Perspectives

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Memories of a Mentor: Charley Steinberg

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CHARLES M. Steinberg (see pictures) began his scientific life as a geneticist and always said he felt more comfortable with that epithet than with "molecular biologist" or "immunologist," although he was indeed those too. He was awarded a Ph.D. in 1961, at the California Institute of Technology, under the supervision of the late Max Delbrück and Frank Stahl. As a student he worked on a variety of problems in the genetics of bacteriophage T4, but the most important achievement during this period was undoubtedly the discovery (with R. H. Epstein) of the *amber* mutants of T4 (Epstein *et al.* 1963).

In 1970, after time in Cologne and Oak Ridge, he received an invitation from Niels Jerne to join the newly formed Basel Institute for Immunology. As Charley said, "It was a small intellectual leap from worrying about mutator mutants and the origins of spontaneous mutants in yeast to getting involved in the controversy over somatic mutations vs. germ line as the origin of antibody diversity."[1] Immunologists of the 1970s seemed to consider genetics to be a subject more suitable for polemics than experiments. Charley was primarily responsible for the Basel Institute becoming one of the pioneers in the application of molecular genetics to the problems of immunology, especially in the drive to uncover the mechanisms of antibody diversity (for examples: Hozumi and Tonegawa 1976; Bachl *et al.* 1999).

The Institute's format nurtured the qualities in Charley that led to these successes. The Basel Institute was a group of 50-odd scientists—"Members"—of whom around 10 were "Permanent Members." Members were at the Institute for 2 to 4 years or so, with their research fully supported by Hoffmann-La Roche—a scientist's Nirvana. Charley, as a Permanent Member, was a constant. He maintained the lore of the Institute; many people sought him out over the years, for many reasons. He had an office with a huge blackboard and was always interested in talk over coffee in the cafeteria. He was the Institute's guru and remained so past his retirement in 1997.

Charley died September 17, 1999, after 9 years with leukemia. His contributions to science bridged many fields. But as we are all more than our publications, so was he (von Borstel and Cairns 1999; Du Pasquier 2000; Melchers 2000). Charley was a mentor.

The word mentor comes from the Greek. Mentor was the name of a friend whom Odysseus entrusted with the education of his son Telemachus. While Odysseus wandered after the Trojan War, Mentor was Odysseus's trusted counselor (Homer 1942). The ancient Greeks had it right. One mentor was chosen, and that was your trusted counselor. Just as Odysseus's wanderings were marked by many changes of fortune, so are those of scientists, although today our intellectual wanderings are sidetracked by grant writing, scrambling for faculty positions, becoming computer literate, serving on committees, and so on. It was on these subjects that Charley's skills in mentoring came through. The best mentorship is a careful balance of listening and advising behind the scenes and not destroying it all by being discernibly judgmental. He was fond of saying: "Don't let the turkeys get you down," when somebody was unfairly treated. Charley's mentoring had many facets; we wanted to reveal some of these through the words of a few recipients.

THE EARLY MARKINGS OF A MENTOR

From the time he first became visible as a scientist, Charley was a mentor.

Millard Susman (Wisconsin):

> I entered Caltech as a graduate student in 1957. By that time, Charley—three years my senior—had already be-

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[1] Charley Steinberg quotations, for the most part, are from e-mails sent to, or copied to, G.W. In some cases, which are obvious from their context, they are from the memories of contributors.

Charcoal drawing of Charley Steinberg. In April 2000 Louis Du Pasquier of the Basel Institute for Immunology drew this charcoal of Charley as he was in the Spring of 1999. Charley and Louis were long-term friends and colleagues and shared office space after Charley's retirement in 1997.

come a legend in the Biology Division. Everyone knew that, if you had a question, Charley was the person to ask. Max Delbrück, our major professor, had already come to the conclusion that he had nothing to teach Charley and that it was time for Charley to write a dissertation and get on with his life. Repeatedly, Max would suggest that Charley write a review article on one of the many subjects on which Charley was an authority. Anything that Charley wrote was certain to contain enough of Charley's original thought to qualify as a Ph.D. dissertation. Charley was cagey, however; he loved the anonymity and freedom of life as a graduate student, and he resisted until Max made him an offer he couldn't refuse: Max was going to Cologne, and Charley could either go with him with a Ph.D. or leave the lab without one. Charley wrote his thesis in two weeks and went to Cologne with Max.

