

Public Policy and the Health of the Public

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Introductory Remarks

I am honored to have been invited to give this year's Simon Lecture – especially so in light of the distinguished speakers in whose footsteps I follow. In conversation with Dr. Epstein I ascertained that an important theme underlying the lecture series is that of activism. That word has many meanings, but to me it connotes involvement – a way of taking one's knowledge and expertise and putting them to best use in a community context; and so I chose as a title for this talk: "Public Policy and the Health of the Public."

I was a bit abashed at the "hype" advertising my lecture; but at least it makes the point that I have had a varied – indeed, one might say, a checkered – career. Over the years, particularly as I became noticeably involved in public policy matters, students have occasionally asked me "How do I get to do what you do?" During this talk I will give you a partial response to that question – at least I will tell you a bit about how I got to do it. But a short answer is: you must work to become as good as you can be, aiming your best talents at things **you** consider important and interesting; and then you must "look up from the detail" at least long enough to find ways to make your trained self useful to the world.

My career meanderings were governed by that principle, along with two others that served as useful guides, both for me and later for my children. First, don't burn any bridges until you are sure you are done using them; and second, try to make yourself as **uniquely** useful as possible. With those precepts in mind, I went from med student to pediatric resident to virology/infectious disease post-doc to medical school faculty member – and that finally is where I began to recognize the importance of the "unique" part; for by being dually trained in both clinical and basic sciences I began to play a bridging role across the fault line between science and health care that

was just opening then but which has become a gaping chasm in present times. I'll pick up on the further evolution of my career in a few moments, but I wanted to be sure to make those points before getting distracted with anecdotes and stories.

Let me return to my title just briefly. You may notice that I didn't use the term "public health." Public health as an organized field of academic and professional endeavor is related in important ways to the health of the public, but the **terms** are not congruent in their meaning – a fact that is sometimes lost in policy discussion. There is a regrettable tendency to mix and match indiscriminately between "medicine" and "health care," between biotechnologic advance and "major public health benefit." And there is a pervasive assumption, at least on the part of the **medical** profession, that the entire domain of health – public and otherwise -- and all related good works flow from a **medical** education – or at least would, if physicians just had enough time....And therein lies the seed of a serious problem, for in point of fact, there are **several** health professions **for a reason**, and in addition there are many other fields of expert endeavor that impinge directly on the health of the public. To the extent that we are currently in difficulty concerning the nation's health status, not to mention the cost, access to and utilization of care, a very real and affordable part of the solution lies in re-thinking and optimizing medicine's role as part of a teamwork approach in the overall system.

At present, however, the profession of medicine is in the throes of a severe and apparently progressive case of **hubris** – one that seriously threatens our ability to take advantage of what we know just as the blossoms of one hundred years of intellectual endeavor are coming to fruition. In my view we need to back off, to recognize the complexities inherent in our medical efforts in the interest of the health of the public, and to learn to work in teamwork with the other profoundly important components that together constitute the context for optimal human health and well-being.

So teamwork and humility are major themes for this homily – but along the way I will try to give you an idea of how I came to feel so strongly about such things and, in particular, how I ended up from time to time in the public policy arena.

Background stories

Let me tell you some of my own story. First, it must be said that from earliest days I was an inveterate reader. Even as a little kid I can remember the pleasure of squirreling away with a good book in an alcove – sometimes successfully hiding from my mother for hours at a time while she sought me out to do chores. [I grew to suspect that she knew quite well where I was but had just gone along with the ruse, since she was pleased with the rationale.] Anyway, voracious reading has played a huge role in my life, and I am often grateful that I was born before the distractions of television threatened to obscure for me the mesmerizing, transforming effect of a really good book!

I also was of a practical bent, and without realizing exactly what I was doing, I held a series of jobs as a college student that put my wide-ranging curiosity to the test. I worked in sequential summers as a psychiatric aide in a state mental hospital; then as an assistant to the nursing staff in a state institution for the retarded; and next as a medical secretary for the chairman of an academic ob-gyn department. Later on I realized that my early work experience in what one might call “subordinate” roles in the health care system had a lasting effect on my attitudes to the need for teamwork and the efforts of those around me. [In case it sounds like I was all-work-and-no-play, I should tell you that I spent the final summer before medical school occupying – if not always playing -- last chair of the second violin section in a Gilbert and Sullivan troupe on Cape Cod].

When I entered medical school in 1957 it was still that era when it was generally assumed that women (or at least **normal** women) had no place in medicine. Since I had been blessed with an easy capacity to learn, memorize, etc., I wasn't worried about academic success *per se*. Moreover I discovered quickly that my gender could be turned to distinct advantage, in that I stood out, the faculty learned my name instantly, and thus they became more approachable and potentially useful as mentors.

