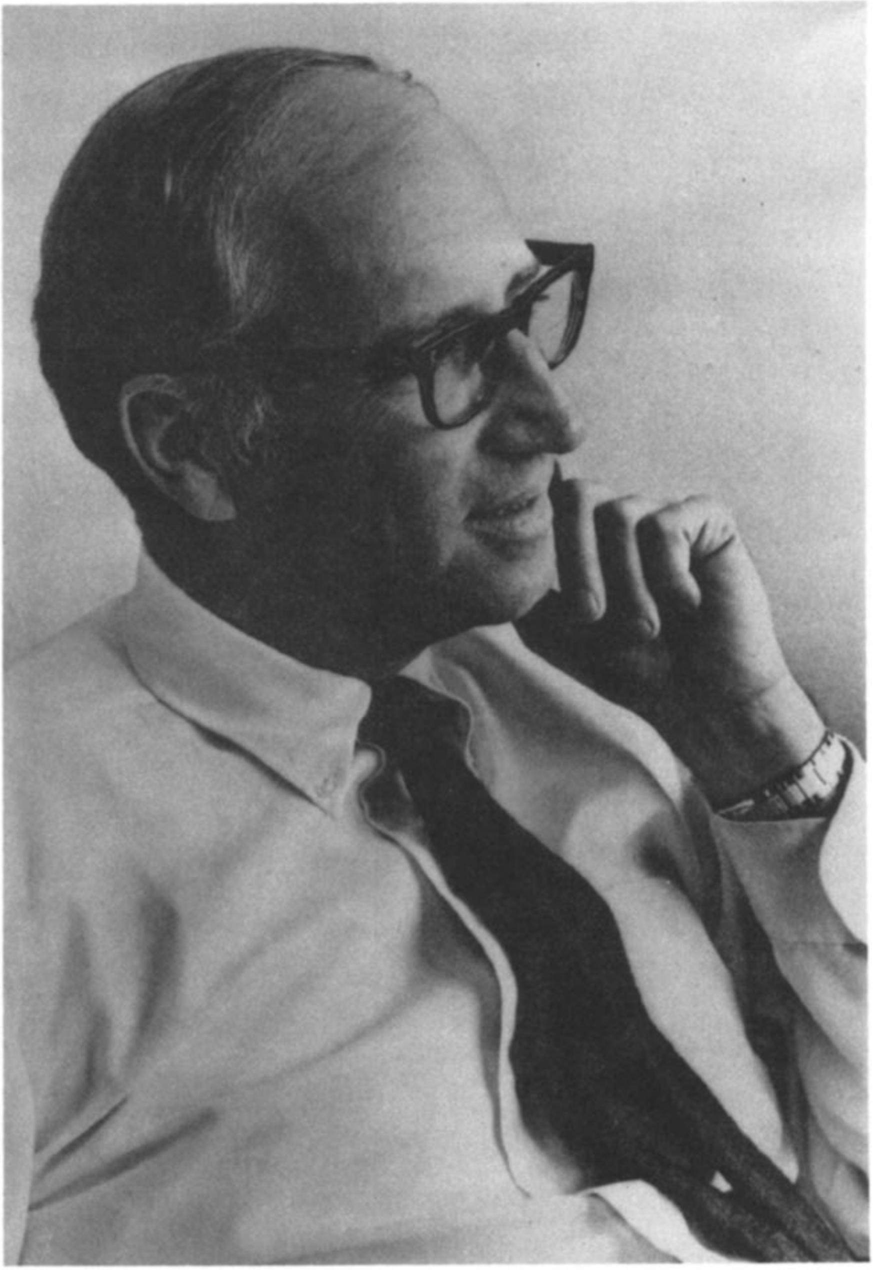

Dan Koshland

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# HOW TO GET PAID FOR HAVING FUN

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CONTENTS



## *Introduction*

When writing a prefatory chapter for Annual Reviews a scientist is confronted with the question of what in his or her life might be interesting to others. In my case I was appalled at the absence of material that generates good novels: no broken homes, no misunderstood childhood, no criminal youth gangs, no disastrous liaisons. A landscape of boredom from sea to shining sea. If there is one overlying theme it is that I got paid for doing what I enjoyed all my life. I wish I could say I had cleverly plotted to achieve this nirvana by a series of Machiavellian measures. The truth, however, is closer to the course of the Lord High Executioner in the Mikado: I was "...wafted by a favoring gale as one sometimes is in trances."

