of antigenic drift, and
a few episodes of shift for epidemic influenza; these do show up
as measurable spikes in seasonal mortality statistics for more
elderly age groups. Whether more intensive vaccination could
have prevented these consequences for familiar strains is an
open question, but the answer is presumably yes, at least in
partial measure. Almost certainly, a recurrence of pneumo-
nogenic influenza like that of 1918 could well overtake the
research and development cycle of new vaccine development
as now constituted, taking into account the acceleration of
spread that derives from present-day travel. Recall that the
1918 pandemic claimed about 20 million lives worldwide, not-
able for its attack on the young and vigorous, and sparing no
country. As backup to new vaccines, we do have some chemotherapeutics, but as with the viral armamentarium generally,
these are imperfect, partial measures at best, though perhaps
still worth stockpiling. And while we may have learned better
treatment of pneumonia than was known in 1918, just visualize
how that would overwhelm our hospitals.

So our prospects are, at minimum, rising exposures to fa-
miliar agents globally spread and increasing treatment failures
with antibiotics. We are at plausible risk from uncontrollability
of, say, pneumococcal pneumonia, and from the resurgence of
a 1918-like flu pandemic. There is an outside chance of a zoo-
carin case, like Ebola escaping more broadly, with increasing ad-
aptation to person-to-person spread, and perhaps some mudding
of mortality that would keep the virus from burning out before
it spread further. Existing viruses might mutate or recombine
to present new challenges to our control measures, or perhaps
simply diffuse to areas like the southeastern United States,
which already harbors many competent mosquito vectors.

Most of these contingencies are, in principle, manageable
with the old standbys of vaccines, passive immune globulins,
and antibacterials. These can be reinforced with very exciting

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fruits of biotechnology, both for parasite control and for modification of the pathogenic processes. Most of the “new” microbial agents do not display HIV’s nasty evasions of the immune system; but they could still go a long way before we actually mounted a response unless we are nimble and more foresighted than has been evidenced so far.

The program needed in response follows fairly self-evidently from the delineation of the problem:

1. Concerted global and domestic surveillance and diagnosis of disease outbreaks and endemic occurrence. This must entail the installation of sophisticated laboratory capabilities at many centers now lacking them.

2. Vector management and monitoring and enforcement of safe water and food supplies.

3. Public and professional education.

4. Scientific research on causes of disease, pathogenic mechanisms, bodily defenses, vaccines, and antibiotics.

5. Cultivating the technical fruits of such research, with the full involvement of the pharmaceutical industry, and a public understanding of the regulatory and incentive structures needed to optimize the outcomes.

Largely through the diligent work of the National Center for Infectious Diseases at the Centers for Disease Control and Prevention, there are clearly outlined plans for epidemiological surveillance, and most of the other elements fall within the established responsibilities of government, particularly the National Institute of Allergy and Infectious Diseases. These simply await political decisions about the allocation of resources to bolster existing programs. Other forms of surveillance and intervention will require devoting substantial new resources and personnel. Conceptually, we probably have the least clarity about the evident market failure in the pipeline for new antibiotics. We need to learn how best to orient the industrial sector, and its inevitable coupling with the Food and Drug Administration, to efficient attention to developing new antibiotics and vaccines.

Understandably, private entrepreneurs are unlikely to invest in purely anticipatory development, the equivalent of war reserves for the military, against future and problematic contingencies. When the volcano does erupt, the industrial sector will be denounced for profiteering when it prices the priceless in accord with market principles, at levels justified by the risks to which it puts its capital. So there is an unavoidable responsibility for the public sector-hard news at a time when disinvestment is the political name of the game in Washington. This is compounded by the status of public health as a poor relation of remedial health care, a subordination that is bolstered by the long-standing economic and political structures of our medical establishment and its associated educational institutions.

Hence the importance of this Emerging Infectious Month, the reinforcement and clarification of our consensual medical scientific perspectives, and the reinforcement they give to public explicators of contingencies. These are often the hardest to convey with balance, without gratuitous scares, with simply a hard-nosed prudence to anticipate threats we hope will never materialize, but some of which surely will.

Joshua Lederberg, PhD


Infectious Diseases
A Global Approach to a Global Problem

A little more than a decade ago, Harrison’s Principles of Internal Medicine proclaimed that “infectious diseases are more easily prevented and more easily cured than any other major group of disorders. . . .” A new disease called “acquired deficiency of cell-mediated immunity in young homosexual men” occupied less than a column of text. “Slim disease,” recognized possibly as early as 1962, did not warrant an entry, but the dramatic decline in tuberculosis seen during the previous decades was noted to have “levelled off.” This complacency, reflected in the textbook and documented throughout this issue of JAMA, allowed a greater focus on heart disease and cancer. Ten years later, cardiovascular disease mortality has declined, and much of the public knows that high cholesterol and blood pressure should be controlled. Infectious disease mortality, meanwhile, has climbed to the third leading cause of death in the United States.

In 1996, we view infectious diseases with a humbler eye. The victories of a quarter century ago ring hollow as AIDS ravages, enterococci become resistant to all standard treatments, and the once easily treated pneumococcus gains a plethora of antimicrobial drug resistance. Unknown diseases develop with disconcerting frequency, and Ebola virus has been identified outside the confines of Zaire. Once considered unique and isolated, these events penetrate every corner of the globe. As was recognized in 1892 when the first international sanitary convention on cholera was adopted, infectious diseases cannot be observed, battled, or understood street by street or country by country. A global approach is necessary.

With this perspective, three editors set about creating the first-ever global theme issue of medical journals. Last December, Linda Hawes Clever, MD, editor of The Western Journal of Medicine, Magne Nylenna, MD, editor of the Journal of the Norwegian Medical Association, and George D. Lundberg, MD, editor of JAMA, contacted the editors of 78 journals worldwide to invite them to participate. Now, 1 year later, 36 journals in 21 countries have agreed to devote all or part of one of their