Furthermore – and much to the point – my professors were, in general, very grateful to find out that I had a sense of humor. Political correctness had not yet begun to permeate academia (to put it mildly), and so a sense of humor came in very handy on occasion. I could regale you with superficially sexist anecdotes; but in truth I can only remember two or three

men who seemed to be genuinely and unfairly sexist – the rest just didn't quite know what to make of the likes of me but were sufficiently flexible to find out and to give me the benefit of the doubt (which is, after all, the most anyone can ask for).

Luck was with me, too, in my choice of medical school. I had been accepted at Harvard, where they were eager to attract and admit women, having started to do so only eight years earlier. Instead, however, I enrolled as a member of the fifth class in what was then Western Reserve University Medical School's "New Curriculum," an audacious educational experiment that had just broken the lock-step of twentieth-century medical education irretrievably.

The changes were so drastic that the term "new curriculum" survives to this day; but most people use it rather narrowly to connote the conversion of standard curricular material into an integrated, multi-disciplinary format. However, there was much more to the "new curriculum" than that; for the goal of the ambitious cadre of faculty revolutionaries who launched the new program had been to acquaint medical students with **all** facets of medicine as a profession, from which we could then select a specific career path while at least being aware of the myriad alternatives that coexisted.

Thus, over and above the startling innovations of an integrated curriculum with a pass/fail grading system, we were required to do research one day a week, to continue it in the summers if possible, and then to submit a thesis as a graduation requirement. We were also required to have a family under our care for whom we were shepherded into the role of primary care physician over the course of our four years. And we were strongly encouraged to do something outside of our strictly medical-school endeavors in order to "stay human." For that purpose there was allocated another day a week of "free time," and I interpreted that as an invitation to study art history (which was an hiatus in my liberal arts education), and to do volunteer work sweeping the floors of the Cleveland offices of the American Civil Liberties Union on Saturdays.

Now, experiments like the new curriculum tend to lead to a "Hawthorne effect" – the very fact that an optimistic experiment is in progress leads to an enhanced result. We certainly experienced that; as the fifth class to enter the experimental program, most of the fine-tuning was done and yet ennui had not yet set in. We were excited! I joined (and later

led) something called the Student Educational Policy Committee [think of it – we’re talking mid-fifties here! I have often taken pains to point out that being “radical” in the 1950s was easy: one only had to entertain non-traditional thoughts to qualify].

And I, and a like-minded group of activist classmates, banded together to invite a series of speakers who were well outside of mainstream medicine. One time we asked Walter Reuther to come talk to us about health care and the UAW. On another occasion we invited the head of Kaiser-Permanente to tell us about the earliest incarnation of “managed care,” which was very *avant garde* at the time. Proponents of family planning told of their efforts – keep in mind that this was not only before *Roe v. Wade* but pre-pill! And Dr. Tom Dooley told us about the rigors of saving lives in Laos [which so inspired me that it nearly aborted my future plans as I gave serious thought to climbing on a plane and going to southeast Asia for a prolonged “elective.” That was one of several times when my enthusiasm threatened to get ahead of my ability to be helpful – so it was good that I calmed down in due course.]

On what might be termed the “home front” we had prime seats from which to experience, at a safe distance, a blast of racism so torrid that it was within just a short while of burning down whole chunks of Cleveland (and lots of other parts of the world besides). As students we lived in apartments in the Hough area of Cleveland that were being unabashedly converted from decent to indecent housing. Between our first and second year we were told to **move out** because both the rents and the occupancies were about to be doubled. The landlords didn’t want majority witness to the outrage, and the city fathers winked.

But we hung in there: we joined community groups, and in a city of posh suburbs with names like Cleveland Heights and Shaker Heights, we had stationery printed up with “Hough Heights” as our generic address. [That the times had not yet changed as radically as they soon would was evidenced by the fact that, when I climbed on the bus to go make house calls on “my family” in the Hough Area, I wore my short white coat and carried a black bag as **protection!** Drugs were still a few years away].

So medical school was full of facts and rigorous discipline; but also of broad awakening to the health care issues accumulating and to the racial and

economic fault lines that were about to open wide. But rather than hunkering down, we engaged! In fact, we interpreted our entry into the world of medicine as a pass – an invitation – to involve ourselves with the world at large. I am rather sure I didn't think of John Donne **then**, but hundreds of times later in my medical career his words echoed forward across centuries of pain and progress: "No man is an island. Each is a part of the continent, a piece of the main. Any man's death diminishes me, for I am part of mankind."

Before I go further with the narrative, let me divert briefly to one particularly important course I took in my last year at Oberlin. I saw pre-medicine as something of a non-major. As a liberal arts student I was supposedly becoming broadly educated; but I had learned the word "dilettante" along the way and was worried. I toyed with the idea of doing a double major, but instead I decided to take advanced courses to follow up on "101" in each of as many fields as I could, working on the assumption that if a little knowledge was a dangerous thing, a little more would at least serve a cautionary purpose.