Charley was good at the bench, but it was his brain that inspired awe in everyone. He and I shared a lab with Dick Epstein and the communal coffee pot. For Charley, the best thing in life was to sip coffee and talk science with the endless stream of people who dropped in to be stimulated by caffeine and Charley. The talk was not always about science. Charley, for example, was interested for a while in Manchester Guardian crossword puzzles, which we worked on as a team, with anyone dropping in for coffee becoming a member of the team. Most of the talk, however, was science of one sort or another, and an impressive group of scientists came in to talk. I'll name just a few: Bob Edgar, Frank Stahl, Jean Weigle, Howard Temin, Matt Meselson, John Cairns, Dick Feynman, and Harris Bernstein. Max would often have famous visitors whom he would bring into the lab specifically to meet Charley. Especially vivid in my memory is the day when Max walked in with Niels Bohr, looking for Charley.

I have always said that I learned humility at Caltech, and I learned most of it by comparing myself daily with Charley. I've never met anyone as bright as Charley. He was a modest genius, who loved to share his knowledge and his good ideas, but never seemed to want any of the glory that comes to geniuses. He was approachable. His clothes, often a bit ragged and spotted; his beard, a scraggly affair that anticipated by several years the popularity of beards among undergraduates; and his posture, a virtually supine position in a front-row seat in the seminar room, all seemed intended to let you know that Charley had no pretense. The extraordinary thing about Charley was that you never sensed any feelings of superiority in him. Charley was smart enough to be frightening, but he wasn't. He chose to be a mentor.

ADVICE FOR THE YOUNG SCIENTIST

Many other young scientists entered their field because of something Charley did or said.

Marc Shulman (Toronto):

I remember a heady week as a graduate student in which I encountered both Charley Steinberg, the molecular geneticist who later became an immunologist, and immunology, a branch of microbiology which later became a branch of molecular genetics. Charley had written a mathematical analysis [*"A formal theory"* (Steinberg and Stahl 1958)] of genetic recombination in phage, and Cyrus Levinthal had assigned it as a trial by fire for us first year graduate students. In our microbiology course, Salvador Luria led us in a Socratic exercise to consider the unlikelihood of allelic exclusion and then revealed that it had been confirmed experimentally. And so I began a career as a phage geneticist with allelic exclusion as my hobby because of this Charley Steinberg.

And many, many others were influenced during his times at Caltech, Oak Ridge, and of course, Basel. It is from Charley's Basel mentoring days that most of the stories emerge. A mentor listens to the babblings of a scientist trying to figure out the data. Charley would hand us a chalk and say: "Start from the beginning, I am a simpleton, I don't know anything about this area, explain it to me." And by explaining it to him, you would begin to understand yourself, and then:

Louis Du Pasquier (Basel):

"A silent Charley made you think twice."

There are many anecdotes relating how Charley helped me when I was confronted with strange results or with a dilemma—explaining to me why the bacteriophage I used was likely not the one whose name was written on the label by the lab of origin, and this just from the shape of the inactivation curve by antibodies. Or . . . picking up patterns in somatic mutations in frogs just by gazing at sequence, leading Melanie Wilson and me to the hypothesis that, compared to warm-blooded vertebrates, somatic mutants might not be optimally selected in Xenopus. Or . . . insisting on keeping the good old genetic technology of analyzing families to try and understand the fate of duplicated genes in polyploid Xenopus. Or . . . encouraging bold experiments when, with Matthias Wabl, we were planning to do nuclear transplantation using Xenopus lymphocyte nuclei.

All this is very well, something all mentors should do, but there was something deeper in Charley's mentoring.

