PRESIDENTIAL ADDRESS

Science as a Way of Life: Perplexities of a Physician-Scientist

Floyd E. Bloom

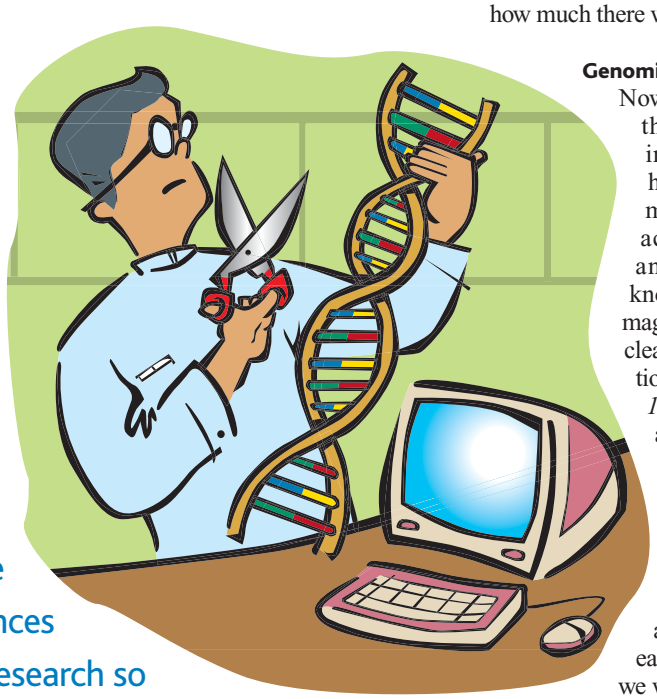
A growing problem of major proportions has been staring us in the face for many decades. Until solved, this long-neglected problem presents a gigantic obstacle to the application of the discoveries flowing from biomedical research into deliverable standards of medical practice that could benefit all of society, both in the United States and globally. This problem is the imminent collapse of the American health system. Unless steps are taken soon to undertake a comprehensive restoration of our system, the profound advances in biomedical research so rapidly accruing today may never be effectively transformed into meaningful advances in health care for society.

Today's term for such evolutions of discovery into application has been dubbed "translational research" (*1*). The appealing notion that research advances travel from bench to bedside is laudable, but conceptually flawed. Even though the U.S. Congress fully anticipates that funding to the National Institutes of Health (NIH) will result in advances in clinical medicine and that other forces, presumably nongovernmental (*2*, *3*), will translate the latest in exciting science into health technologies, under the systems of health care we have today, this advancement is not likely to happen.

Unless steps are taken soon to undertake a comprehensive restoration of our system, the profound advances in biomedical research so rapidly accruing today may never be effectively transformed into meaningful advances in health care for society.

The Delusions of Success

I have been reflecting on the decisions that led me to abandon my incomplete training as a physician for the exciting vistas of what has now become the field of neuroscience. My goals as a student and resident physician were to learn enough about diseases to help others by treatment and prevention of diseases. My introduction to clinical neuroscience research in the setting of the National Institute of Mental Health's Clinical Neuropharmacology Research Center at St. Elizabeth's Hospital in Washington, DC, a massive federal hospital for the mentally ill, allowed me to focus on understanding the pathophysiological mechanisms of depression and schizophrenia. It was my good fortune to be present at the dawning of psychopharmacology, and to work in one of its principal centers of discovery, the NIH Intramural Research Program. In that era, we were thrilled when recognition of the common emotional responses to drugs affecting brain chemistry in humans and experimental animals led to testable hypotheses of depression (*4*); when studies of the adopted-away children of patients diagnosed as schizophrenic helped to sort out the genetic influences in that disease (*5*, *6*); and by the initial efforts to image the brain's blood flow and infer regional changes in underlying neuronal activity (*7*). How little we knew about how much there was to learn.



Genomic Aspirations

Now fast-forward 40 years to the announcements of the initial compilations of the human genome (*8*–*10*), a monumental coordinated achievement, outstripping any other prior biological knowledge base by orders of magnitude. This deluge of data clearly has enormous implications for medical science (*11*, *12*). The pages of *Science* and other learned journals have been loaded with anticipations of postgenomic medicine (*12*–*15*). These vistas predict a time when we will be able to recognize an individual's vulnerabilities to inheritable, disease-causing factors and when we will be able to help those individuals prevent the onset of their diseases. Even though most human heritable diseases are not the result of single dominant or recessive genetic mutations, the studies of strongly inheritable diseases have provided solid clues to help understand sporadic and complex, multigenic diseases such as cardiovascular, metabolic (*16*), and brain diseases.

Nevertheless, even diseases whose genetic origins have been fully defined are not always easily treated. Two that continue to baffle modern medicine are Huntington's disease (*17*) and Lesch-Nyhan syndrome (*18*). Although the dysfunctional proteins of the mutant genes are known, the causes of their unique neuropathologies and behavioral outcomes remain unknown after decades of study. Tellingly, expression of the mutant genes in mouse models or its knockout fails to replicate the human neuropathology (*19*).