So I took courses in international economics, in abnormal psychology, in modern European history, in biochemistry and – notably for these purposes – I took advanced readings courses in the philosophy of education and of science. In the latter pursuit two life-long insights took form. First, that the basic **strategy** of science is reductionism; and second, that the basic **methodology** of science, when done right, is to attempt to **disprove** testable hypotheses. Those two features of the scientific method twist and turn around the pillars of biomedical progress that now seem so solid. But I think they are poorly appreciated, and failure to recognize their importance and impact can lead to serious distortions.

I'll get back to reductionism later. But the **disproof** of hypotheses deserves a moment of attention, for – while I didn't see it then – it is the most difficult aspect of the scientific endeavor, precisely because it runs so counter to human nature. One observes, one reduces and isolates variables, one sets up possible explanations and then designs and conducts experiments that, ideally, are constructed to shoot down one's very own best ideas! How can one help but be invested in those ideas? Yet how can one do the experiments dispassionately if one is embracing a central dogma? That is the rationale for double-blind controls, of course, for indeed, without

blinding it is rare to watch someone remain entirely uncommitted to a given experimental outcome, much less to stick to his guns in the face of flak.

Later, during my faculty career, I had the privilege of watching at close range as my wonderful colleague, Dr. Howard Temin, stayed tenaciously with his experimental data over many years before the world (and then the Nobel committee) would accept the notion that he (and, subsequently, David Baltimore) had upended the central tenet of molecular biology with the demonstration of reverse transcription. But don't underestimate the flak! It is now legendary, but no less true, that people would walk out of sessions in which Howard was presenting papers with experimental data suggesting ever more strongly that DNA could be copied from RNA; but he slogged on.

Let me return to my main theme, however, for I promised to focus on how I ended up in the public policy arena. Unquestionably my credentials as a so-called "hard scientist" brought me credibility at critical junctures. I'm not going to say much about my several-years career as a laboratory or "basic" scientist (except to tell you that I was a modestly successful one, publishing and not perishing, getting grants and serving on NIH's Experimental Virology Study Section).

But I must admit that I was very susceptible to the distorting effect of that paradox in scientific method, whereby one needs to conjure up one's best ideas but then to attempt to disprove them. I am, by nature, an enthusiast and I tended to love my ideas. When I was just getting started in his laboratory, I was distressed when Dr. John Enders cautioned me that "ideas are cheap" – for coming up with new ways of explaining biological phenomena didn't seem all that easy or cheap to me. A colleague who was a much better scientist than I was summarized my problem well when he commented, during those years, that I was forever having "ideas that deserved to be right." My tendency to iconoclasm was a potent generator of such schemes and theories; but in general, they weren't right. Nevertheless I always went after them with enthusiasm and often had to be "shot down" by tougher-minded colleagues.

Early on, my post-doctoral professor, Dr. Donald Medearis, had spotted that potentially fatal flaw of enthusiasm in my scientific armor. There was a time when I had bounced into his office with a rather flimsy research finding that seemed to lend marginal support to my idea of the day;

and he was clearly worried about my capacity for self-criticism. He said, in anxious annoyance: "By all that's holy, June, know ye that ye may be **wrong!**" Actually he didn't just say it – he **shouted** it! Believe me, that captured my attention. And while, when we later became close friends, he learned that my tendency to enthusiasm wasn't quite as distorting as he feared, it happens to this day when I find myself climbing on another bandwagon about something, that I mutter to myself "...Know ye that ye may be **wrong!**"

So the scientific method *per se* interested me. Dispassion, and a willingness to be wrong, were added to my arsenal, although they needed much attention and care in order to flourish. And I kept on reading with zeal although somewhat furtively. There was a time in my residency at Massachusetts General Hospital when, sitting with the same group of junior and senior staff at lunch every day, I let it slip three times in one week that I had recently read one or another non-medical book. On the third such occasion, one of the faculty at the table turned to me and said, with ill-concealed disapproval: "My, you read a lot, don't you!" From that point on I was much more careful about letting people know of my bibliophilia.

I said I'd get back to reductionism, for that is the other concept that grew in importance for me over the years. I am working my way towards a discussion of hubris, as I said earlier, and much of the source of that hubris resides in a forgetfulness about the intellectual reductionist tricks we play in order to achieve step-by-step progress toward new biomedical insights. I am not enough of a science historian to know if reductionism **originated** with bacteriology, but certainly the microbiologists of one hundred years ago exemplified the approach. From a sea of bacteria they would fish one single bacterial cell and give it a clear pond of its own on an agar plate or in a test tube. That allowed them to ignore the gaudy, confusing variety of its surroundings, and instead let it do its own pure biochemical and physiological thing in splendid isolation.

