SLIDES NOT ATTACHED

MOLECULAR MEDICINE: SOLUTIONS

Guy's-Johns Hopkins Fiftieth Anniversary Symposium
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I am left with the simple task of offering "the" solutions to the remarkable array of challenges in molecular medicine as described by previous speakers. Quite clearly, we are embarked on a new dimension in medicine which, as we have heard, offers prospects of being able to diagnose and correct, perhaps someday prevent, genetic abnormalities, conceivably even those intrinsic to the cascade of events culminating in cancer or heart disease.

As we probe this new frontier, I believe we face two different sets of problems. First, there are those which are shaped primarily by the advances in molecular medicine, specifically the ethical and legal quandaries as well as the challenge to medicine of accommodating new research modalities--such as structural and computational biology. The second set of problems pertains more broadly to medicine and science today, encompassing new questions of resource allocations, priorities and motivations in science; of how industry, government and academia collaborate and conflict. There is no way to now anticipate the magnitude or shape of all the challenges any more than one could have anticipated a conference such as this as recently as 10-15 years ago. However, it is appropriate to ask whether suitable mechanisms for coping with change are in place or are coming into place.

I am encouraged, even cautiously optimistic, about efforts which have been initiated to come to terms with the new issues posed by molecular medicine. At the very least, the problems are widely acknowledged and have begun to be addressed. The

Human Genome Project, from the beginning, took cognizance of the difficult social issues to be faced and, as you may know, established a Working Group on the Ethical, Legal and Social Implications of the Project--familiarly referred to as ELSI. The Project now supports social science research at a funding level which exceeds all other NIH support for the social sciences. That is a remarkable phenomenon. Meanwhile, on October 3 last year, these issues were given greater scope in the United States through a Presidential Executive Order which established a National Bioethics Advisory Commission. It reports directly to the National Science and Technology Council, and that council is chaired by President Clinton. The Commission's two first priorities are spelled out in the executive order--issues in the management and use of genetic information, including gene patenting and protection of the rights and welfare of human research subjects. It should be noted that commissions with similar concerns for bioethics have been established or are now being established in several European countries.

Meanwhile, the burgeoning research modalities of such as structural and computational biology and informatics are, I believe, effectively and creatively insinuating themselves into the research matrix and are gradually gaining relevant support. There is much to be done but it seems to me there is both good direction and momentum.

Less hopeful of solution are the growing, difficult problems which molecular medicine shares with other parts of our biomedical research establishment as well as with science as a whole. Foremost is the question of resources--for both basic and applied research. We have witnessed in the United States an extraordinary transformation from

the halcyon, optimistic days of the 1960s and 1970s when research support grew rapidly, to a current once unthinkable debate, now engaging both our political parties, as to how deeply basic research budgets should be cut over the coming decade. This debate is being driven, of course, by a chronic federal budget deficit. Lest we forget, however, the primary cause of that deficit is the growing cost of entitlement programs--and medical care is one of its largest components. For the medical community as a whole, I believe it is fair to say in Pogo's words, "we have met the enemy and they is us!"

The broader debate in the United States is over allocations of a gradually shrinking pool of discretionary federal funds from which research is supported. One implicit question in that debate is what serves the nation's longer-term interests best--what sort of balance should be struck between investments in medical care and investments in research?

This is a debate in which United States medical science has not heretofore participated. Until now, the growth of medical care expenditures has been minimally constrained. New drugs, new diagnostic methods and new procedures have steadily been incorporated into the medical armamentarium with few questions and even fewer studies as to costs and benefits. We have debated the extent of entitlement for Medicare and Medicaid and methods for reimbursing health care costs but we have yet to decide how much, as a nation, we wish to assign to health care. Eventually, we have no options but to do this. Difficult, painful choices are necessary as to which medical services we will provide and to whom, and which we will not. Rationing, if you will, will assume an explicit rather than an implicit character.

Likewise, levels of support for biomedical research and training have grown steadily over the years--never, of course, growing as rapidly as we in the biomedical research community feel they should--but growing steadily nevertheless. Allocations of federal funds, which support the bulk of basic science, have been defined primarily by a science community which has had little cause to weigh the potential implications to the health care delivery system of alternative research initiatives. But this situation, too, is changing, forcing conscious decisions to be made.

Hotly debated now, for example, is the question of what balance should be struck in federal funding between research particularly germane to the development of an HIV vaccine versus development of drugs to treat AIDS. How much should be allocated for basic research pertaining to a better understanding of the impact of nutritional and environmental factors on human health versus funds for development of improved cancer chemotherapy? Should we be spending $200 million per year for gene therapy research or should more be devoted to a better understanding of disease pathophysiology? In making these decisions, it is gradually being recognized that the ultimate products of research translate finally into medical care costs and which avenues are favored have substantial cost implications for that system. This is not a new phenomenon. Bear in mind that, at one time, decisions were made to support research relevant to polio vaccine at the expense of improving the Drinker respirator and Sister Kenny's hot packs and physiotherapy.