ILLUSTRATIONS: TIM SMITH

The author is in the Department of Neuropharmacology, The Scripps Research Institute, La Jolla, CA 92037, USA. E-mail: fbloom@scripps.edu
This essay is adapted from his Presidential Address to the AAAS annual meeting in February 2003; a portion of these remarks was also presented to the Class of 2002, University of California–San Diego, School of Medicine, in June 2002.

Complex Genetic Diseases of the Brain

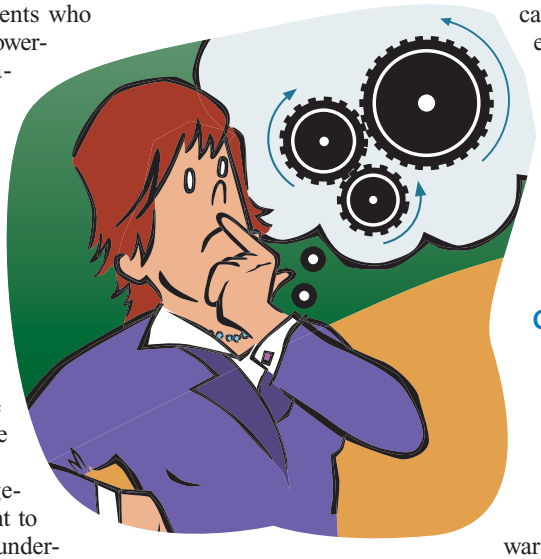
In many of the most prevalent human brain diseases, genetic vulnerability arises from multiple interactive inheritable factors. Scholars of Alzheimer's disease, for example, recognize that at least four different genetic mutations can render members of some families at high risk to the disease (*20*–*25*). Mutations of the gene encoding amyloid precursor protein (APP), a protein of unknown function, on human chromosome 21, and of two alleles (alternative genetic forms) of the apoliprotein E gene on chromosome 19 create conditions that greatly increase risk for the disease, especially at younger ages. Treatments aimed at preventing the inferred consequences of these mutations are currently hoped to be new strategies for the treatment of Alzheimer's. They range from vaccines for absorbing the bad fragments of APP (*26*, *27*) to enzymes to block the abnormal proteolysis, a possible function of the two presenilin vulnerability genes on chromosomes 1 and 14 (*22*, *28*–*30*). A surprising clue may come from the reduction in risk for Alzheimer's disease seen in patients who are taking the lipid-lowering statin medications, an effect that occurs for reasons that are not yet clear (*28*, *31*). A treatment for Alzheimer's disease no longer seems hopeless, but converting today's clues into tomorrow's medications will require considerably more effort.

Other exciting genetic leads may point to new approaches to understanding the origins of schizophrenia and depression, diseases that have been recognized for centuries but were considered untreatable until the last 40 years. One recent study (*32*) has applied powerful genetic sequencing methods to study a segment of chromosome 13 in several hundred adults in France diagnosed with schizophrenia, yielding highly suggestive support for one of the hypothetical neurochemical intermediaries of schizophrenia (*33*, *34*), namely, the NMDA (*N*-methyl-D-aspartate) glutamate receptor (*35*, *36*). These findings, enabled by the power of high-throughput sequencing, make this intervention target even more promising [see (*34*) for review]. Other genetic and cellular abnormalities in schizophrenia are being hotly pursued [see (*37*) for review, and (*38*–*45*) for recent examples of ongoing studies]. Leads are emerging for factors that predict treatment successes with serotonin selective reuptake inhibitors (*46*, *47*), and vulnerability to depression (*48*) and suicide (*49*). Clearly, we are only now beginning to know what we didn't know (*50*).

> There has been enormous progress in the biomedical understanding of disease mechanisms, and the consequences for health promotion have been equally enormous.

Behavioral Steps in Health Promotion

These examples illustrate that taken at its best, there has been enormous progress in the biomedical understanding of disease mechanisms, and the consequences for health promotion have been equally enormous. These sorts of advances have resulted in reductions in cardiovascular illness and in deaths from cardiac causes through scientific insight into the biology of vascular endothelial cells, blood-borne lipids, the early warning signs of ischemic heart disease, and the multiple ways to open and keep open the coronary arteries. Today, lipid-lowering drugs are among the most widely prescribed drugs in the United States.



> Converting today's clues into tomorrow's medications will require considerably more effort.

Times Have Changed

Most medically oriented scientists who were trained in the golden age of academic medicine, that is, before 1965 (*2*), have believed (if they have been healthy) that the health care delivery system would implement their discoveries when the weight of evidence was sufficient to merit clinical application. We recall a time when the indigent ill were welcomed into our academic medical centers (they were not yet termed "health" centers) and their affiliated municipal hospitals of the city and county governments. In return for allowing young physicians to learn responsible diagnostic and therapeutic problem-solving methods, these generally willing patients were able to receive the best treatments available for little or no out-of-pocket expenses. Our faculty taught us the art of taking a medical history and of performing a physical examination, and took the time to help us analyze and hone our problem-solving skills, which we in turn passed on to still more inexperienced student physicians in shoulder-to-shoulder service at the bedside (*2*). Those of us who took a turn away from the bedside to pursue opportunities at the research bench made the assumption that our clinical experience would always be a foundation to which we could return through our research. Regrettably, we were wrong!