Reducing the complexity of life thus permitted study of phenomena that were unique to that bacterium – but it also sometimes misled the researchers, for the answers they derived in pristine surroundings had to hold up in an intricately complex world of limited nutrients and competing organisms, susceptible hosts and hostile environs. Pure reductionist science is almost the exact opposite of the chaos of "real life."

In the same way, clinical researchers in more recent years have been trained, appropriately, to isolate one set of questions – does a small dose of daily aspirin influence the risk of heart disease? Does a serum lead concentration above a certain level hurt a child's neurologic status and potential?...and so forth. In a well-designed experiment, new levels of understanding emerge about **that variable**, while all else is held constant. But in the real world, "all else" almost never holds constant – so that the daily dose of aspirin will rarely be the **only** change in heart-disease risk factors, and an environment containing lead is likely to contain other toxic elements that threaten a child's developmental potential as well.

The reductionist approach to human health and disease, backed up by increasingly sophisticated biostatistical and epidemiological sciences, has proved to be a mighty scalpel – dissecting out risk factors and mechanisms of disease and yielding insights that have liberated us from many fears, while identifying specific threats that can be dealt with. It is good, and useful...but it is subject to the same interpretive hazards that pertain to laboratory-based reductionism: individual idiosyncrasy, familial malfunction and potent societal poisons are very active factors in the final therapeutic or preventive equilibrium and it is dangerously misleading to forget them or pretend they are not there.

The great physicist Leo Szilard took up biology in the years after his recantation of work on atomic weaponry. Throughout his career he was a brilliant, iconoclastic thinker who tried to see science clearly and in human context. As the shadow of nuclear war began to glower in the late 1930s, he wrote his own set of Ten Commandments, the very first of which opened with an admonition to **recognize and remember the connectedness of things**. (Another, which grows increasingly relevant as interventionist medicine gathers steam, was "Do not destroy what you cannot create.")

My awareness of the pitfalls of reductionism as they pertained to clinical medicine allowed me, increasingly, to recognize that one must commit to putting pieces back together after having taken them apart for purposes of diagnosis – to seeing the whole picture in the context of patients and their complicated lives. It is superficially attractive to think of **disease as the enemy**; but one needs to be aware that such a mind-set could lead to a sense of failure or rejection if a patient's problem proved chronic or

intractable. Reductionist biomedical science allowed some things to be **cured** – a wonderful fact that was almost never true one hundred years ago.

But in the glow of that success, physicians began to resist involvement with chronic or multifactorial disease, and to resent or even to **blame** patients for what was called “non-compliance.” [In fact, one could actually argue that so-called “failures of compliance” are at least equally the fault of the putative care-giver, if indeed the proposed interventions are truly in the best interest of the patient]. And of course in the real world, cures are uncommon and never guaranteed to last forever – but illnesses and lives tend to go on, and so does the need for care and compassion. One must, indeed, yield up the superwoman cloak from time to time to keep in mind the connectedness of things.

A Fast-Forward to My Faculty Career

I have paused over those special aspects of scientific method and of reductionism because they grew in importance to my thinking as I progressed in my career in medicine. As a medical student, the excitement implicit in their marvelous power was exemplified by the creation of polio vaccines and the addition of new antibiotics to the short list that was available when I started. And technology brought further wonders: I vividly remember the film of the first cardiac catheterization which was shown to us in class (since it was done in Cleveland, or so I was given to understand at the time – and one needed to maintain a positive view of being in Cleveland). We had to accept with faith the assertion that the snaky, jerky whitish shadow was indeed a tube that had been threaded through someone’s blood vessels; and that the intermittent plumes of white cloud that the tube emitted were radio-opaque materials lighting up the inner workings of the human heart. What a leap of faith! But the leap was extended well beyond those shadows, for the implication was left that abolition of human heart disease was just a few steps further down the technological road.

Indeed, there did follow a veritable cornucopia of biomedical advances, wondrous and seemingly all-powerful. But the advances were, in fact, only incremental – leading mostly to what Lewis Thomas referred to as half-way technologies; and the sad fact was that all that extraordinary progress was occurring against a background of racism, classism and social

turmoil that would soon explode with enough fury to slash, scar and then reconfigure our world.

I am glad to remember that I was at least somewhat aware of that discordancy – but ashamed to realize how little it seemed one could do. I guess that is where, over the years, I changed most profoundly – for over the years I have found that it is a truly remarkable fringe benefit of being a well-trained professional and maintaining one's awareness of the needs of one's community to find out just how **much** one can do. My beloved friend Jonathan Mann, who died at age 51 in the Swissair crash in 1998, had managed to change the world in stunning ways before his tragic and untimely death. He was the quintessential activist, and he chose the hardest path possible, working within the stiff and bureaucratic constraints of the international health community. And concerning activism, he said: "Some people say that you can't change the world. But if we don't try, will it change?"