To many, the broader social policy planning implicit in reaching such decisions is repugnant. The mantra which we have heard so often in the United States is that we

have the finest health system the world has ever known--and the finest research establishment; that our citizens have never been healthier; and that, if the government would simply leave well enough alone, all would be right with the world.

Certainly, our citizens do enjoy better health and a better quality of life than ever in the past and, at the same time, health care expenditures are at an historical peak. What are the implications of augmenting or perhaps diminishing our investments in health care and health care research?

For purposes of this presentation I thought it might be interesting to share with you a longer-term look at what our investments in health care have been and how these relate to one marker of health--longevity. Accordingly, I went back to 1900 which, in effect, provides data for the ~~45~~ 50 years preceding the Hopkins-Guys relationship, and for the ~~45~~ 40 years after--data from 1900 to 1990.

~~SLIDE 1~~ ~~Note~~: Life expectancy at birth in 1900 was ~~47~~ 48 years. (table) It rose to ~~66~~ 69 years in ~~1948~~ 1950--a remarkable increase of ~~18~~ 21 years or ~~39~~ 44%--primarily accounted for by better nutrition, water and housing. It was not curative medicine, as you know, because curative medicine didn't then have that much to offer the populace as a whole. From ~~1945~~ 1950 to 1990, longevity increased by ~~ten~~ seven years, a gain of just ~~14~~ 10%, despite a dazzling new array of antibiotics, diagnostics and therapeutic procedures.

But if we ask the question as to how long a 20-year-old might live, we see a somewhat different picture

(SLIDE 2). In 1900 the average 20-year-old could expect to live to 63 years; in 1945 to 71 years; and in 1990 to 77 years. There has been progressive improvement but far less dramatic than for longevity measured from birth.

Now, we know that 40% or more of our medical expenditures are devoted to those beyond 65 years. Accordingly, might we not expect to see more dramatic changes in longevity among seniors **(SLIDE 3)**. Note that a 60-year-old in 1900 could expect to live to the age of 75; in 1945 to the age of 77 (a gain of two years); and in 1990 to the age of 81 (a gain of four years).

How do these figures relate to expenditures for health **(SLIDE 4)**? Note that in the U.S., health expenditures until 1955 remained at less than 5% of GNP--then they began to climb, reaching 12.6% in 1990 and in 1996, nearly 16%. But there is no apparent relationship between increased expenditures and changes in longevity at any age.

SLIDE 5 Expenditures for the U.K. remained low through 1990, barely exceeding 6%. Life expectancy figures for the U.K., however, are virtually identical to those of the U.S.

The unpleasant fact is that although we have invested increasingly large sums of money in the health and well-being of our populace, and especially of "senior citizens", there is surprisingly little to show based on these measurements.

Now, it must be emphasized that these figures do not reflect "quality of life". Knowing what we do of the remarkable advances in medicine over recent years and given such a substantial health care investment, it would seem, intuitively, that our citizens must be living better quality, if not significantly longer lives. Adequate data to document this, however, simply do not exist. In brief, there are few outcome data which would argue for substantial increases in investments either in biomedical research or medical care. Indeed, as one appraises the advancements in molecular medicine, one views with some apprehension, the potential costs associated with wide-scale genetic screening, and, indeed, with some alarm as to the potential costs of such as preimplantation genetic screening.

We face difficult questions as we endeavor to deal with Archie Cochrans's "margins of impossibility", as we confront the dichotomy of "what should be done" and "what can be done". The laissez-faire environment in which contemporary medicine has emerged is passe. This is reflected now in a burgeoning interest in technology assessment. It is also apparent that managed care organizations, as never before, are questioning both costs and benefits of products, procedures and regimens. New products and new procedures, I suspect, will be subjected to increasingly close scrutiny and in the future will find it more difficult than ever to enter the marketplace. These changes in the clinical care environment will predictably impact both private sector investment in molecular medicine and the translation of its discoveries into clinical products.

It is critical as to who makes these choices. From my experience in the White House and in the Department of Health and Human Services, it seemed to me that

economists, politicians, entrepreneurs and professional administrators have dominated the agendas, joined more recently by special interest groups concerned with the aged, specific diseases and selected organs.

We need to reexamine fundamentals, and the bottom line has to be the healthiest population given the resources available. Epidemiology and Public Health are especially critical to the success of such an enterprise and I am happy to acknowledge a now 13-year-old Hopkins School of Public Health-St. Thomas's collaborative exchange program which has been one of the most productive and contributory of all programs in which we have engaged. Now that Guys' and St. Thomas's have merged, I would hope this might be acknowledged in future celebrations.

Major policy decisions such as we are now discussing demand the input of a diverse constituency but, it seems to me, any process must more actively involve our academic medical centers and in a leadership role. Might this be the time to look to the establishment in both our countries of broadly constituted Committees to examine and decide the balance of priorities in prevention, diagnosis and treatment and to decide broadly our research priorities? Such an effort would require a far more active and public persona from the academic community than that to which we have been accustomed but without that leadership, I fear for the short-term, financially expedient solutions which could cripple our academic health centers and, no less, the future of molecular medicine and medical research as a whole.