The Crisis in Medical Care Cannot be Ignored

As numerous strong reports from the Institute of Medicine over the past 4 years have repeatedly pointed out, the U.S. health system is failing in front of our eyes (*51*–*53*), despite consuming a very significant and growing percentage of the gross domestic product, and representing the biggest employer in many communities (*54*). The president has recently reacted to some of these concerns by proposing new legislation limiting the malpractice awards to patients suing their physicians for errors leading to major pain and suffering. Yet capping awards will not end the pain and suffering from errors committed in a system that is no longer able to cope with the pressures of daily practice. This failure is not due to incompetent practitioners, but rather to the systemic failures among physicians, patients, and nursing staffs to communicate rapidly and effectively. Several states have previously enacted similar legislation, which does seem to have held malpractice rate increases in check. Yet even those states are experiencing consistent annually rising rates of health care cost coverage.

In states where no caps exist on malpractice claims, the accelerating pace of insurance coverage premiums, combined with

ILLUSTRATIONS: TIM SMITH

loss of practice profits as third-party payers set rates for service provision, is forcing physicians out of practice, a concern especially onerous for radiologists, neurosurgeons, and emergency care physicians. Furthermore, intrusions into the traditional physician-patient relationship by increasing regulatory compliance requirements and third-party payers deciding issues of clinical practice are not simply onerous, but have soured the joys of practice and further reduced the time available for doctors to spend with their patients and to teach the next generations of physicians.

There is now a serious shortage of medical expertise, particularly in those states with the highest rates of malpractice insurance, such as New Jersey, Pennsylvania, and Nevada. Not only are we experiencing shortages in physician-specialists as care becomes more and more sophisticated, but the health system has an even greater shortage of career nurses and nursing educators. The system has more than a million fewer nurses than are currently needed for adequate hospital care; the more patients assigned to a nurse, the lower the expectations for patient survival (*55*).

The current economic downturn has given profit-strapped employers cause to pass a rising fraction of health costs to employees. When employees opt to conserve their funds, more people lose medical insurance coverage. This year, owing to the budget deficits facing states with obligatorily balanced budgets, many states may be unable to provide their share of Medicaid Insurance for the indigent and unemployed, or those employed who are unable to reduce their assets sufficiently to qualify. Furthermore, in border states of the South and West, the cost of caring for indigent foreigners coming to emergency and urgent care facilities has added further unbudgeted expenses to already overburdened operations.

Further expected changes in the demographics of our population and the diseases they face will almost certainly compound today's problems. Thanks to past gains in the treatment of acute cardiovascular and infectious disease emergencies, more adults are living well beyond the previous generations' expected lifetimes. As the population ages, the diseases from which the elderly and not-so-elderly suffer are becoming chronic illnesses, more demanding of care and treatment resources.

Patients loudly express their unhappiness with the lack of choices in physicians, tests, and treatments, and the lack of information to make decisions about their own lives. With multiple unconnected caregivers seeing the same elderly or chronically ill subjects, each for separate conditions, complex, potentially adverse medication interactions will go unchecked. These adverse reactions resulting from miscommunication lead to medical errors, and the spiral into worse and worse care continues.

Patients loudly express their unhappiness with the lack of choices in physicians, tests, and treatments, and the lack of information to make decisions about their own lives.

Everyone has a suggested problem for a part of the crisis. But despite all of the reports and outraged statements by leaders and consumers, no one has offered even partial solutions to the continually rising costs among the employer or private providers, the lack of trained personnel, the rise of the uninsured, and the insatiable hunger for more and more health services. The United States, like Canada and the United Kingdom, has recognized for years that unless we act to implement better programs of individual life-style education for health promotion, we can only expect the costs of fixing preventable health problems to continue to rise (*3*).

Lastly, young physicians are carrying extreme burdens of debt accumulated during their medical education, while managed care has imposed time constraints on the provision of medical education for students (*2*), residents, and fellows [at a time when resident hours are severely reduced (*56*)]. Those concerns and the recognition that nursing personnel are at an all-time low (*55*) tell me that the prospects for receiving good medical care have never looked more worrisome.

How Did We Get into This Mess?

We can trace the origins of today's health dilemmas to 1909, when President Theodore Roosevelt endorsed the enactment of workman's compensation insurance to protect workers in an increasingly mechanized industrial society (*54*).

During the 1930s, in part based on experiences of large military battlefield efficiencies, and the rise of major hospital technology, such as radiology, anesthesiology, and pathology, community and private hospitals became the bastions of health technology, and private physicians deferred to these settings for their access to expensive technology. At the same time, communities saw the rise of Blue Cross and Blue Shield Insurance plans as a means to pay in advance for hospital and physician services. Such "third party" health subscription or insurance plan systems allowed our U.S. hospitals to retain their private, nongovernmental, and independent status (*54*).

Although there had been much discussion in this country of going to a government-sponsored plan similar to the British National Health Plan, which provided access to general practitioners when it was enacted in 1911, the consensus in the United States was against compulsory coverage and in favor of voluntary actions by communities [see (*54*) for more extensive documentation].