Again, I must get back to business. I finished medical school, did pediatric training in Boston, virology and infectious disease training at Johns Hopkins and at Pittsburgh, and then began my faculty career. Again, luck and fate took a curious guise – nepotism laws were still in sway at the University of Wisconsin where my about-to-be-husband was being sought by the Department of Pediatrics. The rule was that spouses could not have dominant appointments in the same department. I was co-equally trained as a pediatrician and as a virologist at that point. Furthermore, they already had a pediatric infectious disease person. And so I became, officially, a medical microbiologist and took over the teaching of infectious diseases in the preclinical curriculum for the medical school. That suited me well, since I happily had a son and then twin daughters fifteen months later, and I felt that when I needed to cut corners in the interest of my kids, my career (rather than someone else's children) was what would be at stake. In fact I later ended up doing plenty of pediatric infectious disease, since the Department of Pediatrics suddenly lost the faculty member who had been playing that role; but by that time I had control of the situation and was able to call my shots.

And as a virologist, I had fallen into a veritable bed of clover – for I had colleagues like Duard Walker and Howard Temin, Roland Rueckert and Bob Hanson, who were preeminent leaders in the newly emerging field of virology. We team-taught graduate courses together, ran joint seminars,

served on doctoral students' committees, and kept each other current and on our toes. When Howard won the Nobel Prize in 1975 it was a particular thrill since he was as modest, analytical and thoughtful as anyone I had ever known; and when his critiques of my science seemed particularly cutting and I complained, he would say "You'd rather hear it here at home, wouldn't you?"

Howard's rigor had a profound effect on me in many ways, but one is worth noting in view of what happened next. In 1975 a new virology study section was created at NIH, since the original one (on which Howard was serving) was being flooded with applications. I was asked to be on the new one and said to Howard, when my first stack of 135 applications arrived: "I understand what to do with the fifteen for which I am primary or secondary reviewer...but what do I do with the rest?" His reply was: "That's everybody's own decision. As for me, I read them."

So I did too, and thus ended up inadvertently well prepared for what was looming in our future. Over my years on study section (1975-1980) we reviewed dozens – in fact hundreds – of research proposals having to do with retrovirus infections. I used to complain about that, muttering sourly that I thought it was outrageous to give them so much time and attention when there wasn't a single known retrovirus infection of humans! I was, of course, about to be VERY wrong – for HIV was spreading silently and relentlessly in human populations around the globe even as I complained!

And then came a final factor that impelled my entry into matters of public policy: in 1972 Eliot Richardson, then-Secretary of Health, Education and Welfare, declared that HEW advisory committees should include women in their representation. I'll never know how he came up with 42% as the appropriate fraction, but he did – which meant that nearly 600 positions should be filled by women at a time when there were only 300 tenured women faculty in all the nation's medical schools. My colleague Duard Walker spotted the announcement of Richardson's fiat in Science and put it on my desk with a note attached that read like a Chinese fortune cookie, saying "You will get many offers; hold out for what you want." And boy, was he right!

The first several requests were highly inappropriate to my expertise, and I was in full turn-down mode when I got a call one day from Saul Krugman asking me to serve on an FDA panel whose charge was to review

all existing licensed viral and rickettsial vaccines – both the generic licenses and the specific products on the market – for safety, efficacy and appropriate labeling. Efficacy had only just been added to that list of FDA mandates and a number of the vaccines for such diseases as yellow fever and smallpox predated the criteria that had later become available to judge them. I was torn; there was no question that I was appropriately trained for **that** task, but it sounded so dull....never have I been more wrong! Over the years from 1973 to 1979 our panel (composed in equal numbers of members over 60 and under 40, in order to achieve a balance, I suppose) not only reviewed those licenses, but we got caught in a maelstrom of dissident complaint and legal protest that threatened to depose the very capable leadership of the Bureau of Biologics at the FDA.

There are some talents you don't know you have until they are called for. In my case it turned out that, under those kinds of circumstances, I was able to remain cool and analytical in the face of ferocious attack and, furthermore, that I could communicate clearly and in plain language with the press. As time went on it became customary for the "feds" to cast me in lead roles, and when in 1977 Russian flu followed quickly in the wake of "swine flu," I was pressed into service to chair and/or summarize meetings at the level of the Secretary of HEW, who by then was Joseph A. Califano, Jr. [To this day Joe has remained both a public policy mentor and a wonderfully supportive personal friend.]