As I look back, each new chapter in my life seems to have been a mutation of Pasteur's phrase "chance to the prepared mind." Once I had decided to be a scientist, the events seemed to flow as if by accident. However, in retrospect I see that the experience of each phase of my life presaged the next "accidental happening." But I was surprised at the "random walk" nature of my life.

## *The Making of a Scientist*

What started me on the course of being a scientist and why did I stay the course? I can retrospectively say I decided to become a scientist in the eighth



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grade when in quick succession I read *Microbe Hunters* by Paul DeKruif and *Arrowsmith* by Sinclair Lewis. *Microbe Hunters* told the adventures of early microbiologists and their extraordinary success in curing diseases. *Arrowsmith* described what being a scientist really means and how a scientist has to make choices that differ from the practice of medicine. Being a scientist seemed highly desirable, so when I entered high school I enrolled in college preparatory courses and took all the math, physics, and chemistry I was allowed.

Today I am still a scientist. Am I typical or abnormal? In my job as a professor at the University of California, I make a point of asking students when they first decided to become scientists, and their stories are amazingly similar to mine. Though not all have read *Microbe Hunters* and *Arrowsmith*, some have. But additional patterns in their lives fit with my experience. All of these students got good grades in mathematics in elementary school and went on to do the same in high school. Not all were equally enamored of math by the time they were graduate students, but elementary school math was a common denominator of the elements of logic I think are essential for a scientist who does puzzle solving for its own sake.

This experience points out lessons that are sometimes forgotten in oratory regarding the supply of scientists. Almost all scientists decide on careers while very young, so if we are to have more scientists we had better entice them at the elementary and high school levels. Colleges are in the business of retaining scientists, but only rarely in the business of generating them. I have heard some speakers who wish to recruit minorities and women into science (a desirable goal in my opinion) who seem to have the idea that anybody who is interested in science is going to be good at it. In fairness to the recruits, recruiting should be targeted to those whose skills correlate with success in science. Exceptions will occur: Pasteur got a "C" in chemistry and Albert Einstein was renowned as a mediocre student, but most scientists like math and get good grades.

## *Background*

From high school I went to the University of California. Tuition at that time was about $100 a semester for which one got free medical care and education. The school was a perfect opportunity for all, with no barriers of wealth or privilege; an egalitarian democracy. The college of chemistry, however, which I entered, was run by GN Lewis, who was an intellectual elitist and made no apologies for it. In freshman chemistry all students took an examination in the first week of classes. Although all students in chemistry had the same general lectures, assignments to lab sections were based on the rankings from the examination. At each hour there was a "number one" lab section composed of the top students, a number two section composed of the 30 next best students, a number three section composed of the next 30 and so on (chemistry was taught at 9:00, 10:00, 11:00, and 1:00 p.m.). The lab instructor for section one was a full professor of chemistry, something GN Lewis believed was important to keep his best students challenged and stimulated. The number one lab sections got no extra edge in course material, but a good deal of added stimulation. I also enjoyed the turbulent social and political life at Berkeley. Those early influences became important later.

Another event I thought minor at the time that turned out to be important was an encounter with Wendell Latimer, chairman of the department and one of the distinguished names at Berkeley. I took a summer course in which I was one of two students in Wendell Latimer's advanced inorganic chemistry. Both of us studied very diligently, and as I was walking out of a three-hour final exam, Wendell Latimer looked up at me, picked up my final exam, and asked "Would an 'A' be sufficient?" I laughingly said yes (I had gotten "A"s in three midterms), but then he started to tear up the exam implying that I had done so well in the course that he didn't need to read the final. With the typical impetuosity of youth I reacted angrily and said, "I spent three hours working on that exam; you owe it to me to correct it." In retrospect I wonder what was on my mind, but fortunately for me Wendell Latimer only laughed. He did correct the exam, and the incident passed without apparent further notice. When I recounted the incident to some classmates at the time they uniformly said that I had acted like an idiot. But shortly thereafter I received the James Monroe McDonnell Scholarship, which is given to the senior student deemed most likely to succeed, and I was later asked by Latimer to work with Glenn Seaborg on the Manhattan Project. I will of course never know whether my grade point average or some inner amusement of Latimer's at the antisocial behavior of a young student lead to those two appointments. But I concluded that being obnoxious was not all bad.