In taking the path advocated by community activists, local employers, and charities—that local hospitals should function autonomously as community enterprises—important and far-reaching policy decisions were set in place. One rejected alternative was for the hospitals to become elements of state or federal governments as the agencies of health service provision. A second rejected alternative would have been for groups of hospitals to organize themselves into regional or multistate networks that would constitute an additional form of public, and for-profit, utility. Such health utilities could have been regulated, as were the rising local electricity, gas, and water utilities, as a necessary service provided to the citizens. Instead, the hospital system became the center of the health system and remained independent, distributed, and voluntary—with many municipal and charity hospitals providing care to the indigent (*54*).

Subsequent steps also seemed well intended. Shortly after the end of World War II, the United Mine Workers demanded a plan that would include "full" health benefits in their first new contract negotiations. In the same year, Congress passed the Hill-Burton Act to develop community hospitals for populations of fewer than 10,000, and widespread expansion of the hospital-based health system began.

In 1965, in the midst of struggles over the priorities of guns and butter, Congress passed the Medicare Act (part A for hospital services and part B for physician services) to provide health coverage for the elderly (above 65) and the Medicaid Act to cover the indigent and incapacitated. Suddenly, hospitals that had previously cared for the indigent for little or no cost in return for a steady base of patients for medical education were now entitled to bill the federal government for full reimbursement for those services (*2*).

Congress developed the Medicare and Medicaid programs out of earlier legislation under which the federal government had issued grants to states to cover the cost of care for the indigent. Upon their implementation,

ILLUSTRATIONS: TIM SMITH

the country experienced a massive, pent-up hunger for care that unexpectedly led to enormous cost-overruns, quadrupling the budgetary requirements for such care within 10 years.

In response to their suddenly lucrative opportunities, enterprising physician groups in the 1970s formed Health Maintenance Organizations, that is, groups of specialists practicing to provide integrated coverage. Many enterprising Academic Health Centers saw this as a means to enhance the general levels of care and return some profits to their medical centers and universities. Within the decade, however, for-profit hospital corporations and health insurance companies formed networks of hospitals for greater efficiency and profit, generally with little or no role played by physician leaders. By the 1990s the sense of growing dissatisfaction was unavoidable, and the system was clearly out of control.

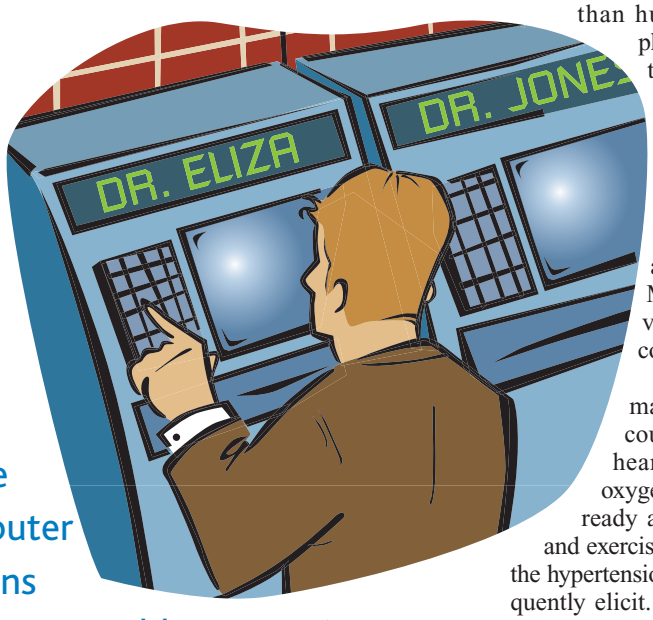
Automated Doctor Machines?

As noted by David Kipnis and Jeffrey Gordon of Washington University in St. Louis, many academic health centers confronted the economic pressures created when, in the early 1990s, the once-profitable clinical practice plans ceased being profitable by a reactive focus on the bottom-line as an end in itself (*57*). In the 1970s, these "practice plans" had provided large subsidies for research and teaching, and for the expansion of faculties. However, as the for-profit systems grew ever more competitive, and as employers resisted cost increases, maintaining profitability for many academic centers became impossible (*2*). When the only goal of a health care system is financial solvency or profit through cost control and increased patient throughput, one can only imagine what the future might hold.

"Eliza" is a so-called artificial intelligence program written in the late 1960s by an MIT professor of computer sciences, Joseph Weizenbaum (*58*). Although intended to demonstrate how badly mainframe computers could emulate human conversations, the results were quite the opposite. Eliza was one of the first computer applications in which users could communicate with remote mainframe computers through the use of a teletype-style input, to which the computer could respond by presenting the user with texts that it generated.

In the guise of a Rogerian psychoanalyst, Eliza would respond to banal comments from the user by syntactically shuffling the words typed on her keyboard and spitting them back out in the form of an assertion. If you asked Eliza a question, "she" would usually respond with another question. Occasionally, she would change directions by focusing on the subject's feelings about their mother or their job.

The results were so convincing that people refused to believe they had been conversing with a computer instead of a skilled analyst. People looked forward to their time with Eliza. People who were charged for their time with Eliza gladly paid. Why would people do this? Because people want to be paid attention to, and to know that the person with whom they are speaking is paying attention to them and their complaints. Eliza always responds with complete sentences. She never just says "Mmmm" or "un-huh," while writing notes in a chart or shuffling through missed phone-call memos between beeps from the pager or tweets from a Palm Pilot.



