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SHEER LUCK MADE ME AN IMMUNOLOGIST

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A Head Start

The luck began when I was four years old and my younger brother contracted typhoid fever from a carrier in the local dairy. It was not a lucky event for him, of course; he became desperately ill and was not expected to live, so my parents spent months in the hospital by his side.

It turned out to be lucky for me, however, because I was farmed out to the next-door neighbors who had two preteen daughters. For some reason, the girls decided to undertake my education. They knew nothing of the techniques, neither the do's nor the don'ts; they just taught me to read simple words and sentences and to count. Proud of their handiwork, they took me to school and had me show off my accomplishments. This was very heady stuff for a four year old who was feeling, rightly or not, somewhat left out by her parents.

My brother finally recovered from typhoid fever, but his immune system was so depleted that he promptly succumbed to every known childhood disease. As a consequence, I was quarantined at home for a year, and my martinet father took over my education. When I finally was allowed to go to school, it was clear that the tutoring by the girls and my father had put me ahead of my contemporaries, and this assurance served to support my conviction that "studies" was the one thing I was good at.

Upward Bound

My second piece of good luck was provided by three Jewish boys who were my main friends during high school, particularly during the last two years. I emphasize the word "friends" because in those days religious differences meant that I could never for a moment be considered a "girl friend." We were simply a gang who did things together, and since they came from a more cultured

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and ambitious tradition than mine, I was challenged to go along and keep up with them both outside and inside school. Outside of school during the 1930s depression, we went to WPA theater productions such as *One Third of a Nation* and *Murder in the Cathedral*; we sat at the top of the Metropolitan Opera House to hear Kirsten Flagstad and Lauritz Melchior sing *Tristan and Isolde*; we visited the downtown fish market at dawn and browsed through Chinatown. Inside school, when my friends chose to take a physics course, I went along and, much as I disliked it, learned to wire a light box and measure gas pressure. When they got A's in American history, I had to do as well. And when they picked up a three-foot constrictor black snake in biology class, I followed suit. And then I had to eat the canned rattlesnake meat that was the prize for the only girl who dared to touch the reptile. Thus, I was not only intellectually stimulated during my teen years, but I also escaped the usual pressures to be a "girlie."

Start of a Research Career

I was a sophomore chemistry major at Vassar, bored with memorizing organic reactions, when I was saved by a third stroke of luck. The College hired a PhD fresh from Yale to teach bacteriology and, on the side, a little immunology. The young professor, Catherine Dean, was such a good and enthusiastic teacher that within her first year she collected twelve majors from my class alone—a number that surpassed the usual total of science majors at the College. It was her introduction to the new science of immunology that provided me with a research career for a lifetime. Only a year before, Tiselius and Kabat had finally identified serum antibodies as members of the γ-globulin fraction, and one of the critical questions that arose from these studies was whether the various serum antibody activities—agglutination, precipitation, neutralization, complement-fixation—were carried out by different immunoglobulin molecules or were different manifestations of the same molecule, the so-called Unitarian Hypothesis.

I was much more intrigued by the ability of immunoglobulin molecules to recognize and eliminate an almost infinite number of foreign invaders. I read Karl Landsteiner's *The Specificity of Serological Reactions,* (Charles C. Thomas 1936), which had been published just four years before, and I was determined to try my hand at resolving the basis for the diversity and specificity of antibody reactions. How fortunate I was at the age of nineteen to be able to select a research area that, despite a few dips here and there, has grown and developed over the years and is even more fascinating and important today than it was when I began.

Graduate Reinforcement

My choice of graduate school was based on hard cash: Having spent my life in the East, I wanted to go as far West as my limited amount of money would

allow. The University of Chicago won out as the best institution with the lowest traveling costs, $16 for an overnight coach ticket from New York. Little did I realize that the University had become a hub of wartime research, not only for the development of the atom bomb and various explosives, but also for the control of infectious diseases among the troops. But being broke and having to work my way through graduate school turned out to be the source of great luck because it gave me the opportunity to work on two such projects. Each experience emphasized the need to understand the fundamental mechanisms of immunity, and both reinforced my desire to participate in such research.

