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Prologue: For years, award-winning author Lewis Thomas has been interpreting the mystifying and marvelous world of biomedical research for the layman. Through his words in this regard, Thomas has become the most distinguished figure of his time in unlocking for the citizenry—which, by and large, pays the bill—some of the secrets of the research enterprise. Thomas, president emeritus of Memorial Sloan-Kettering Cancer Center, is an unabashed advocate of research and its potential for improving the health status of humankind. Writing from this bias, it is interesting to note, as he does in this paper, how his view has changed on the likelihood of stunning successes in society’s war against cancer. At first, Thomas concedes, he was a genuine skeptic when Congress declared its resolve to sharply increase the federal effort to unlock the mysteries of cancer. More than a decade later now, Thomas reports that the most talented of America’s younger scientists are streaming into cancer research because “it has turned into one of the most exciting and enchanting of all problems in biology.” Sure, money helped, he says, “but the phenomenon was not caused primarily by money.” What happened was that basic science “produced an overwhelming surprise—two surprises, in fact.” In stressing the importance of basic science to the improvement of medical care, Thomas issues a call for local health departments to earmark some of their scarce monies for research. Given their position at the front lines of disease, Thomas argues, local health departments could appropriately conduct research on the AIDS syndrome, or on the long-term effects of dioxin exposure in human beings. In short, Thomas seems to be saying, for health departments to remain relevant, they must restore a capacity to conduct research.
State and local health departments in this country were created principally to deal with problems of infectious disease: at first the great epidemics of cholera, yellow fever, and typhoid, and later on, the endemic and sporadic outbreaks of contagious disease. Early in this century, health departments began to take responsibility for maternal and child health because of the particular hazards posed by infectious disease in pregnancy and early childhood. The greatest threat to public health was tuberculosis, feared by the populace at large much as cancer is feared today. Group A hemolytic streptococci and the syphilis spirochete were high on the list of public health priorities because the incidence of rheumatic heart disease and tertiary syphilis was high throughout all levels and classes of the population. Health departments directed their educational efforts chiefly toward sanitary practices, early detection of tuberculosis and syphilis, and the improvement of nutritional habits. The term “preventive medicine” meant simply the prevention of infection. There was no such thing as “lifestyle.” The Health Care System had not yet been invented; charity hospitals, run (badly, most of them) by counties and municipalities, looked after the poor, and private practitioners earned modest to moderate incomes looking after everyone else. The technology of medicine consisted mainly of measures for accurate diagnosis and prognosis, and medical care consisted largely of reassurance, explanation, and good nursing care.

In the decade following World War II, infectious disease came largely under control. What had been major public health concerns a few years earlier no longer seemed to require the existence of large, elaborate professional agencies. During the 1950s, health departments began steadily to shrink in the scale of their operations and the size of their budgets. The major problems brought before the New York City Board of Health from 1955 to 1969, when I was a member, involved the regulations affecting the milk industry; the long public debate over fluoridation of the water supply; and jurisdictional disputes with other city agencies over the responsibility (and budgets) for rat control, unsanitary housing, and restaurants. Medicare and Medicaid seemed to have eliminated the need for public health clinics operated by the health department. The research activities of the health department (for which New York City had been distinguished since the late nineteenth century) were kept alive for ten years or so by the department’s Bureau of Laboratories, by the Public Health Research Institute, and by Commissioner Leona Baumgartner’s introduction of the Health Research Council, which supported biomedical research in the city’s medical schools and hospital centers. During the 1970s, these research activities were gradually reduced and they have now nearly faded away.

It seems to me that the public has always expected a health department to be the central governmental mechanism for the prevention of
disease wherever possible. In the decades ahead, this expectation may extend to the treatment of disease as well, if public dissatisfaction with the quality, equity, and cost of medical care continues to deepen.

This prediction allows me to move directly into my topic. I believe that the capacity of health departments to deal with their responsibilities will depend directly, and almost solely, on the quality and scope of biomedical research, both basic and applied, in the years just ahead.

One Scenario—Make Do

I can imagine two courses of action with respect to biomedical research. Both are imaginary, and in describing them I may overstate the case somewhat in order to make the point that coincides with my bias.

In one scenario, we cease doing basic biomedical research altogether, and make do with today's scientific information about human disease. A typical health department will continue to carry five major responsibilities—epidemiology, health services delivery, environmental monitoring, education, and mental health—but it will be able to make only a marginal contribution to the prevention or alleviation of illnesses chiefly responsible for premature death and incapacitation in the United States today. These diseases have different manifestations, but they share one all-important feature. We do not understand their causes, or the underlying mechanisms by which they run their course, nor (with a few exceptions) how to prevent or cure them. It is conventional to treat them separately, as the discrete, unrelated health problems, which of course they are, but taken in the aggregate, they comprise the public health agenda for the 1980s 1990s and (under this scenario) beyond.

