

## Presidential Address to the American Society for Clinical Investigation, Baltimore, Maryland, 2-6 May 1992

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Thank you for granting me the singular privilege of serving as President of the ASCI during this past year. After I learned of my election last spring I looked up the list of my predecessors. The previous presidents of the ASCI comprise a very impressive group. The list includes a Nobel laureate, members of the National Academy of Sciences and the Institute of Medicine, a cornucopia of deans and department chairs, founders of great departments of medicine, editors of our premier clinical and research journals, and authors of landmark textbooks. I feel deeply honored that you have seen fit to allow me to add my name to this list.

I have enjoyed being President. The duties are few; the effort required is modest. It is well documented that no ASCI president has ever suffered excessively from overwork due to the demands of the office. The president helps to organize this spring meeting, presides at the mid-winter council meeting during which we pick our new members, deals with occasional matters of policy and finance that arise, and, most importantly, nods obediently when the JCI editor speaks from atop his trust fund. These tasks were, for me, far more pleasurable than taxing because they were done in conjunction with an outstanding group of officers and councilors who quickly became my friends. I would like to thank the council members with whom I have worked during my five years as councilor, president elect, and president, and to acknowledge their contributions to the Society. Their friendship and collegial approach to their responsibilities made my time as an officer thoroughly enjoyable.

There is only one onerous task attached to this position, and that is the preparation of this presidential address. I have not relished the prospect of giving this talk. Like most scientists, I am far more comfortable with the reportorial, rather than the philosophical, mode of discourse. On the other hand, this is a once in a lifetime opportunity for me, a chance to share with you my own feelings about our lives in academic medicine. That is what I offer you today: my own subjective, intuitive, highly personal, and undocumented views about our present state of emotional health, and about the ways that we are reacting to realities that challenge our futures. I will focus most especially on the way that our attitudes are perceived by our potential successors.

I have a premise. It is the following: I believe that we have become far too engrossed with the problems that we face. We forget how much we enjoy our work. We no longer project the positive image of either our careers or our lifestyles that is necessary to attract the next generation of young scientists. Whether intentional or not, our negativism is driving talented young

physicians away from careers as physician scientists. My contention is that we must and can do a great deal to solidify the future of academic medicine by simply delivering more positive messages in our positions as mentors and role models. We think a great deal about our responsibilities as scholars, practitioners of the healing arts, teachers, and administrators. For today, at least, I shall concentrate on how we are doing as ambassadors of academic medicine.

It would be folly to presume *a priori* that you will share my sense of the importance of these issues, agree with my formulation, or even find the exercise worth remembering. Addresses by outgoing academic society presidents, however well or badly done, do not enjoy a history of lasting impact upon their audiences. Nonetheless, I feel emboldened to address these issues by my intuition that many of you share at least some of my concerns. In fact, my remarks have been strongly influenced by correspondence and commentary that have reached me this past year because of my position as president. In this regard, I am indebted to those of you who responded to my open letter of this past August, and shared your thoughts about these matters.

This is what has come to me from those letters and my conversations with many academic physicians: we presently suffer from a crisis of confidence. I note, with alarm, the symptoms of a syndrome of self-doubt. For the past 40 years we enjoyed the largess of the NIH and the unquestioning approbation of the citizenry. Now, reality is intruding upon our idyllic, ivy-encrusted edifice. We lament the loss of many things we have taken for granted in the past. Let me recount what I have read and heard from so many colleagues: first on the list of woe is loss of security, because NIH funding is becoming so difficult. There is also a considerable fear that we're losing our ecological niche as clinician researchers. We are told that the triple threat is dead. Clinicians can't do research, researchers can't do clinical medicine, no one can teach. We also resent the loss of our innocence. Some reporters and politicians would have the public believe that we cheat, steal each other's data, perform horrid atrocities on household pets, and misappropriate Federal funds. We are stung by a seeming loss of respect. We hear that the Ph.D.s have no respect for us as true scientists, practitioners have no respect for us as real doctors, and hospital administrators just plain have no respect for us. We are experiencing a collective loss of self-esteem. We are glum about the future.

This self-doubt and our consequent gloomy demeanors are far more threatening than tight grant money, an intrusive bureaucracy, a carping press, or even the strident purists who claim that our research can be done better and less expensively by Ph.D.s and biotech companies. I do not deny that we have real problems; times are truly tough. We would be suicidal to trivialize these issues or their ominous implications; however, I am much more concerned about our morale than any of these problems. All of our problems are soluble, yet we tend to magnify and overstate the gravity of our situation. It was not so long

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ago that we projected enthusiasm, excitement, and confidence in our labs, on rounds, and in our classrooms. Now, too many of us, in too many places and on too many occasions, emit a miasma of dejection and despair. All too often, we incorrectly lead people to believe that we are teetering on the brink of extinction.

Our melancholia is being sensed by those who take us very seriously, namely our students, house officers, and fellows. We are discouraging promising young scholars at a time when the very problems we face demand for their solution an infusion of youth, vigor, and talent. Academic medicine needs more than ever to enlist gifted, perceptive, and energetic individuals. Negative messages will turn these people off. I am thus far less anxious about what our future will hold than I am about who will be there to deal with it.