Eliza was one of the first computer applications in which users could communicate with remote mainframe computers and the computer could respond.

As noted by Leon Eisenberg, a Harvard social psychiatrist, encounters between patients and physicians are increasingly marred by mismatches between what patients want and what physicians are able to provide (*59*, *60*). Patients want enough time to tell their story, to be listened to, to be cared for as individuals. Time and trust are key ingredients of patient-physician relationships (*2*). Regrettably, the pressures of the present version of health care management diminish both time and trust. Interestingly, a recent survey of physicians and patients reported that what concerned them most about today's health care was not medical errors but rather the costs of malpractice, lawsuits, the cost of health care, and the cost of prescription drugs (*61*, *62*).

As the executives in charge of the managed health care systems strive to renew their contracts in the face of this year's 15% cost increase, and next year's projected 22% cost rise, something will have to be done. How can they ratchet up the system's efficiency one more level to see more and more patients, faster and faster, perhaps faster than human physicians and even physician's assistants can do on their own?

Given the ability of Pixar and virtual-reality simulators of the human form (like Lara Croft in Tomb Raider), surely a computer-generated physician version of Eliza in an Automated Doctor Machine must be among the very next developments being contemplated.

This sort of development may not be all bad. Dr. Eliza could immediately assess your heart rate, blood pressure, and oxygen saturation with devices already available in most drug stores and exercise clubs, and probably without the hypertension that initial doctor visits frequently elicit. Dr. Eliza could listen to today's chief complaint, compare that problem with your prior diagnoses in her online records, and reconcile that history with your known allergies, family history, and current medications, all of which will have been instantly updated from authenticated information resources. Any recently reported adverse interactions and contraindications will be duly noted and alerts placed in your records automatically. With proper programming, Eliza will then suggest the proverbial "lie down, take two aspirins, and come back tomorrow," while nature triages the course of your problem.

Dr. Eliza could also complete the insurance papers and e-mail them for reimbursement before the next willing user arrives. And just like the ubiquitous Automated Teller Machine—the ATM—Automated Doctor Machines will be everywhere and gratefully received (when was the last time you remember going into a bank to do banking business?).

The Information Synthesis Challenge

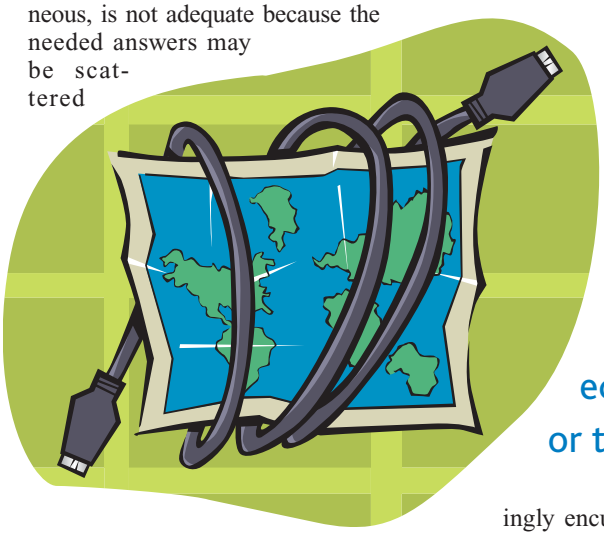
In all scientific disciplines, the database of the published literature is growing exponentially and will soon be unmanageable without intelligent tools to guide us. This is a problem

ILLUSTRATIONS: TIM SMITH

that scientific publishing has recognized for a long time (*63*), but to which clinical practice has generally remained oblivious.

Synthesis of information can be as important as data itself: Wisdom and insight today are being lost in a sea of overwhelming knowledge. The issues are especially important in clinical medicine (in life-and-death situations, where there is a need to act without the luxury of time and without burgeoning new rules) (*64*). In medicine, for example, there are 10,000 drugs, more than 100,000 diseases and conditions, thousands of guidelines, and millions of rules governing them. The rules that should be followed implicitly in practice plans (often essential to life and limb) lie buried inside a sea of facts that is constantly being modified by the clinical literature (*64*).

Document retrieval, even when instantaneous, is not adequate because the needed answers may be scattered among dozens of sources. For example, a typical elderly patient may have 10 major medical problems, be taking a dozen medicines, have numerous allergies and laboratory abnormalities, and have undergone several surgeries. A start-up company launched in San Diego called MyOwn.MD (and on whose board of directors I sit) has created a tool that addresses this problem in a very powerful way. They have converted literally millions of clinical rules into machine language to provide answers to the most complex of medical questions in real time and without physician effort.