The aim of the first project was to develop a vaccine that protected troops in the Far East against cholera. Since the infection is confined to the lumen of the gut, parenterally administered vaccines were of little efficacy. Our studies used an experimental disease in guinea pigs to show that oral administration of a nonlethal dose of vibrios prevented the disease, and the protection was associated with the secretion into the gut of antibody, politely called copro- rather than fecal antibody. These findings provided an important precedent for the subsequent development of the oral polio vaccine and left me with a lifelong interest in antibody secretion into the body cavities.

In the second project, the Commission on Airborne Diseases was charged with reducing the incidence of respiratory disease during Army basic training. Streptococcal infections were particularly prevalent among recruits from rural areas; they had little previous exposure to the causative organism and often developed serious autoimmune complications, such as rheumatic fever and glomerulonephritis. In this case, the problem was solved not by immunological approaches but by controlling transmission of the pathogens. Epidemiological studies showed that the incidence of disease could be significantly reduced by measures that reduced the number of airborne pathogens in the barracks sleeping quarters—measures such as spraying a thin layer of oil droplets on blankets and clothing to prevent the release of bacteria during bedmaking.

Career Crisis

Perhaps the greatest luck of all was the support and advice my husband gave at the end of our postdoctoral training at Harvard. Up to that time, I had proceeded along the usual route, marriage, graduate school, two children, postdoctoral studies, and had blithely assumed the usual outcome, a full-time academic career. An unexpected complication arose, however; namely, the arrival of twins, which meant that our family suddenly consisted of four children under the age of five. Reality struck as I had to face how I could do both—be a good mother and a good immunologist. When I told my husband of my decision to become a full-time mother, he would have none of it and instead suggested part-

time work as a solution. He overrode my objections with two arguments; first, that most tenure-track scientists did research only part-time because of teaching and administrative duties, and second, that a half-time research adjunct could remain competitive by being creative and undertaking high-risk projects that a tenure-track scientist could less afford to do.

I followed my husband's advice for twenty years until our youngest son finished high school. It meant that I had a great time doing "crazy" research and did not suffer severe guilt pangs about the children.

A Paradigm for Science Education

Many of the chance events that shaped my career as an immunologist are now the basis of educational programs aimed at generating an interest in learning. Thus, preschool tutoring, such as I had, has been employed by Head Start to remedy the backgrounds of children from disadvantaged homes. The program has an impressive record of turning out children who perform better on entering school and thus like the learning process. Maintaining that performance and liking of learning during the teen years, however, requires programs that can successfully counteract the anti-intellectualism inherent in some social traditions and teenage peer groups. My father was a good example of the traditional problem. His ambition was for me to be a "lady," which translated into taking courses that aimed to produce a good hostess and a good housekeeper rather than a good physicist or a good mathematician. He didn't approve of my Jewish friends, but fortunately he could not override the stimulation and security of their friendship. Programs such as Upward Bound are providing support to high schoolers equivalent to that provided by my Jewish friends. Their aim is to combat not only social pressures but also peer pressures that place the highest values on being a cheerleader, or starring on the football team, or wearing expensive clothes. Organizations such as the National Science Foundation are trying to create rewards for scientific achievement that can compete with the publicity given high school sporting events or prom queens. The best science students in each state and his/her high school teacher meet in Washington and have their pictures taken with "big shots" like the President's Science Adviser or the Director of National Science Foundation.

"Hands-on" experience is a powerful career attractant. A research project in my senior year at Vassar and the subsequent wartime projects completely destroyed any notion I had of alternative careers, even medicine. The research bug had bitten! And my bite has been duplicated hundreds, thousands of times. The Oberlin Report clearly documented that it is an undergraduate research project conducted in close contact with a professor that is responsible for the high turnout of scientists by the small liberal arts colleges and for the high rate of success among those scientists. As a result, "hands-on" laboratory work

has been adopted as a lure by many public and private organizations to interest minorities and women in scientific careers. The MARC program of the National Institutes of Health and the undergraduate programs sponsored by the Howard Hughes Medical Institute are good examples of how effective the hands-on approach can be.

Where Is Creativity?