I submit that it would be a good idea to set our worries aside for awhile and focus more energy on the issue of how to attract the best talent. At the risk of being remembered as the Pollyanna President, I have to confess that I simply do not believe that things are bad enough to justify all the crepe hanging. I agree with one of my mentors, David Nathan, who said, in his letter to me, "There are too many dirges and not enough joy." All dire predictions to the contrary, we continue to do the very things that people say we cannot do. Somehow we stay well enough funded to do our work. We teach, we give excellent care to patients, we give the public an outstanding return on its investment. It is harder, much harder, than it was, but we prove every day that it is possible to endure, and, yes, even to prosper, in the face of all this doom and gloom.

I maintain that we are doing quite well. The NIH budget is far too tight for our needs. We should push hard to maintain and enhance funding. However, let us never forget that we enjoy greater security and more generous public support than any other scholarly group in the history of this country. Let me ask you a rhetorical question: would you rather depend for your salary on the NIH or the National Endowment for the Arts? The sky is not as blue as it was, but it is not falling in, either. There are still splendid opportunities for young physician scientists to thrive as faculty in our clinical departments. I think that now is a good time to pay particular attention to the day to day role we play as ambassadors for careers as physician scientists. It is more important than ever that we attract top flight people, nurture them through their early career development, and launch them as productive independent investigators who also know how to take care of patients.

In order to accentuate the positive, we must feel good about what we are trying to do. We must believe that we are uniquely situated to contribute to the future of biomedicine. I have read and heard too much about how we no longer have a niche in science. I have even been told by some people that it is unethical to entice young people into a field that has such a dim future. We must not buy into this nonsense. I, for one, thus have an absolutely clear conscience about persuading our best young scholars to join our ranks. Our professional lifestyles are more stimulating, challenging, worthwhile and, yes, affluent, than they ever have been.

The recent incursion of molecular biology into the study of disease defines more sharply than ever the need for scientists with our hybrid vigor. During the past decade, molecular genetics has been spectacularly successful as a strategy for exploring normal physiology and the fundamental causes of disease. Recombinant DNA technology is providing us with reagents of unprecedented power. Gene therapy is a virtual reality. We

have benefited enormously from a reductionistic era of science that has allowed us to slice through layers of physiologic complexity and to excise from the genome that bit of DNA that seems to determine a particular physiologic behavior or disease state. A great deal has been learned by a simple conceptual approach: clone the gene that determines the phenomenon.

The next era will be much more complicated. Witness the often bizarre and unpredicted phenotypes of animals modified by transgenes or gene knockout strategies. Their complex behaviors strike me, at least, as strong affirmation of the continuing need for individuals trained the way that we are. Delineation of the true biological impact of the many genes and gene products that we are characterizing at such a rapid pace will require a sophisticated understanding of integrative physiology and pathophysiology. Medical practice will need physicians able to understand clinical phenomena at the structural and molecular level; biomedical science will need scientists well versed in the subtleties of human disease.

Consider, for a moment, the set of human diseases that have been better characterized at the molecular level than any other—the human hemoglobinopathies, diseases to which I and many other people in this room have devoted a large part of our careers. Hemoglobin is produced only in red cells, yet mutations of the globin genes cause clinical syndromes that affect every organ system in the body. How is it that severe  $\beta$  thalassemia, the failure to make  $\beta$  globin chains, a single gene defect, causes not just anemia but also pathologic fractures, deformed facies, glucose intolerance, and cardiac failure? How is it that different mutations in the same  $\beta$  globin gene can also produce jaundice, leg ulcers, gallstones, polycythemia, rosy cheeked patients who are actually quite ill, and pale cyanotic patients who are in fact quite healthy? None of these phenomena are directly predictable from knowledge of the globin genes or the biochemical properties of hemoglobin. To decipher these diverse clinical phenotypes one must understand the interactions of tissues and organs with the abnormal hemoglobin molecule and the responses of one organ system to perturbations in the others. Hematologists understand the phenomena that I have listed. Their pathophysiology has been explained, but this achievement required individuals who were equally comfortable with the nucleotide sequences of the globin genes and the clinical interpretation of arterial blood gases to pull it all together. These very necessary individuals sound a lot like those of us who sit in this room. We can stop worrying about whether or not the triple threat is dead or whether the future includes a prominent place for us. As clinical medicine depends more and more on basic cellular and molecular biology, our role will be enhanced, not diminished.

We must also not underestimate the importance of what we are trying to do. A colleague, Dr. Barry Coller, in recent testimony before the House Appropriations Subcommittee, made a statement that I'd like to paraphrase. He said: "To harness the power of the scientific method for the purpose of relieving human suffering from disease is among the highest achievements to which one can strive."<sup>1</sup> I subscribe to that point of view. We will need more, not fewer, people in the future who will be able to strive for this goal in a meaningful way. We must be sure to give those individuals messages that will draw them into this field.