The System Must Be Repaired if We Are to Benefit from the Scientific Advances

Several conclusions can be drawn from this analysis. The health care system has become more and more automated and rigid in the pursuit of cost reduction. This evolution has occurred just at the time when science is revealing the need for a highly flexible system with a different focus. The transition from symptom- and disease-driven medicine to a predictive, preemptive, preventive postgenomic medicine will be slow and costly. The very skills and time that will be necessary for the wise clinicians of the future to invest in the study of individual patterns of disease progression are the very features that profit-driven, high-throughput care systems eschew and that insurers will refuse to cover. If predictions that the medications of the future will be molecularly tailored to individual needs hold true, the cost of getting such tailored medications through a drug-approval process that demands that consumers receive risk-free efficacy will simply be prohibitive. The current system can scarcely meet today's needs, let alone the costs of such a transition.

In a recent report, the Institute of Medicine's Clinical Research Roundtable concluded that "clinical research is increasingly encumbered by high costs, slow results, lack of funding, regulatory burdens, fragmented infrastructure, incompatible databases, a shortage of qualified investigators and willing participants" (*65*, *66*). According to this latest analysis, we do not have sufficient capacity to incorporate new knowledge, let alone new ways of using that knowledge for the diagnosis or treatment of disease.

We do not have sufficient capacity to incorporate new knowledge, let alone new ways of using that knowledge for the diagnosis or treatment of disease.

The physician-scientists of the past are an endangered species (*67*–*69*). Those who remain the most viable candidates for the translation of science to health are indeed a vanishing and fragile resource that must be part of any restorative process (*66*). We urgently need to begin the expansion and training of a new cadre of academic health practitioners to fill the gap between basic scientific discoveries that inform us about the unknown elements of the life process, and the practical steps needed to provide societal benefit from those insights. It is a form of science termed by the historians Holton and Bonnert "Jeffersonian Science" (*70*, *71*)—a form of use-inspired engineering of the kind that delivered transistors and lasers from the insights provided by physics, and the novel products provided by modern chemistry.

A Call to Fix It

Scientists must now unite to insist that the system be prepared for the discoveries of the future and that we fulfill as quickly as possible the major needs of today's global health problems. In my view, it is time to seek a New National Consensus to Restore the American Health System, enabled by a Commission from the President elected by the 2004 ballot. The consensus must consider all of the problems noted here: restoring the incentive to be a physician or nurse; restoring medical care and treatment affordable by the consumer, the provider, and the payer; standardizing the best practices for diagnosis, treatment, and outcome assessment so that systems of care provision can be compared; reducing the occurrence of practice errors by implementation of a modern system of communication; accelerating the recovery from the diverse published literature of information on clinical issues and their interactions; and implementing preventive medicine with a renewed emphasis on public good health in which the consumers of health services accept responsibility for their own health maintenance (*72*). Indeed, to benefit from the discoveries that have already flourished as the NIH's budget has doubled, we must create a translational health system in which research discoveries flow to clinical trials to best-practice standards to those exceptions that will define the feedback to fuel new discoveries. We must restore a system that can welcome the new insights and exploit them.

While AAAS alone cannot drive such reform, our commitment to advance science and serve society demands that we seek such reforms and do so promptly. We must gather the full rosters of stakeholders who can make decisions to go into the why's and wherefore's of what we are about, what we want our health care system to provide, and what we are willing to spend and invest to make that happen. The decisions of the 1930s that made the hospital systems of America into a self-standing emporium of then-modern technology may well require reanalysis. Hospitals were once seen as community-based, charity-based, teaching-intensive institutions, and yet in their zeal to become the profit-based vehicle of today, they have degraded, if not lost, all of these attributes.

If we agree that we must have a system that can provide for the dissemination of the best of modern medical technology [and clearly, some communities have been able to do so (*73*)], then, as the Institute of Medicine has said, we must be prepared to

ILLUSTRATIONS: TIM SMITH

pay that price. But what system should that be? One possibility is that the basic medical system should be available to all who live in and contribute to our society in the same way that clean water, gas, and electricity are available, as closely regulated utilities with profit margins fixed by regulatory commissions and with charges to the users for the amounts consumed.

Perhaps, as Oregon's Governor Kitzhaber (a physician as well as an elected administrator) has noted (*74*), we need to turn our attention back to community responsibility for health promotion, and to provide individuals with incentives to maintain their health rather than allowing the expectation of free care now paid for by federal and state governments and employers. Richard Mahoney, former CEO and chairman of Monsanto, has proposed that American business should stop providing specific health care plan coverages, and move to a system where the employees, when properly educated, can spend their own money for the care they deem necessary. Business would therefore get out of the annual coverage dilemma decisions that small businesses increasingly cannot afford (*75*). Suppose, for example, that in order to qualify for a basic level of universal coverage, one were required to have check-ups at various critical life points, the way new automobiles were required to be inspected in order to maintain the factory warranty?

Clearly, there is a pressing need for innovative and extensive reevaluation of the U.S. health care system. To do less would be tantamount to never having done the research of the last 25 years. Doing nothing is a severe form of doing less. Inaction will extend the period of nontranslation of the discoveries of the next decade that the past discoveries have enabled to flourish. Those of my era simply do not want to see their lifelong career investments contribute nothing to our global society's health.