Of these twenty-five or so common varieties of illness, the most important are generally conceded to be cancer, arteriosclerotic heart disease, stroke, the senile dementias, schizophrenia and the manic-depressive psychoses, diabetes, nephritis, hypertension, cirrhosis, multiple sclerosis, rheumatoid and osteoarthritis, pulmonary fibrosis and emphysema, and the medical consequences of drug abuse and alcoholism.

If we leave biomedical science where it now stands, and if the incidence of these diseases increases, as it will for some in an increasingly aged population, the prospects for any health care system are bleak indeed. It has been estimated that the annual cost of institutional care, entirely custodial, for the cases of senile dementia during the coming decade will exceed $40 billion within a few years. The management of schizophrenia has undergone an illusory improvement because of the mandated emptying of state hospitals, but the patients, quieter but still disabled, and the incalculable costs to society, are still there on the streets. We have introduced new and peculiar sorts of engineering technologies for the replacement of damaged organs—the artificial heart, chronic renal dialysis,
transplanted hearts, kidneys, livers, pancreatic islet cells, and bone marrows—with varying degrees of success but at such high expense that these half-way technologies threaten the solvency of even the most spartan health care system. We can do very little to prevent cancer, despite the common (and probably unfounded) assertion that 80 percent or more of human cancers are caused by environmental carcinogens, and today’s best therapy can cure less than 50 percent of patients with cancer. The claims being made by proponents of “health education and promotion,” and the assurances that changes in “lifestyle” will greatly reduce the incidence of heart disease, seem to me totally unproven and highly unlikely. As for mental health, we have already learned, at a very high dollar price, that the installation of community mental health centers in cities all across the country has provided employment for professionals and paraprofessionals but not much else that can be measured.

In short, medicine remains in a state of ignorance or, at best, incomplete knowledge, about each of the major diseases that make up the public health agenda for the foreseeable future, and the costs of applying what little we do know for technological “fixes” are becoming insupportable. Meanwhile, new and equally mystifying diseases, such as acquired immune deficiency syndrome (AIDS), may be coming in from the wings, finding medicine even more unprepared.

Second Scenario–More Research

In the past, scientific research has yielded highly effective and inexpensive technologies for the prevention and cure of human disease. The whole contemporary array of vaccines, antibiotics, and synthetic antimicrobial chemicals is testimony to the usefulness of basic biomedical insights and the ultimate applicability of such insights. It may not be justifiable to extrapolate achievements of research in infectious disease to other, more imponderable illnesses, such as the senile dementias. The modern applied sciences of microbiology and immunology did not emerge full-blown with penicillin and, a few years later, poliomyelitis vaccine. Edward Jenner administered the first smallpox vaccination in 1796. The recognition of the existence of bacteria and their toxins, and of viruses, took the better part of another century. At least fifty years of painstaking research into the cultivation, taxonomy, and metabolic properties of bacteria had to precede the very notion of anything like penicillin. Controlling infectious diseases took centuries and the lifetime work of countless investigators.

Today’s question is whether understanding, and then coping with, the mechanisms of today’s major diseases will take a similar stretch of time, or whether, indeed, some of today’s diseases are so complex as to lie forever beyond reach.
Take cancer, for example. Only twelve or thirteen years ago, before I became connected with a cancer institute and while I was busy with the affairs of a medical school and with research on various problems of immunity and infection, I could not imagine a scientific problem less attractive than cancer. It seemed, at that time, too hard a problem for anyone. I wondered at the zeal and courage of my colleagues who were engaged in cancer research, but I believed that they would never get anywhere with it and I felt sorry for them, trapped in a scientific blind alley.

Cancer then seemed not just one problem but a hundred different problems, each requiring its own separate solution. And all of them had the look of unanswerable questions. Cancer simply stood there, the most profound and imponderable of all puzzles in biology. Carcinogenesis seemed to encompass almost every discipline in biomedical science—virology, immunology, cell biology, genetics, membrane structure and function, and all the rest.

I knew, even then, more than fifteen years ago, of a few people here and there who were doing clinical research on cancer. They were bright, ambitious, and hopeful, and my heart bled for them. They had discovered a few chemical agents—dangerous, toxic, and difficult to handle—that seemed to have a modulating effect in the leukemias of childhood. They were made hopeful by these things, but as an outsider I was not. In the late 1960s if any young post-doctoral student or M.D. had asked me about the advisability of going into cancer research, my advice would have been to stay away, and instead to pick a field such as immunology or molecular biology, in which things are clearly moving along.

