

Notes for Presentation to Senate Committee on Labour & Health
Joshua Lederberg, President, the Rockefeller University, New York
1/12/87

Three main pillars to health goals:

Access to care; Prevention; Research.

In fact access also needs more analytical research to assure the efficient use of the enormous funds expended. Health care and prevention both look to research for badly needed knowledge for diagnosis, survey, medications and other interventions. In view of limited time, my remarks will be confined to the medical research enterprise.

HEALTH RESEARCH STRATEGIES:

Matrix of

- a) public health challenge, given by statistics
- b) scientific opportunity: where is existing frontier of knowledge.
- c) resources -- funds, facilities, organizations, people
- d) constraints -- ethical and legal regulate pace of much research of human importance

Public Health Challenges

Statistics give us clear guidance about problems!

The principal sources of morbidity and death are listed below. However, we cannot overlook the myriad of ills that afflict us, especially with aging, even if they are not among the top killers - problems of vision, hearing, skin.

Not every challenge is equally amenable to solution - need understanding of the scientific opportunity.

In almost every case it is our fundamental knowledge of the biology and chemistry of the cell that is the limiting factor.

Killers:

Heart Disease

Cancer

(AIDS as national emergency - subject of other hearings)

Psychiatric disorders

Schizophrenia; depression (constant and biphasic)

Anorexia / bulimia -- epidemic

Substance Abuse

Aging Population

Arthritis: Vertebral syndromes

Alzheimers & other senile dementias

Diminished, altered immune response

Birth Defects

major anomalies

subtle impairments

Third World Disease is neglected

How it gets back to US!

AIDS should teach us that lesson

Parasitic Disease

Diarrheal disease: cholera and treatment of pediatric US

RESEARCH OPPORTUNITIES :: EXCITEMENT OF LAST DECADE.

{I will mainly elaborate on these, as reflecting my own specialized interests. Research Briefing Papers of the Institute of Medicine offer more detail on many.}

Most advances came without any way to foresee what the detailed application to disease would be

Molecular Biology

Last 40 years -- spanning my own career in science -- have been of the greatest excitement. The substance DNA is found to embody the blueprints of the cell. We can deal with DNA in material terms, diagnose its detailed structure in health and disease, move sections of DNA from cell to cell.

This has also spawned the new biotechnology, enabling the production of powerful physiological agents not otherwise available (e.g. pituitary growth hormone, TPA (for blood clots), interferons, interleukins, many enzymes, etc.) as well as new vaccines.

Whatever headway has been made in understanding AIDS virus in the last few years has come entirely from molecular biology.

Gene therapy (misnomer) also proposed, to "fix" defective body cells -- not hereditary traits in germline!

Most important, however, is not those technologies, but the understanding we can get of how the cell works.

Mapping the Human Genome - how DNA works and is regulated

There are about 3 billion "nucleotide" units in the DNA of every human cell. Proposal for systematic project to map the totality. We should get there, and need new technology, but in my view better by problem-focussed research than by brute force. E.G. one investigator will want to type all the DNA that has to do with the development of the retina, another with susceptibility to virus infection, and so on. However, some systematic mapping is a good idea -- like getting the baseline maps of the geodetic survey, but more selective approach before we drill deep holes in every square inch.

Oncogenes are an important subset of these genes. Found in normal cells, but also in cancer-causing viruses in animals, and in altered form in cancer cells. Our best clue to what cancer is, and how it is caused. About two dozen different oncogenes now known, just being sorted out what they do. Already being used for diagnosis; help us understand hereditary cancer, with inborn propensity for cancer (retinoblastoma). Some genes suppress cancer; cancer develops when those genes are damaged. Helps explain why same kinds of chemicals and radiation cause hereditary mutations and cancer.

Concept of "receptors" -- important new organizing concept.

Cells need to exchange signals with each other and with the immediate environment. Cell surfaces have specific signal-receivers or receptors. applications to everything from heart disease: how cells recognize cholesterol and take it up from blood

cancer: signals control pace of growth of cells

immunology: activation of lymphoid cells to make antibody
derangements in auto-immune disease, AIDS, other infections

brain: how one nerve cell signals another, it puts out a chemical signal that binds to the receptor (across the synapse) of the next cell. Problems arise when receptors are overstimulated (schizophrenia; mania) or under (depression) in specific parts of brain.

virus infection - how viruses attach to cell surfaces, then penetrate and harm them

Monoclonal antibody; cellular immunology

Exquisitely specific reagents for diagnosis and treatment.

acquired by culturing (cloning) single cells of immune system involved in making one specific antibody. Then trick of fusing these with a cancer cell line that makes them grow and work overtime in making antibody.

Blood supply can now be protected from AIDS

Exploration of auto-immune diseases (arthritis?); Multiple sclerosis?

Computer science

Diagnostic Imaging: CAT scanners; Magnetic Resonance Imaging which avoids excess radiation exposure in diagnosis.

Spillover: Research on Artificial Intelligence in Medicine.

originally directed at the development of diagnostic assistance in medicine, led to the development of expert systems, which are the leading edge software for industrial application today.

Neurobiology

Organization of the brain

How the nerve impulse works; chemistry of neurotransmitters and application to new medications for psychiatric disorder and blocking agents for treatment of drug abuse.

MEANS OF RESEARCH AND TRANSFER INTO PRACTICE.

facilities

people

maintaining integrated perspective

e.g. clinical research

institutional performers taken for granted

need for investment outlook - people not projects

capital needs; overhead issues

(Detailed discussion in White House Science Council Report
on Health of Universities)

private sector

main avenue of technology transfer

three sectors working better than ever

international competitiveness in biotech

medical education

equally important avenue of tech-transfer

research setting not excessively driven by project performance
but by quality of mind and effort indispensable

how attract gifted, dedicated people into medicine and medical
research? Offer stability of opportunity, confidence of
pursuing long shots, that years of arduous training will be
rewarded with confidence in their own judgment.