1. Testimony before House Appropriations Subcommittee, 30 April 1992.

In my open letter of last August, I asked for responses to several questions: What made you choose this career? What keeps you in it? What would you tell a young person contemplating a similar career? The general tenor of the responses that I received was actually quite congruent with what I myself would have answered if someone asked me that question. We speak in cosmic terms. We emphasize the joy of discovery. Some of you captured quite eloquently our hopes to combine a love for science with a desire to aid humanity. Others noted the gratification we feel when a student's face lights up because we have successfully explained a difficult concept, or the sense of fulfillment we enjoy when a former trainee "makes it" as an independent investigator.

These are indeed worthy and lofty motives. In one form or the other, we have all felt them; we are very sincere when we emphasize their importance in our career choices. But, at the risk of committing blasphemy, I submit that these were not the true activators that led us to choose our careers or at least to stay with them. These ideals were tropic factors. They caused us to consider the possibility, and to investigate further. I'm willing to bet that our choices were more strongly influenced by considerations that were far less idealistic and far more human. Someone motivated us to give research a try while we were students or fellows. Someone made us feel good about our chances for success. Someone taught us the strategy to succeed. More importantly, someone seemed to be having a good time, good enough to make us feel that we could be reasonably happy doing the same thing. The quality of our contacts with these "someones," our teachers and mentors, had a greater impact upon the career choices that we made than any other single factor.

During my own career I have been lucky to enjoy the mentorship of three outstanding individuals, David Nathan, Bernie Forget, and Arthur Nienhuis. Each of these people is a superb scientist. Each taught me a great deal about science, about how to do research, about the tactics and strategies I needed to succeed at the bench and in the profession. But these weren't the most important messages that I received from my association with them. In truth, these tools alone could not really provide me with either the emotional strength or the sense of belonging that it took for me to stay in this field. I garnered those very necessary assets from my personal association with each of them, by virtue of both the overt and subliminal messages that they transmitted to me.

When my experiments weren't working in the laboratory, my mentors were always there to help, not just by trying to solve the practical problem at hand, but also by making it clear that they were confident that things would work out well. They always made me feel that I would succeed, even before my potential to succeed was apparent to me. That for me served as the light at the end of the tunnel. By their encouragement and by the way that they treated me as someone who belonged in the field, they instilled confidence. By their enthusiasm for their work, they made it clear that academic medicine was a highly stimulating and worthwhile way to spend a career. They kept me in the field by their attitudes even more than they did by their skills as teachers. I would be willing to bet that most of you had similar relationships that led you to choose lives as physician scientists. Consider for a moment that if it was important for us to have excellent mentorship during relatively "easy" times, how much more important is it that our protégés receive outstanding mentoring during these very difficult

times? Today's young physicians face even more daunting challenges to their futures than we did. Their need for guidance, protection, and encouragement is exponentially greater.

In order that these young individuals succeed, they must first know that they will have a fair chance to succeed, that the words "approved but not funded" are not a death knell, that it is normal that success might take longer to achieve during these stringent times and that we, their mentors, are deeply, sincerely, and patiently committed to their success and security. They must also feel that they are embarking on an endeavor that is not only worthwhile, but also stimulating, fulfilling, and, often, even fun. These neophytes look to us for cues; they are highly sensitive to the messages and metamessages we deliver by our actions, attitudes, and conversations. We have the power to affirm or negate their interest in us.

My thesis today has been that we must be highly aware of these messages that we broadcast to our students and fellows. If we walk around looking gloomy and unhappy, no one smart enough to succeed in our business will be dumb enough to sign up. Those gifted in science will drift off in one direction, while those with clinical talents will go in another. The physician scientist will become extinct, and we'll have made prophets out of all those naysayers. On the other hand, we could try to appreciate just how well off we really are. We could admit, at least to ourselves, that we cut a pretty good deal when we chose academic medicine. We might even confess, all of our bellyaching notwithstanding, that we truly enjoy our work. If we let these feelings out, and share them with our protégés, then our behavior will attract successors of sufficient quantity and quality so that we can pass them the torch. Physician scientists will continue to make their mark, and the purveyors of gloom and doom will have to take their catastrophes elsewhere.

I think that it is fair to presume that we all share a desire to leave behind something of lasting value before our careers wind down. What I have to sell today is a sure fire formula for earning that very good feeling of leaving an honorable legacy when the time comes to settle into our emeritus chairs and cash that first check from TIAA-CREF. We must work very hard to inspire the very best students, the ones who have the best chance to succeed in these trying times, to give a research career a try. We must sustain and nurture them during what will be the difficult embryonic years of their careers. Most importantly we should set as our goal that their work and their success will outshine our own. If we accomplish these aims, we are guaranteed the warm glow of satisfaction that comes from knowing we left our profession and its beneficiaries better off than when we entered. The method is easy: first, be more sensitive to the many blessings that we already enjoy in our lives. Second, enjoy them. Third, share the joy. It will work. Thank you for your attention.

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