Finally came AIDS. People have asked how I happened to be involved in it so quickly, for by January of 1984 I was made chairwoman of the NIH's advisory group on AIDS and the nation's blood supply, a role I held until 1989 when I was elected chair of the National Commission on AIDS. But there wasn't much mystery about why they turned to me: it was as if I had been in training for the epidemic, with both virology and clinical infectious disease in my background, and plenty of time logged as both a federal advisor and as a communicator to the press. And all of that was needed, as you know, for the complexity of the AIDS epidemic begged every question I had ever pondered and added vastly more to the long list of unknowns with which we were grappling. All of my awareness of complexity, of the social context within which dreadful epidemic things were happening, and of the need to bring both expertise and compassion to the approach to matters of public health were put to the test. And all the eclectic reading I had been doing suddenly took on the value of my most

cherished resource. Even so, as I look back I am humbled to realize how little I knew then, and what a steep learning curve I had yet to mount.

Cases in Point: Public Policy and AIDS

Obviously there is a long story there that won't be told today; but I started this talk by saying that, to do what I did, one needed to be deeply trained and then look for ways in which that competence could help. At the outset of the AIDS epidemic we had to deal with raw fear, and later (and still) with the public's insistence on what I call "**their perceived right to be fearful.**" But with time, reductionism served; HIV was identified and vaccines suddenly loomed as the putative way out of a worldwide mess. Firm data had shown that the routes of transmission of HIV were few, were avoidable, and that prevention worked when those concepts were implemented with conviction.

Yet the world in general was in the habit of associating viruses with vaccines and invoking the word "vaccine" almost worshipfully as the ultimate solution to nearly anything. I found that attitude particularly unsettling, since I had just spent years fending off dissidents and nay-sayers who declaimed about the imputed evils of demonstrably wonderful vaccines for relatively straightforward diseases. The idea that a vaccine against HIV would somehow be a "magic bullet" to ease the world's fears (and thus erase its need to rethink sexual and drug-using mores) was astonishing to me.

That reliance on a vaccine approach was problematic was all the more clear to me, given that HIV was one virus that actually could be **avoided**, and my years of viral vaccine review told me that there was no vaccine as good as that. The very best vaccines we had – against measles or yellow fever, for instance – were live and attenuated, and they imitated natural protective immunity; but while they were good they were only 98% effective, not 100%, and then only against sporadic **epidemic** pressure. HIV was a sexually transmitted agent that was difficult if not impossible to attenuate, for which there was no known protective immunity to be imitated, and that was rapidly becoming endemic, as well as presenting a steady threat throughout a sexually-active lifetime.

Altogether, then, I found it very worrisome that the public viewed a vaccine approach as the ultimate solution to the AIDS pandemic, and indeed

in 1991 I gave a talk entitled "What would we do with a good AIDS vaccine if we had one?" The "we" I was talking about in that case was Americans -- for there never was any question that a vaccine would be **crucial** to parts of the world where double-digit seroprevalence was already a fact of life. But in the U. S. it was not then (and, I might add, is not now) clear to me what we would do with an HIV vaccine that wouldn't displace, and do less well than, other prevention efforts.

Needless to say I was not always very popular with the leadership of NIH when I said such things. [In fact, there was one amusing episode in which I was being interviewed about some facet of AIDS vaccines on Good Morning America in New York, and Tony Fauci, Director of the National Institute on Infectious Diseases, was being interviewed from a studio in Washington. Unbeknownst to Tony, he was visible on our screen in the New York studio even when he wasn't talking, and when I went into my prevention-not-just-vaccine routine, he all but crossed his eyes and mouthed "There she goes again!"] To be fair to Tony, we were and have remained good friends over the years, and in fact he is one of my strongest supporters in trying to keep behavioral prevention on the table when so-called "hard science" threatens to displace it entirely.

Anyway, I persevered -- which I suppose is the other quality I should mention about being a public policy person. If your data are appropriate and pertinent, then being scowled at or shouted down becomes irrelevant, and it doesn't make much sense to take it personally. Indeed, one of my favorite anecdotes about that appeared just as my involvement in policy matters was starting. I had begun to enjoy reading the comments of an analyst named Daniel Greenberg, who wrote about health and public policy in a Washington biweekly publication. One day he had a column entitled: "On the importance of stamina in the political process." In it he told a story about the grand opening of Lincoln Center in the early 1960s, for which event Victor Borge had been asked to perform and to comment in his usual fashion.

On the appropriate evening Borge played the piano while expressing, from the stage, his admiration for all the lavish and plush accoutrements -- the carpets, the tapestries, the chandeliers and so forth. He then proposed to go into the audience to solicit their reactions. He got to the edge of the stage holding his microphone, but then its cord stopped him; assuming that it was snarled, he turned to untangle it, but it turned out that that was all the cord

there was. So he turned to the audience, sighed loudly into the microphone, and said "Ah, and to think that for \$1.29 more they could have gone all the way!" [I can't tell you how many times I have whispered to myself in public policy discussions: "Only \$1.29 more."]