## *The Manhattan Project*

When I graduated from Berkeley the war clouds were forming in Europe, and I tried to enlist in the Navy, but with an eyesight of 20/400 was told by the interviewing officer that, "As far as the Navy is concerned you are legally blind." As the war progressed Navy standards slackened, but at that time they wanted all recruits to be potential deck officers. I explained that my competence in mathematics and calculations would be useful below deck for this new discovery radar, even if I couldn't see the horizon, but I received no sympathy.

The rejection was fortuitous because shortly thereafter I received the call from Wendell Latimer saying that Glenn Seaborg was recruiting people for something called the Manhattan Project at the University of Chicago. By that time I had a job working on aviation fuels, and I told Latimer that my job was classified and getting approval for a transfer would be difficult. Latimer said, "Don't worry, this is the most important job in the world." Knowing Latimer's expertise and relationship to war efforts I accepted his word. A couple weeks later I was on my way to Chicago not knowing on what subject I was going to work, what I was going to be paid, or where I was to be located. I got one hint from Latimer who gave me Rassetti's book on nuclear physics and said to me slyly, "You might find it useful to read this on your way east." When I arrived in Chicago I was greeted by Glenn Seaborg who told me I would be working on an atomic bomb that could win the war, and he said the work was top secret and could not be mentioned to anyone. These were the unexpected events, far from Paul DeKruif and *Arrowsmith,* that started my research career.

Seaborg was not only a brilliant scientist but a superb organizer who could have been successful in any field (he became in fact a winner of the Nobel Prize, Chairman of the Atomic Energy Commission, Chancellor of the University of California, and scientific advisor to four presidents). As a bachelor student who had much to learn I could not have gone into a better training atmosphere. Seaborg's people all knew the job they had to do, and their assignments to projects made for interactions that maximized productivity. For example, we were using radioactive isotopes in an era in which simple Geiger counters were very untrustworthy and commercial instruments nonexistent. We sometimes went through an elaborate experiment to produce an isotope that had a half-life of hours only to have the Geiger counter break down, wasting the work of the experiment. Seaborg, whose primary goal was chemistry, hired instrument experts to develop his own set of reliable instruments that satisfied the needs of the chemists in his group.

Our major job was to purify plutonium from fission products and other impurities to obtain a product of unique purity that could be reduced to a metal and made part of a bomb. Since plutonium was a man-made element of unknown chemistry this charge was a tall order, and we scientists, under Seaborg's guidance, had to work out the chemistry of plutonium with amounts detectable only by their radioactivity. Moreover, this element whose chemistry was totally unknown had to be separated from many transition-state elements whose chemistry was largely ignored in classic textbooks and graduate research programs. Our success is an enormous feat in chemistry in which many young and totally untrained chemists like me were productive only because we were channeled into appropriate paths by an organizational genius.

When I was first hired it was explained to me that plutonium was extremely lethal, a conclusion based on calculations showing it to be much more dangerous than radium which had caused many deaths in the radium-dial industry. We were told to take precautions such as wearing gas masks and performing elaborate pippetting procedures to protect ourselves from inhaling the plutonium. Almost unanimously, we young scientists discarded this advice because we believed we were in a necessary war against an evil Hitler bent on global domination. With our friends dying on battlefields, slowing research to be extremely cautious about our own lives seemed inappropriate. We routinely worked six and often seven days a week, spurred on by our reading of a captured document in which German scientists speculated on the possibility of a German bomb or nuclear power capability. Later we learned that the German nuclear effort never really got going because leaders like Heisenberg discounted these possibilities of nuclear potential. But fission had been discovered in Germany, and the secret weapon Hitler was bragging about could have been the bomb as far as we knew.