I look forward to hearing your suggestions as to how we can help a great enterprise restore itself to effectiveness at reasonable expense and how we can help ourselves learn to accept responsibility for the decisions we make that can adversely affect our health. In closing, let me remind you of some excerpts from last year's Presidential Address by Peter Raven: "The challenges that we face are enormous and deeply rooted in relationships neglected for far too long. We must find new ways to provide for a human society…" (*76*)—and from the 2002 Plenary Lecture by Ismael Serageldin: "For science to realize its full promise and become the primary force for change in the world, it requires that scientists work to engage scientific research in the pressing issues of our time" (*77*). We must ensure that we have a health system that will be able to deliver on the important biomedical discoveries of the past 25 years and the bounties to come from postgenomic medicine—we owe it to our colleagues and to society. Join with the AAAS in this effort; together, we can do more (*78*).

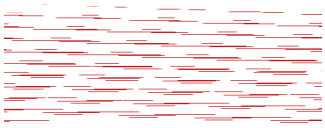
Scientists must now unite to insist that the system be prepared for the discoveries of the future, and that we fulfill as quickly as possible the major needs of today's global health problems.

ILLUSTRATIONS: TIM SMITH

References and Notes

1. D. Nathan, *J. Am. Med. Assoc.* **287**, 2424 (2002).
2. K. M. Ludmerer, *Time to Heal* (Oxford Univ. Press, New York, ed. 1, 1999).
3. A. Robins, P. Freeman, *Pharos* **65**, 22 (2002).
4. J. J. Schildkraut, S. S. Kety, *Science* **156**, 21 (1967).
5. D. Rosenthal, P. H. Wender, S. S. Kety, J. Welner, F. Schulsinger, *Am. J. Psychiatry* **128**, 307 (1971).
6. S. S. Kety, D. Rosenthal, P. H. Wender, F. Schulsinger, *Am. J. Psychiatry* **128**, 302 (1971).
7. M. Reivich, J. Jehle, L. Sokoloff, S. S. Kety, *J. Appl. Physiol.* **27**, 296 (1969).
8. E. S. Lander *et al.*, *Nature* **409**, 860 (2001).
9. J. D. McPherson *et al.*, *Nature* **409**, 934 (2001).
10. J. C. Venter *et al.*, *Science* **291**, 1304 (2001).
11. A. Cravchik, G. Subramanian, S. Broder, J. C. Venter, *Arch. Neurol.* **58**, 1772 (2001).
12. G. Subramanian, M. D. Adams, J. C. Venter, S. Broder, *J. Am. Med. Assoc.* **286**, 2296 (2001).
13. B. Childs, D. Valle, *Annu. Rev. Genomics Hum. Genet.* **1**, 1 (2000).
14. G. Jimenez-Sanchez, B. Childs, D. Valle, *Nature* **409**, 853 (2001).
15. F. S. Collins, V. A. McKusick, *J. Am. Med. Assoc.* **285**, 540 (2001).
16. S. O'Rahilly, *Eur. J. Endocrinol.* **147**, 435 (2002).
17. A. B. Young, *J. Clin. Invest.* **111**, 299 (Feb. 2003).
18. J. E. Visser, P. R. Bar, H. A. Jinnah, *Brain Res. Brain Res. Rev.* **32**, 449 (2000).
19. S. H. Elsea, R. E. Lucas, *ILAR J.* **43**, 66 (2002).
20. G. Ermak, K. J. Davies, *Drugs Today* **38**, 509 (2002).
21. J. Hardy, *J. Alzheimer's Dis.* **3**, 109 (2001).
22. P. J. Harrison, M. J. Owen, *Lancet* **361**, 417 (2003).
23. J. M. Schott, N. C. Fox, M. N. Rossor, *J. Neurol. Neurosurg. Psychiatry* **73** (suppl. 2), II27 (2002).
24. D. J. Selkoe, *Science* **298**, 789 (2002).
25. S. S. Sisodia, P. H. St George-Hyslop, *Nature Rev. Neurosci.* **3**, 281 (2002).
26. D. M. Holtzman, K. R. Bales, S. M. Paul, R. B. DeMattos, *Adv. Drug Deliv. Rev.* **54**, 1603 (2002).
27. D. Schenk, *Nature Rev. Neurosci.* **3**, 824 (2002).
28. L. Bertram, R. E. Tanzi, *J. Mol. Neurosci.* **17**, 127 (2001).
29. S. Gandy, *Neurobiol. Aging* **23**, 1009 (2002).
30. P. M. Mathisen, *Drug Discov. Today* **8**, 39 (2003).
31. T. Hartmann, *Trends Neurosci.* **24**, S45 (2001).
32. I. Chumakov *et al.*, *Proc. Natl. Acad. Sci. U.S.A.* **99**, 13675 (2002).
33. J. P. Mothet *et al.*, *Proc. Natl. Acad. Sci. U.S.A.* **97**, 4926 (2000).
34. M. Williams, *Curr. Opin. Investig. Drugs* **4**, 31 (2003).
35. J. W. Olney, J. W. Newcomer, N. B. Farber, *J. Psychiatr. Res.* **33**, 523 (1999).