Even in the early 1970s when the National Cancer Institute (NCI) and the Nixon administration were launching what was then called “The Conquest of Cancer,” with a substantial infusion of new funds for the support of cancer research, I remained skeptical about the whole venture, and so did many of my colleagues outside the field. It is just too early for a crash program, we said. Biological science is not ready; we do not know enough. Some of us even went before the congressional committees responsible for the program to testify that the problem of cancer would not be reliably approachable for another fifty years.

And then, still in the early 1970s things began to change at a great rate, and they have been changing with stunning speed ever since. Now, in 1983, work that was the state-of-the-art just three or four years ago has a sort of antique look. The brightest and most talented of our youngest scientists are streaming into cancer research everywhere in the world, because—best of all news—it has turned into one of the most exciting and enchanting of all problems in biology. It is beginning to look like an approachable problem, even (although on this point everyone tends to speak softly) a soluble problem.

What changed? Well, the money had something to do with it at the
outset, and more money will surely be needed to keep the work going at
its present pace, but the phenomenon was not caused primarily by money.
What happened was that basic science did what basic science tends to
do, by luck, every once in a while: it produced an overwhelming surprise—
two surprises, in fact. The first was the technology of recombinant DNA,
which makes it possible for an investigator to ask almost any question
that pops into his head about the most intimate details of a living cell’s
genes, and to get sharp, clear answers. These techniques made it plain, a
couple of years ago, that there are indeed such things as cancer genes—
oncogenes as they are now called. Now it is possible to learn how chemical
carcinogens and cancer viruses change and switch on such genes.

The second surprise was the discovery of cell fusion, and then the
development of cell factories for making monoclonal antibodies. With
these new tools, it is now possible to identify the gene products that are
elaborated by switched-on oncogenes, and also to examine with a high
degree of precision and specificity the changes that take place at the cell
membrane when a normal cell is switched to the mode of living of a
cancer cell.

The virologists are having a field day. The immunologists are ready to
claim the whole cancer problem, including cancer therapy, as their own.
The biophysicists, the nuclear acid chemists, the geneticists, the cell mem-
brane people, and the cell biologists are falling over each other in the
race to final answers. I have never known a period of such high excite-
ment and such exuberant confidence in any field in biology. It begins to
resemble what one reads about the early days of twentieth century phys-
ics when quantum theory was just beginning to take shape. All the
researchers, especially the youngest ones, know that what is being discov-
ered about cancer amounts to a revolution in biological science. No one
can be sure what lies ahead, but it will certainly be brand new informa-
tion of profound importance.

Two aspects of this phenomenon seem to me remarkable in their impli-
cations for public policy and for the future of the health sciences. First,
no committee sitting around a table in Washington or anywhere else in
the world in 1972 could have predicted any of the things that have taken
place. What we are observing is basic science at its best, capitalizing on
surprise, following the new facts wherever they seem to lead, taking chances
and making guesses all the way, driving the problem along toward its
ultimate solution, not by following any rule book or long-range plan, but
by playing hunches. Basic science may be the wildest of all human activities,
and it can only work in its own wild way.

Second, a vast range of biomedical territory seems to be opening up as
this work goes along. I have not the slightest doubt that cancer itself has
turned into a soluble problem, although I have no way of guessing what
the specific solution is. It may lie in gaining control, pharmacologically or
immunologically, over the switching mechanism responsible for the activation of oncogenes. Or it may lie in the chemical nature and mode of action of the protein gene products coded by oncogenes. Or a set of signaling events occurring at the cell surface, or within the cell membrane, may have final responsibility for transforming a normal cell into a neoplastic one. Or it may be something I cannot imagine at this stage, something totally surprising. The important point is that whatever the mechanism is, the research technologies now available are becoming so powerful and precise that it cannot remain hidden much longer.

As this work progresses, cell biology advances as a huge new enterprise in biology, quite independent of the cancer problem itself. Cellular immunology has become, also just within a decade, one of the most sophisticated of biomedical disciplines, capable of opening the way into problems of autoimmune diseases, such as, perhaps, rheumatoid arthritis and multiple sclerosis. Virology, which played an important role in opening the way to the recombinant DNA technology, is beginning to reveal its own deepest secrets to that same technology; vaccines can now be manufactured by the particular viral genes that code just for the antigenic fragment of the virus, without risking the presence of the whole virus. Modern virology and cellular immunology have joined forces, opening up a new approach to understanding (and eventually reversing) the mechanism that damages pancreatic islet cells in juvenile diabetes.