Later, when I was at Berkeley in the 1960s, many discussions of "generation gaps" filled the newspaper. Many were nonsense, but I did think there was one real difference in generational attitudes. A generation that has gone through a great "war for a noble cause" can never look on death in the same way as one that has lived in an unthreatening peace. We had to realize that some things are worth dying for, and pacifists in peacetime preaching that nothing is worse than boys dying on the battlefield are not convincing.

## *Graduate School*

When the war came to an end I decided to return to graduate school and was tempted to stay in nuclear chemistry. Seaborg was a superb teacher, and I knew I would benefit greatly by working with him. On the other hand my initial attraction to biology was still very strong, and I decided that I should go back to that subject with a chemical approach. Chemistry's application to biology is so obvious today that one need not elaborate on it, but at that time it was a frontier, so I chose to go to the University of Chicago. There, a young assistant professor named Frank Westheimer was interested in applying chemistry to biology. As a result of our mutual interest, I ended up in his laboratory, which was enormously stimulating. A variety of graduate students were working on classical problems of physical organic chemistry, whereas I was something of the "odd man out" working on a chemical approach to biology.

My radioactive experience was valuable so I volunteered to apply carbon 14 ($C^{14}$) to the glycolytic pathway, a problem envisioned by Westheimer for an incoming graduate student. The only available $C^{14}$ at that time was supplied by Oak Ridge National Laboratory in the form of barium carbonate. To obtain useful $C^{14}$ for my synthesis I needed to make hydrocyanic acid (HCN) which I did by placing barium carbonate in a mixture of liquid ammonium and metallic potassium. The result was a big explosion that resulted in a small amount of potassium cyanide. That amount was sufficient to follow the classical Fisher -Kiliani synthesis of glucose 14 starting with arabinose and HCN. I used the glucose-1-$C^{14}$ to trace metabolic pathways.

Getting a PhD was great fun for me, not only because of the excitement of Westheimer's laboratory, but also because the department of chemistry at the University of Chicago was a pioneering and intellectually stimulating group. Harold Urey was studying cosmology, Henry Taube was introducing a whole new approach to inorganic chemistry, and Bill Libby was starting his carbon-dating work.

I remember one Saturday afternoon when Frank Westheimer burst into the laboratory and said, "Come right away. We need you at a conference." I followed along dutifully to find Frank, Bill Libby, George Whelan, two other professors, and some assorted graduate students and postdocs assembled in a room. The problem put to us was that Libby wanted to know how to ash a penguin. Someone had told Libby that he should have a verified modern sample of carbon composition to compare with his ancient samples of carbon dating and that he should accumulate animals from the North Pole, South Pole, Equator, etc.

The Penguin had been flown from the Antarctic and we were charged with converting all the carbon in the flesh, beak, claws feathers, etc. to $CO_2$. The group started with obvious answers such as fuming sulfuric acid, aqua regia, fuming nitric acid, chromate solutions and so on. Each suggestion was discarded on the recommendation of someone whose experience showed it couldn't do the job. Finally, in frustration, the group dispersed for dinner. Several days later I happened to meet Libby, and I asked what had been decided. Libby said no chemical solution had been found, but he had mentioned the problem to his wife. She pointed out that all body materials were synthesized from a common source, and she therefore suggested that we cook the penguin and collect the grease, which of course could be easily oxidized to $CO_2$. We followed her advice and the problem was solved. Both this imaginative solution and the exchange of ideas among professors and students over the course of several hours are typical examples of what made the atmosphere at Chicago so exciting at that time. When I went to Harvard for my postdoctoral studies the competence level was the same but the mood was more sedate and regal.

Although my PhD program had only taken three years I was convinced I was a very old man because of the four-year war delay, so I wanted to skip a postdoc. But Frank Westheimer talked me into doing a postdoc and helped me get into Paul Bartlett's laboratory at Harvard. Bartlett's lab was at the forefront of organic chemistry mechanisms, and my years at Harvard were fascinating and challenging because I was focusing on enzymatic reactions, an area Bartlett's group respected but in which they had little interest.