One of the elements, perhaps the most important one, that shaped my career as an immunologist has, however, fallen through the cracks of most science education programs. That is an emphasis on creativity. At the beginning of my senior year at Vassar, Catherine Dean led the bacteriology majors to a room in the basement and said, "Here is a centrifuge, a pH meter, an incubator, media on the shelf, and various bacterial strains in the icebox. Dream up your research project!" We did, because senior research was a requirement for graduation. In the graduate program at the University of Chicago, students (that included me) were expected to develop a thesis proposal and then sell the project to the appropriate professor in the Department. In the postdoctorate scene at Harvard, appointments could be made to do independent work provided that the proposed work passed faculty review. I took full advantage of the opportunity. The emphasis on originality in these programs reflected the notion that students could be trained to think creatively and that such training was critical to their success in their subsequent careers. This notion was amply supported in my own case because the training enabled me to follow my husband's advice and to remain competitive by concentrating on more "far out" research ideas.

Many of the devices used in the past to foster creativity, e.g., graduate students designing their own thesis projects, have been discarded. They became impractical as the biological sciences grew more sophisticated, more team-oriented, and more competitive. Unfortunately, the emphasis on training in creative thinking has disappeared along with the devices. The de-emphasis has occurred as young scientists have a harder and harder time creating research niches to establish themselves, as study sections award their limited amounts of money to safe rather than innovative proposals, as the number of scientists being trained is reduced without any criteria for selecting those with the most original minds. The de-emphasis has also occurred at a time when creative thinking is needed for young scientists to tackle socio-scientific problems such as the dealing with the question of a second job for a spouse or significant other, the division of time and effort between research and parenting, etc. In my opinion, the immunological community would do well to focus on such issues and devise techniques for encouraging creative thinking that are applicable to the current state of the science world and its teaching.

Bad Luck

At this point in my recital, you may ask whether there were any unlucky events that affected my career. Of course, there were. To give a few examples: A professor at Chicago gave me a foretaste of things to come as I was going off to Harvard for my postdoctorate. He said that I had been an excellent graduate student, but because I was a woman, I should not entertain any hopes of being hired by the faculty of the Department of Bacteriology and Parasitology. At another institution, the head of the department proclaimed he would never hire the wife of anyone, not even the janitor, so my husband and I had to look elsewhere for the second job. Early in my career, one or two immunologists would get up after each of my research presentations and say they couldn't reproduce the data. Although their criticisms were never documented, the constant voicing of doubts had the effect of delaying recognition of my work.

To be fair, there were also many helping hands along the way. The faculty at Chicago sponsored me for membership in the American Association of Immunologists before such well-deserving male peers as David Talmage, Maurice Hilleman, and Riley Hauswright. Dr. Howard Mueller, head of the Harvard Department of Bacteriology, went into the shop and personally made 24 guinea pig metabolism cages that I could not afford to purchase on my fellowship. Dr. Wendell Stanley, head of the Virus Laboratory at Berkeley, bought some $25,000 worth of equipment for my research without any guarantee that I would get a grant and pay him back. I suppose the unkindness and kindness come out about even.

As I look back, I think my one significant piece of bad luck may have been not playing a team sport. Recent analyses have indicated that women scientists tend to be loners who do not belong to a network of collegial associates. Typically they run small laboratory groups and are relatively unaggressive about promoting their research accomplishments. These characteristics contrast sharply with those of the average male colleague, and the question is, why? A number of explanations have been offered: differences in mentoring, in standards for masculine and feminine conduct, etc. One of the most intriguing is the difference in athletic experiences. Most men have participated in some form of team sport throughout their education, whereas most women have not. Moreover, men continue to participate in their adult years; the male graduate students, postdoctorates, and able faculty from our immunology floor still get together for a basketball game using a net rigged up outside the laboratory building. In these team sports, the players get the opportunity to practice competitiveness; they learn how to develop winning strategies and, at the same time, how to work cooperatively and form successful liaisons—very valuable lessons for any

subsequent competitive endeavors. The idea of a contribution from team sports came much too late to affect the education of my three daughters. However, all seven of my granddaughters, ranging in age from five to eighteen, have been or are currently playing on soccer teams! We'll see what happens.