Reductionism and AIDS Vaccines: Some Further Comments

So to diligent training applied in an appropriate context and in teamwork with others who bring different backgrounds to the table, I add stamina as a necessary ingredient if one wants to change the world. That sounds like a rather trivial comment, unless you realize that many professionals try to **substitute authority for stamina**. Once having declaimed, they feel good about having done so; and if their authoritative assertions are not quickly and fully embraced, they stalk off, congratulating themselves that they have done their best. That isn't their best! It is in the "heavy lifting" between having expertise and making it useful that the public policy issues are at their most tendentious and important, and it is there, too, that the awareness of reality constraints and of the intermeshing roles of multiple kinds of expertise become crucial.

And that brings me back once more to the topic of AIDS vaccines, for as you know there is now a much-increased and broadened set of efforts being devoted to their development as the global disaster of HIV/AIDS continues to unfold.

My role with the National Commission on AIDS ended in the fall of 1993, but I was pressed into service in a few contexts thereafter. One of the most interesting was a fascinating series of discussions – co-sponsored by the AIDS Action Council and by NIH over an 18-month period to ascertain what social and cultural impediments there might be to the large-scale (Phase III) **testing** of an AIDS vaccine should one become available. The idea was to anticipate and grapple with as many problems as possible so that time wouldn't be lost later; and the group was the most heterogeneous collection of bright, earnest, dedicated individuals you could imagine – in fact, the heterogeneity went well beyond what I could have imagined. I think it is enough to say, for purposes of this discussion, that I was one of very few so-called health "credentialed" participants in the group, and the temptation to pull rank was dangerously attractive.

But the deeper into our charge we dove, the more challenging it became, for, as the group “gelled” and began to trust one another, whole worlds of fear and anxiety surfaced. We were shown a videotape of African American men and women berating a peer because he had participated in a phase I trial of a candidate HIV vaccine – they were implying that he had been “duped,” and he looked miserably embarrassed, as one does when castigated for naivete. We heard anecdotal accounts of the bad things that had happened to people who had lined up for such trials out of altruism: even though by definition they had to be “low risk” in order to participate in the Phase I trials, suddenly they faced the threat of spousal mistrust or even (in one case) divorce. Problems with the military or with travel were documented for it was, and still is, illegal for someone who is HIV-positive to enter the United States. And we learned to know of all sorts of other uncertainties about their fates that arose from the fact that they might become seropositive in the context of vaccine trials.

Equally worrying, on the other hand, we heard detailed accounts of people who completely ignored the careful, cautious disclaimers from investigators in such trials that they might be given placebo. The concept of placebo is difficult for most people in the health care setting, and enthusiastic trial participants would state with great confidence that they were quite sure they were “getting the vaccine” and that it would protect them because “that nice doctor wouldn’t do anything to hurt me.” And, throughout, we heard that the world considered behavioral interventions too difficult, although it was acknowledged that they had worked and could continue to work when applied with diligence and conviction.

Finally, to do any Phase III trial that could yield meaningful evidence of protection from vaccine, one needed populations with 1-2% annual seroincidence of HIV infection. It was uniformly assumed that no trials would be ethical if the highest level of valid behavioral interventions were not offered to everyone throughout, but it was problematic as to how that could be done in settings where untreated substance abuse, homelessness and lack of access to health information and care provided the very backdrop against which such trials (in the U.S.) were even statistically feasible, given seroincidence data. Oh dear! A genuine Catch-22! The magic glow emanating from that word “vaccine” certainly began to fade during those discussions.

That was in the mid-1990s. With the energy and resources now being devoted to AIDS vaccine efforts, things have moved along. The very strategies have shifted as recognition has come that cytotoxic T lymphocytic responses, rather than antibody responses, are more likely to correlate with protection; and at last people are trying to develop vaccines with HIV-1 subtypes appropriate to the populations that need protection. But the **disconnect** between high science and earthy reality remains, as I was reminded the other day.

I was skimming through Science magazine, when, in the correspondence section, I noticed a thoughtful letter about use of a DNA vaccine against simian immunodeficiency virus in rhesus monkeys. The vaccine itself was only marginally protective, but it seemed, when augmented, to have been greatly enhanced in its capacity to prevent clinical AIDS. The augmentation effort was targeted at eliciting CTLs and other TH1 responses, using a purified fusion protein (representing IL-2 and the Fc portion of IgG). That augmentation had a very impressive effect, raising the DNA vaccine from marginally to distinctly protective in rhesus monkeys when they were subsequently challenged with virulent virus. So far so good.

The letter writers, from South Africa, applauded the study and commented on the therapeutic effect noted with interleukin-2 treatment in people living with AIDS. From their vantagepoint, however, those findings raised the potentially complicating problem of a high prevalence of parasitic infestation in sub-Saharan Africa – especially helminthic infections which have been shown to impair pathways leading to IL-2 (and related) responses. Their query was: should not treatment or prevention of helminthiasis be considered as a necessary prelude to HIV vaccine trials, since otherwise one might be misled and fail to demonstrate potential efficacy in helminth-infested trial participants.