Fritz Lipman, whom I met during my postdoctoral fellowship in Bartlett's laboratory, invited me to an important symposium because of my acetyl phosphate work and in spite of my youth and immaturity. He later offered to have me come to his laboratory for a few months to learn something about biology, and I suggested that I might like to crystallize an enzyme. This interest was a very logical step for me because crystallizing organic compounds was a routine matter; but it was a heroic project for enzymes at that time, and I did not realize the processes were so different. So word got around Massachusetts General Hospital that a young guy named Koshland was coming over to work with Lipman for a month and planned to crystallize an enzyme, a source of great humor to many. I did not succeed in crystallizing an enzyme in that short time, but I did learn an enormous amount of biology and fortunately was exposed to a lot of Lipman's philosophy, which was original and keenly perceptive.

## *Brookhaven National Laboratory*

Up to this time I had been the typical happy-go-lucky graduate student and postdoc, but as happens to all such students it began to dawn on me that I would have to get a job. The job situation was very tight in the early 1950s. My varied background in chemistry and biology certainly didn't help, and I did not get an offer for an academic job. One interviewer from Columbia University looked at my record and said a man who had published little by the age of 31 would never amount to anything (all my war work was classified). So I went to Brookhaven National Laboratory somewhat reluctantly with the vague idea that I would stay a year or so and then go back to a university. Fourteen years later I was still at Brookhaven and very happy, and even then I probably would not have left if I had not had an attractive offer from the University of California at Berkeley.

Brookhaven National Laboratory turned out to be an excellent place for the beginning of my independent career. Because I was a chemist learning biology it was probably best that I didn't start teaching students immediately, and the position also gave me time to assimilate the knowledge in the new field. One lucky break during my years at Brookhaven was a rejection of one of my papers. The paper described a theory I had developed about the stereochemistry of enzymatic reactions which lumped group transfer reactions into two categories, single displacement reactions and double displacement reactions. Because the topic was chemistry I submitted the paper to the *Journal of American Chemical Society* using extensive references to the chemical literature for the stereochemistry of the substrates and products. I also chose this journal because they had recently invited theoretical articles. The editors promptly turned down the paper, saying they did not accept theories. When I pointed out that they had specifically asked for theory they told me that meant mathematical ideas. As a result of this rejection, I published in the review journal *Biological*

*Reviews*. Older biologists told me that lots of biologists read *Biological Reviews*, whereas most never looked at the *Journal of American Chemical Society*, and that I was extremely lucky to have picked that journal to bring chemistry to the biologists.

One of the great lessons of my life derived from the publication of the induced-fit theory. I was supposed to give a talk at a well-known symposium on my oxygen 18 ($O^{18}$) work, but decided to speak instead about new research on the specificity of proteins. As I was preparing the talk I was going through the classical explanation for the manner in which substrates are excluded from active sites and decided the "key-lock" or "template" theory of Emil-Fischer was too simple. The theory provided no explanation for the low enzymatic reactivity of water. When I reexamined the literature with this puzzling thought in mind, more and more anomalies arose. I postulated that the enzyme must be flexible and that a new structure of the protein would have to be induced by the binding substrate or activators. This deviation from the template hypothesis of Emil-Fischer met with no approval from distinguished journal editors but finally got published when DD Van Slyke offered to sponsor my paper for the *Proceedings of the National Academy of Sciences*.

Although we did many experiments that in my opinion could only be explained by the induced-fit theory, gaining acceptance for the theory was still an uphill fight. One referee wrote, "The Fischer Key-Lock theory has lasted 100 years and will not be overturned by speculation from an embryonic scientist." We did a lot of experiments, all of which supported the theory, and crystallographers saw small conformational changes that were enough in my opinion to validate the theory, but authors dismissed the changes as being too small. We did more experiments with protein reagents that supported the theory and later the crystallographers, Bill Lipscomb and Tom Steitz, found big conformational changes in proteins on binding ligands, which removed all doubt, and the theory became accepted. Textbooks now routinely include the induced-fit theory.