36. J. W. Olney, N. B. Farber, *Arch. Gen. Psychiatry* **52**, 998 (1995).
37. C. R. Cloninger, *Proc. Natl. Acad. Sci. U.S.A.* **99**, 13365 (2002).
38. G. J. Popken, W. E. Bunney Jr., S. G. Potkin, E. G. Jones, *Proc. Natl. Acad. Sci. U.S.A.* **97**, 9276 (2000).
39. K. Mirnics, F. A. Middleton, A. Marquez, D. A. Lewis, P. Levitt, *Neuron* **28**, 53 (2000).
40. R. Freedman *et al.*, *Am. J. Med. Genet.* **105**, 794 (2001).
41. L. Tremolizzo *et al.*, *Proc. Natl. Acad. Sci. U.S.A.* **99**, 17095 (2002).
42. S. E. Hemby *et al.*, *Arch. Gen. Psychiatry* **59**, 631 (2002).
43. S. Leonard *et al.*, *Arch. Gen. Psychiatry* **59**, 1085 (2002).
44. L. D. Selemon, J. Mrzljak, J. E. Kleinman, M. M. Herman, P. S. Goldman-Rakic, *Arch. Gen. Psychiatry* **60**, 69 (2003).
45. P. O. Koh *et al.*, *Proc. Natl. Acad. Sci. U.S.A.* **100**, 313 (2003).
46. B. G. Pollock *et al.*, *Neuropsychopharmacology* **23**, 587 (2000).
47. L. Iversen, *Mol. Psychiatry* **5**, 357 (2000).
48. A. Neumeister *et al.*, *Arch. Gen. Psychiatry* **59**, 613 (2002).
49. D. C. Purselle, C. B. Nemeroff, *Neuropsychopharmacology* **28**, 613 (2003).
50. S. S. Kety, *N. Engl. J. Med.* **276**, 325 (1967).
51. K. Adams, J. M. Corrigan, Eds., *Priority Areas for National Action: Transforming Health Care Quality* (National Academy Press, Washington, DC, 2003).
52. Institute of Medicine Committee on Quality of Health Care in America, *Crossing the Quality Chasm: A New Health System for the 21st Century* (National Academy Press, Washington, DC, 2001).
53. L. T. Kohn, J. M. Corrigan, M. S. Donaldson, Eds., *To Err is Human: Building a Safer Health System* (National Academy Press, Washington, DC, 2000).
54. R. Stevens, *In Sickness and in Wealth* (Johns Hopkins Univ. Press, Baltimore, MD, ed. 2, 1999).
55. L. H. Aiken, S. P. Clarke, D. M. Sloane, J. Sochalski, J. H. Silber, *J. Am. Med. Assoc.* **288**, 1987 (2002).
56. Accreditation Council for Graduate Medical Education http://apdim.med.edu/acgmereport.pdf (2002).
57. J. I. Gordon, D. M. Kipnis, *Pharos Alpha Omega Alpha* **62**, 9 (1999).
58. J. Weizenbaum, *Commun. ACM* **9**, 36 (1966).
59. L. Eisenberg, *Arch. Intern. Med.* **159**, 2251 (1999).
60. L. Eisenberg, *J. Am. Med. Assoc.* **274**, 331 (1995).
61. R. J. Blendon *et al.*, *N. Engl. J. Med.* **347**, 1933 (2002).
62. T. H. Lee, *N. Engl. J. Med.* **347**, 1965 (2002).
63. F. E. Bloom, *Brain Res.* **886**, 1 (2000).
64. A. Ghouri, in www.myown.md, F. E. Bloom, Ed. (2003).
65. N. S. Sung *et al.*, *J. Am. Med. Assoc.* **289**, 1278 (2003).
66. R. Rosenberg, *J. Am. Med. Assoc.* **289**, 1305 (2003).
67. L. Rosenberg, *Science* **283**, 331 (1999).
68. T. J. Ley, L. E. Rosenberg, *N. Engl. J. Med.* **346**, 368 (2002).
69. R. M. Steinman, M. Szalavitz, *Cerebrum* **4**, 61 (2002).
70. L. Branscomb, G. Holton, G. Sonnert, Eds., *Science for Society* (Belfer Center for Science and International Affairs, Cambridge, MA, ed. 1, 2001).
71. G. Sonnert, G. Holton, *Ivory Bridges* (MIT Press, Cambridge, MA, 2002).
72. R. S. Williams, H. F. Willard, R. Snyderman, *Science* **300**, 549 (2003).
73. Malcolm Baldrige Health Care Quality Award, 2002; www.nist.gov/public_affairs/releases/ssmhealth.htm (2003).
74. J. Goldsmith, *Health Affairs* **24**, 114 (2003).
75. R. J. Mahoney, *Directorship* **25**, 2 (1999).
76. P. H. Raven, *Science* **297**, 954 (2002).
77. I. Serageldin, *Science* **296**, 54 (2002).

78. I thank A. Leshner, W. Peck, J. Morrison, D. Kupfer, and J. Corey-Bloom for their guidance and suggestions.



Editor's Summary

Science as a Way of Life: Perplexities of a Physician-Scientist
Floyd E. Bloom (June 13, 2003)
Science **300** (5626), 1680-1685. [doi: 10.1126/science.1085535]

Science (print ISSN 0036-8075; online ISSN 1095-9203) is published weekly, except the last week in December, by the American Association for the Advancement of Science, 1200 New York Avenue NW, Washington, DC 20005.