I thought that was a terrific question and an unusually fine example of keeping in mind Leo Szilard's connectedness of things. But the response quite took my breath away; for in answering the letter the American investigators who had authored the initial paper, while paying lip service to the importance of the issues raised concerning HIV vaccine trials in Africa, suggested (and I quote): "...a possible solution to this problem might be to co-administer cytokines such as IL-2 or IL-12 with candidate HIV vaccines to drive the vaccine-elicited Th1 immune response, perhaps by using a protocol similar to the one we reported in our research article."

Ta-dah! Their solution to a worldwide pandemic that, in the area in question, threatens to decimate young adult populations, was not a suggestion to attack helminths but rather a proposal to escalate the technology and cost of vaccine with fusion protein or interleukin-2 augmentation, thus rendering it essentially meaningless to the region, even if it proved to be protective! Wow! That is a fine example of what I have been referring to when I speak of hubris – the “piling on” of one technologic intervention on top of another at the expense of common sense and “low-tech” prevention.

And it doesn't just occur in the AIDS arena. That written exchange in Science put me in mind of a talk I heard at a meeting at the Howard Hughes Medical Institute about a year ago in which a molecular genomics enthusiast declaimed brilliantly on progress in the human genome project, noting that soon we would be the proud possessors of data that defined (by his estimate) 80,000 genes and their products. His happy conclusion was that that would give us 80,000 new targets for pharmaceuticals! The idea that anything else might be needed to deploy that information **in the interest of the health of the public** seemed not to have occurred to him.

Such truncated thinking can be found in other aspects of health care. In a 1996 meeting that was called by the Kaiser Family Foundation to try to bring together the entirely separate worlds of managed care and of HIV/AIDS care. As the topic of homelessness came up, I was somewhat startled to hear the managed care types say that they had to draw the line short of providing social services. During the AIDS Commission years I had come away with a very strong conviction that housing was the single most important, fundamental determinant of health status for a person living with AIDS, and so the categorical drawing of a line in that part of the sand astonished me. Before I could figure out what to say, however, a colleague beat me to it, commenting dryly that “...so far as I'm concerned, ‘managed care for the homeless’ is an oxymoron!” Yes!

I could go on like this at even greater length, but time is flying, and I suspect that by now you can tell where I am coming from. I hope no one thinks I am decrying the wonderful biomedical progress that has been made over the course of recent decades. It is crucial, and momentum must be maintained. But it is not available to all – the old, ugly backdrop of

community and social ills that complicate its usage has not gone away. Systematic health care is not available to millions of our fellow citizens, and health care of any kind whatsoever is not available to great numbers of denizens of the global village.

And then there are whole areas of health and of medical care in which we are not even using common sense. Substance abuse, for instance. It has been declared a national problem so severe that we have been conducting a "war on drugs" for decades – but mostly at the borders, rhetoric to the contrary notwithstanding. Actually the war has been on drug users, with no accommodation made for the prisoners of that war; in fact our chief therapeutic weapon to date has been incarceration.

Now things may be changing, with many thanks to the extraordinary efforts of your colleague David Lewis, whose inspiration it was to call together a group called Physician Leadership on National Drug Policy. That group epitomizes almost perfectly what I have been trying to get at throughout this talk, for it enjoys voluntary contributions of the genuine expertise of countless professionals involved in trying to bring substance abuse treatment to the fore; but it is led by physicians **not** in that field who collectively have extensive public policy experience. We are thus able to convey the simple, clear message that substance abuse and addiction are illnesses, that they are treatable in the same way as are other chronic diseases, and that the cost-effectiveness of that approach puts our incarceration mode to shame. And my earlier experience has been strongly affirmed: the very fact that dedicated professionals are willing to make the effort to grapple with complex problems has captured the attention of policy makers and moved us distinctly closer to revising policy. In fact, the response from involved parties in other professions – the judiciary and law enforcement officials, for instance -- has been genuine delight that "doctors are at last willing to get involved."

Let me conclude with a few remarks aimed at those of you who are still early in your careers and to whom it sounds unreal at present to think about doing anything beyond what is required of you. I want to point out that the key role you can play is never obvious in advance, and that the secret lies in your willingness to maintain an awareness of the world around you. In the AIDS epidemic, the critical players were experts in their fields (whether epidemiologists or oncologists or other health care professionals),

but they knew enough about the world around them to recognize an urgent and unprecedented need. Some re-directed their careers entirely. Others, like me, kept close track so that expertise could be brought to bear quickly when called for. And you – who are currently immersed in demanding courses of training – can keep yourselves prepared to do likewise. The needs for activism will change and evolve, but they will never go away! And I assure you that, if you decide to be an active participant, your lives will be greatly enhanced!

Thank you.