The episode made me sympathetic to novel theories and aware of the obstacles to their publication. New and tantalizing results require strong support to overturn well-established principles, but this experience also taught me that sometimes journals and literature can be too conservative. That attitude helped me later when I became editor of *Science*.

At Brookhaven we lived a fairly idyllic life. My wife Marian Koshland had her laboratory in the same institution as I did, simplifying our life. Our children grew up in a lovely small village with fine schools. They and we had great friends, and the laboratory had a stimulating intellectual atmosphere.

I got interested in muscular contraction and used lobster as a good source of muscle. We often ran what we called the "boiled control," and it was the culinary peak of my academic career. I had read that lobster muscle was essentially a pure ATPase, so I deduced that I could simply add an excess of $H_2O^{18}$ to lobster muscle, let the $H_2O^{18}$ exchange with the water in the muscle, and then let the reaction run in the intact lobster muscle. The experiment worked well and had the advantage that at the end I simply lifted out the intact muscle and had a pure water ATP solution without contaminants. I was then able to analyze the ADP and inorganic phosphate that was formed. I submitted the manuscript to the *Journal of Biological Chemistry* where it was accepted. Only later did Mildred Cohen tell me that the manuscript had come to Carl Cori who asked Mildred (an authority on $O^{18}$) what she thought of it, with the comment that "some nutty, young scientist at Brookhaven National Laboratory has added a whole lobster tail to a solution and thinks he is studying an enzymatic reaction." Mildred, with whom I later became good friends, told Carl Cori (with whom I also later became good friends) that in fact she could see nothing wrong with the experiment, and Cori accepted the manuscript.

## *Berkeley*

While I was doing this work, I was offered and accepted a faculty position at Rockefeller University. Because moving five children into New York City did not seem practical I proposed that I come one day a week to teach a course and supervise a laboratory, and to my amazement this arrangement was accepted. I would have blithely continued for the rest of my life with that arrangement at Brookhaven and Rockefeller, but in 1964 I received a phone call from Horace Barker at the University of California asking if I would like to come to Berkeley. My wife, an Easterner, immediately pointed out how happy we were and how good our situation was, and I agreed intellectually that we could hardly better ourselves. One of my senior colleagues advised me, "If you are 95% happy at one institution never move to gain 5%, there are too many uncertainties."

Recalling all the arguments that were made at the time is difficult, but my great love for Berkeley and the campus in my early years cut through all the logic. At our family dinner table we had a brief discussion in which our five children and my wife voted "nay" on moving, and I quoted Lincoln to say the "ayes" have it. Actually, my wife made the decision saying, "Either we stay in the East and I spend the rest of my life making it up to you, or we move west and you spend the rest of your life making it up to me. We move." Berkeley lived up to its reputation of being turbulent as I moved in the 1960s when Berkeley was a center of uproar, but it also lived up to its reputation of being dynamic and exciting. In retrospect, I believe none of us regretted the move.

Being a professor at Berkeley added teaching to my job requirements, and I found it a great joy. Teaching is work, but very rewarding work. I enjoyed the large classes at Berkeley when I was an undergraduate, and since I am basically a ham I consider it a privilege to lecture to the 300 students who annually take our biochemistry major course. The students are very good and constantly keep a professor on his toes. The postdocs who made up my research laboratory at Brookhaven were augmented by graduate students and postdocs at Berkeley.

The pleasures of doing research and teaching made it difficult to pretend I was working instead of merely having a good time. Scientists are basically puzzle solvers, and they get hired to solve puzzles. So someone else is providing the capital for them to satisfy a lifelong desire. *The Organization Man,* a brilliant book by William Whyte explained that people in many professions love their work, but that scientists seem to be particularly lucky in that regard. Tenure can be given because those who love what they are doing work long hours even after such commitment is no longer necessary.