Just in the past few years, neurobiology has begun to take off. The discovery of the endorphins, followed by discoveries of other internal hormones secreted by brain cells, has turned the central nervous system from an incomprehensible computer-like wired apparatus into a chemically governed system of signals now ready for direct study in the most reductionist detail. Experiments with primitive marine organisms are beginning to reveal neural mechanisms and structures involved in both short-term and long-term memory. Selective enzyme deficiencies are being observed in the brain tissue of patients with Alzheimer’s disease, and other forms of senile dementia are now known to be caused by a so-called “slow” virus, the C.-J. agent.

Aspirin works by inhibiting the chain of enzyme reactions that catalyze the conversion of arachidonic acid to one or another of the prostaglandins. Components of the same chain make platelets sticky, and platelets sticking to the inner walls of coronary or cerebral arteries may be the first stage of coronary or cerebral thrombosis. Pharmacologic agents are now becoming available for selective inhibition of individual components of the prostaglandin synthetase system. Bits of information spinning off from the study of this system may help to prevent coronary occlusion and stroke.

When I was an intern, malignant hypertension was a sure death sentence; today it has become a treatable disease. Moreover, new drugs
have been deliberately designed to inhibit a particular enzyme (angioten-
sin converting enzyme) that leads to hypertension. Cardiovascular phar-
macology is emerging as a field in which the chemists can call the shots
before making their chemicals.

The whole field of biomedical science is on the move, as never before
in the long history of medicine. I do not know what will happen over the
next twenty years, but my guess is that we are on the verge of discoveries
that will match the best achievements in infectious disease a generation
ago. My guess is that new technologies based on a really deep understand-
ing of disease mechanisms will turn out to be inexpensive relative to the
makeshift measures that medicine is obliged to rely on these days.

Research on human disease mechanisms used to be a routine function
of certain municipal, county, and state health departments. I would like
to see some of this activity restored, wherever feasible, for a variety of
reasons. One is departmental morale; I am certain the presence of strong
and distinguished research laboratories within the New York State and
New York City Health Departments was beneficial to all the profession-
als who worked in those departments. Another reason is the need, as I
see it, for some degree of decentralization in the national biomedical sci-
ence effort. The National Institutes of Health (NIH) is a marvelous
institution, probably the greatest social invention of modern times, but
the demands on its bureaucracy have become too heavy in recent years,
and might be eased by a modest degree of local and regional support of
science. Industry is showing an increasing interest in biomedical
technology, for the best of reasons. The health departments, which in the
long run have the heaviest of stakes in research, should reenter. Given
their almost unique opportunities in epidemiology, these agencies might
be able to spot openings for bench research before anyone else. Research
on the cause and mechanism for the AIDS syndrome, or on the still-open
question of long-term effects of dioxin exposure in human beings, would
be entirely appropriate problems for local agency research.

One obstacle to this undertaking is money. But I am not proposing
recreating small NIH-like institutions; I am simply recommending that
health departments once again have the kind of research bureaus they
used to have. If health departments are now costing $6 billion, as has
been estimated, an addition of 5 percent—or $300,000,000 countrywide—
would not represent a heavy drain. It might turn into a lucky investment,
and it would make these agencies more interesting places in which to
work than they are today.

Another hard assignment for the health departments of the future is to
provide reliable information about the public health. Fear of malign in-
fluences in our environment is so widespread today that it amounts to
mass hypochondriasis, despite reliable statistics telling us that we live
longer and in a generally healthier state than any generation of human
beings before our time. The presence of any trace of dioxin, insecticide, radiation (even background radiation), food additive, or even a foreign smell is taken as an omen of death and treated as such by the press and television. In fact, we are one of the toughest, most resilient of species in the record of evolution. We should be concentrating our fears and our preventive efforts on the real and immediate prospect of thermonuclear warfare, rather than on imaginary demons. The duties of health departments include assuring people that they can go on living in the presence of saccharine and caffeine, go on breathing air with traces of carbon monoxide or the fumes of automobiles, even go on surviving in the company of people who smoke cigarettes or drink vodka. We will not all die early because of these errors in living. We are more likely to die before our time—and often in misery—of diseases that we do not yet understand. To fill these gaps in our knowledge, we urgently need more and better biomedical research. I would set this research as the topmost priority for public health over the remainder of this century. But if people are looking for a hazard to worry about day and night, I would push the nuclear missiles into public view, over and over again. Now there’s a public health menace, for sure.