One Saturday morning I was working at the University when a student knocked on the door. When I answered the knock she said she had to ask about an anomaly. She asked, "You and Professor Snell, Professor Barker and Professor Hassid are all working on Saturday but you are members of the National Academy and have tenure so why are you working so hard?" I explained that we all enjoyed it. The incident made me remember a small conference during the hectic days of the atomic bomb research in which Enrico Fermi looked up from spirited argument and said humorously, "It's amazing how fascinating blowing up the world can be." Fermi was a kind and sensitive person and was well aware of the horror of a bomb and the importance of its achievement, but he was observing for a moment that developing a bomb entailed a massive puzzle of great difficulty in chemistry, physics, engineering, and mathematics.

## *Science*

In 1984 I received a phone call from David Hamburg asking me to move to Washington to be full-time editor of *Science.* I answered without hesitation that I would not give up my laboratory but added laughingly, "If it was a part-time job I could be interested." I had just been chairman of the department, a time-consuming chore, and decided that one could do two things at once. Two months later I received a call from the same David Hamburg saying the American Association for the Advancement of Science (AAAS) (the owners of the journal *Science*) were willing to offer me the job part time. Then I got scared and asked myself if I could really do the job part time. I decided to visit the magazine and talk to the staff about it. After that initial appraisal I decided the arrangement was possible and said I would do the job with the condition that they would be honest with me if they thought I was doing a bad job and I would be honest with them if I thought I couldn't handle the burden.

But everything proceeded extremely well. Staff at the time were helpful and welcoming, and new staff, which I hired over the next couple of years, were equally enthusiastic and competent. The arrangement in which I spent one week a month at *Science* and the other three in Berkeley actually worked out quite well for both of us. My division of time between editing and research was close to 50-50, since I spent a great deal of *Science* journal time in Berkeley, not only phoning *Science* staff every day, but also soliciting articles and discussing policy from Berkeley.

When I was about to leave the editorship I recommended to the AAAS Board that they continue with the part-time editor for two reasons. First, I felt the editor of *Science* should be a continuing member of the scientific community. Not only because he or she would then speak with more credibility to the public, but also because he or she would be considered a colleague by fellow scientists and would understand policy issues such as funding that fellow scientists were experiencing. Second, this arrangement produced more independence and enjoyment for the staff. The editor was around enough so the staff could understand his wishes and get a feeling for his approach, which is important because the head of any large organization has to provide direction, enthusiasm, and motivation. But since I was not there most of the time, each editor, department, and staff member had an added degree of responsibility. Moreover, I deliberately selected people who could be more independent, and they in turn were the type of people who enjoyed the independence. When I started I was apprehensive that my part-time position would end badly and might cause great friction. When I left, the staff was in almost unanimous agreement that the part-time arrangement allowed the journal to select the editor-in-chief from a far more widespread pool and also to develop a more talented pool of staff members.

I had a wonderful time at *Science* and was tempted to go on forever. But as my ninth year was ending I noticed that I was beginning to lose some of my enthusiasm for new projects, and I was longing to get back to full-time research. So I notified the Board which then started a search for a successor, and I have returned to full-time research. The Board chose an excellent successor in Floyd Bloom. I miss the stimulation and excitement of the *Science* atmosphere and my many friends there, but I believe that any job in this world can only operate at full throttle. Once a manager starts thinking everything is going well, the staff is excellent, and there's nothing to fix up, he or she is on his way to disaster. The show business phrase "always leave them laughing" is a good one and is the indication of the time to move on.

Being able to do full-time research again provides compensation for the loss of the challenge of *Science*. When one is doing research half time, as I was for those 10 years, one can keep up if one stays in one's original field and knows the literature well, but starting an entirely new line of work is very difficult. Pursuing new areas of interest has been possible since I left *Science*, and I am extremely excited, feeling much as I did when I was a starting assistant professor and had to probe entirely new lines of research as part of my need to get a laboratory going.

## *Colleagues*

One of the most easily forgotten ingredients of the life in science is its social aspect. The image of a reclusive curmudgeon solving esoteric puzzles in a badly heated attic is a movie director's idea of a scientist. The real life of a modern scientist involves interactions with many people: students, colleagues, editors, business staff, university administrators, visiting speakers, and so on. A very big social life is needed just to get the job done. That social life is very rewarding and in retrospect no minor part in the joy of science. There is a special camaraderie in science in which colleagues share the frustration of failure and the joy of success in the arduous battle to uncover nature's secrets.

That camaraderie is also part of editing where the challenges of producing a journal of highest quality require the great efforts and high abilities of many people. That enjoyment of a common endeavor is also shared with the business staff at universities, who rise to challenges such as getting the grant proposal in on time even though the principal investigator has left it until the last minute, and the university administrators who struggle to maintain the quality of the institution.

An inadequate step in this direction is to list the coauthors who contributed to the research in my laboratory (see Acknowledgments). Space does not allow me to add all those on the staffs of Brookhaven National Laboratory, Rockefeller University, the University of California, and *Science* magazine who were so helpful and fun to work with, but they are deeply and gratefully remembered for their effective and enjoyable contributions.

## *Summary*

As I look back, I am still amazed that I was actually paid to do something I loved and others could describe as work. Yet my situation is no different from that of most scientists who find that they are asked to pursue their innate curiosity to solve puzzles, the solutions to which fortunately are of value to society. I enjoyed the beautiful logic of mathematics in elementary grades and was entranced by the exciting solution of puzzles described by DeKruif. So I drifted into the scientific profession without a clear idea of what to do or how to do it. Each experience prepared my mind and supplied the base for the next job, creating what was for me a smooth flow from scientist to professor to editor to scientist.

Fortunately for me and fellow scientists the problems of the world never disappear. "The one who rides the tiger can never get off" is an aphorism that expresses society's dependence on science. Automobiles improve transportation and create pollution, medical advantages prolong life and create overpopulation, pesticides bring cheaper food and create soil problems. Each advance brings on the need for more science to solve the new problems. Society, which likes to live well, is addicted to the products of science, and fortunately a peculiar set of humans are addicted to solving the problems. I am one of those typical addicts who finds the obstacle course fascinating and the endlessness of the quest utopia.

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The author owes too much to too many to acknowledge adequately the generators of his unbelievably enjoyable life. It all started with two exceptional parents who expected children to rise to challenges and provided the cushions of love and support that eliminated pain from failure. I had two outstanding scientific mentors in Glenn Seaborg and Frank Westheimer, and a stream of superb colleagues, graduate students, and postdoctoral fellows who not only provided scientific ideas and results but an atmosphere of enjoyment that made the trip as much fun as the destination. They were equaled by the staffs of Brookhaven, Rockefeller, Berkeley, and *Science* who were so good I would even inadvertently admit I liked administrators. Last but certainly the most important colleague and mentor is my wife, Marian Koshland, who has dispensed wisdom with amused compassion as a "shadow government" in all my endeavors.

Because space does not allow me to list all those collaborators who made research so much fun, I have settled for naming an illustrative sample chosen by chance to represent the totality whom I remember with affection. A Kowalsky, A Redfield, B Howlett, B Lynch, C Batt, C Blake, D Filmer, D Hoare, D Mulligan, D Phillips, E Herr Jr., E Kennedy, H Levy, H Weiner, J Spudich, J Thomas, M Erwin, M Kirtley, N Sharon, P Strange, R Macnab, R Weis, S Springhorn, S Strumeyer, W Ray Jr., W Springer, A Shiau, R Cook, R Zukim, R Yount, P McFadden, M Lee, T Ingolia, G Dafform, J Hurley, D Storm, W Stallcup, H Biemann, R Stroud, A Conway, C Jeffrey, K Carraway, R Cook, A Dean, A Cornish-Bowden, J Haber, D Saunders, C Long, M Shapiro, M Snyder, S Clarke, K Neet, R Bell, G Loudon, S Kim, M Brubaker, R Tjian, L Cheever, J Stock, S Mowbray, J Falke, K Walsh, A Goldbeter, G Bollag, A DeFranco, D LaPorte, R Dahlquist, G Moe, S Mockrin, T Terwilliger, B Stoddard, J Wang, D Mochley Rosen, M Smolarsky, S Parsons, A Russo, N Paoni, A Flint, D Aswad, P Thorsness, A Stock, D Clegg, M Fahnestock, A Newton, A Levitzki, and P Lovely.