Like all mentors, Charley raised my standards by making me more critical of my own and others' data. But Charley went further; he modified my way of thinking. Like all good chess players, he was always a few moves ahead in our discussions, and he managed to make me think at least *one* move ahead. This introduced patience and re-

Charley in Paris, 1998. In his last years, Charley took to wearing broad-brimmed hats to ward off the sun's rays—the anti-leukemia chemotherapy made his skin especially sensitive to UV light. This photograph was taken as he posed, in fun, for a fashion photographer who took a fancy to his appearance.

> flection in my behavior when I was in my 30s, and it was a blessing. He did it by diffusion, never by direct persuasion, never by brutally showing how wrong I was. Education and training would come while talking about etymology, secret codes, or French wines over a cup of coffee. First I tried to adapt, adjust, copy—probably in a silly and confused way, and then with some efficiency. I do not really know how it worked. It reminded me very much of my first flute teacher who simply told me, "Listen to me and as close as you can, copy me." With the difference that Charley never said it so explicitly. He did everything silently, gazing at you, letting you discover yourself. The positive suggestions often came as a special look that was an invitation to change something in your way of thinking. That look was not at you, it was a polite, indirect look whose power forced you to think again. The direct look came at the end when I had corrected my reasoning. The result was that I learned to analyze observations in Charley's way. This is perhaps the most important and durable mark of Charley's influence on me.

Charley's judgment was dreaded. Anyone about to make a decision in front of him would think twice. A quick glance at a silent Charley was enough to guarantee a rethinking before a mouth was opened. This style irritated a few, and they would claim that Charley silently ruled everything because everybody was looking for his agreement. Well, this may not have been such a bad thing.

Asking Charley for scientific help was not for those who had something to hide. Charley had no patience with incompetence, no patience with stubborn, unmovable people in any walk of life. His gentleness with young scientists, however, always came across.

For *Una Chen* (*Giessen*) it was back to the basics—

> When I was trying to get a position, Charley would talk to me using language and examples I could understand and which lifted my spirit. He never talked to me in mathematics, or physics, or computer programs (of which I knew little). Instead, he taught me to handle the Internet, to use a Macintosh writing program, to load my own laptop so that I could work while traveling and communicate with him and the rest of the world from all corners of the world.
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> Charley also taught immunology to Lisa-the-artist, such that she could express the concept of the immune system in simple words better than anybody that I know.

For *Marc Shulman* (*Toronto*), it was challenging the intellect:

> Charley arranged a position for me at the Basel Institute for Immunology. Soon after my arrival, Charley pointed out one of the differences between phage genetics in the lab and immunology in the field: over coffee (where else?) he asked me what would happen when a lethal virus was introduced into an animal population. After I gave the knee-jerk answer that the circumstances would select for the animal analogue of phage-resistant bacteria, Charley explained the more subtle and realistic result that circumstances would select for a less lethal virus which conferred immunity. I explained that realism did not bother me, but subtle realism was frightening.

In answering people's questions, Charley spoke gently, but carried a big stick. As one scientist said, "Upon my arrival at BII, I went to see him in his office, he gave me chalk and I talked for 30 minutes about what I saw as the problems and puzzles of IgM and μ-mRNA stability. He listened carefully, then stood up and said in one sentence: 'Your problem is the half-life of μ-mRNA vs. the half-life of μ-heavy chain protein. Next please!' And he walked out."

For *Ellen Hsu* (*New York City*), Charley was someone you could talk with about anything—statistics, ambition, or the act of passing time:

> In her book *"Interview with History,"* the journalist Oriana Fallaci observed that a person who was interesting would come up with an interesting answer to even the most banal questions put to him (Fallaci 1976). Perhaps these anecdotes will give an idea of how Charley Steinberg's responses to problems, scientific and otherwise, were original as well as pragmatic, and always to the point. No one knows how anyone gets that way, but perhaps Charley felt he was just born with it, and he gave it away for free.
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> I first became acquainted with Charley when writing my thesis. Charley had a reputation that daunted almost everyone who didn't know him personally. Because he was reserved in manner, some people preferred to think that he was unapproachable, rather than admit to being afraid of finding themselves intellectually inferior. In fact, when you talked to Charley, he assumed that you really wanted to know the answer to your questions (the true essence of the spirit of scientific inquiry), and it would never have occurred to him to show you up. All of us are acquainted with colleagues who do that when you naively hand over your manuscript for their scrutiny.
>
> I also was afraid of him, afraid of ridicule, but I had a problem with my thesis discussion, and so I consulted him. Charley gave me a long explanation. I grew embarrassed and told him that I hadn't understood what he said. He went to the board, drew diagrams, and explained in a different way. I listened, with increasing misery, realizing that I still didn't entirely grasp it. He asked me whether it was all right. I couldn't look at him, debated with myself,

and finally asked him to repeat himself. He didn't repeat—he explained his answer yet a third way.

Charley respected your wish to know and understand. Because he did so, you realized that you must respect it, too.

When a collaborator repeatedly refused to acknowledge evidence directly contradicting his experimental results and interpretation, I took the manuscript to Charley, who noted that the collaborator had even glossed over internal evidence of artifact in his results. When I expressed my outrage about "bad" science, Charley calmly told me that there were two kinds of scientists. One kind thanks you for catching his mistake before it gets into print; the second prefers that you catch it afterwards. Charley never preached, much less moralized—he would simply get to the heart of the matter and save you time and breath. Although instrumental in developing experiments, Charley also performed an important role in axing proposed efforts that he foresaw would be futile.

Once Charley interrupted me in a rambling speech about the meaning of life and my failure to find it in science and asked how my experiments were progressing. When I informed him, not at all, he remarked that it was possible for scientists to spend an entire day working very hard and to ask themselves at the end of it, What have I done? He went on to advise me to take up a hobby. Perhaps inspired by my glare, he puckishly suggested that I take up making shoes (homonymic with my surname). He said, an activity where you can see concrete progress is good. You can go home at night and count how many shoes you'd made.

He drank some more coffee.

Charley's philosophy of life, which made him such an effective mentor and loyal friend, is shown in a quote he often cited when he saw ambition taking over a once good scientist, "Be nice to people on your way up; you will meet them again on your way down."

CHARLEY THE EDITOR

We entered into Science believing we would be creating science, not literature. We were mistaken, every one of us. Science has to be communicated and communicated well. Although he always said one couldn't, Charley changed our sow's ears into silk purses, at least at some time in our careers. Charley edited abstracts, manuscripts, letters, grant applications, novels, all of a scientist's writing. He changed our muddled ramblings into prose. He was the consummate editor and a gifted writer. As described by one recipient of his editing: "I wrote pages and pages of grant proposals, manuscripts, applications, and he just picked up his brush (pen, computer keyboard), and chopped my document down to 50% or even to 30%. But it still said the same thing or even better."

And Charley celebrated with us when we were successful. As one grantee wrote: "When he learned that I was awarded the grant, he sang 'Lily Marlene' for me. I was in tears." And when he sent back revised manuscripts, they had his terse comments attached: "Leave the two pDR70's. Don't generate more data. Remember to go over the text to change anything that adding the new sequences demands." His attention to details would bring admiration from any editor: "Note that one of the columns does not add up. I get a total of 109 sequences. But you got 108. I did not alter any numbers. You need to reconcile the difference."

Someone for whom English was not the first language asked: "Much vs. many—is it that 'much' modifies a singular word, 'many' a plural? As in many people, much sand?" And Charley's answer: "It is a bit more complicated than that. There are 'countable nouns' and 'uncountable nouns'; many is 'countable.' Countable means just that—you can count it like 1 sheep, 2 sheep, 3 sheep. That is, 'sheep' is countable. Much is uncountable; you cannot count sand, so you write, there is much sand. Sand is uncountable."

We learned to write clearly, or Charley would say: "It is surely a convoluted way of saying it." And a summation: "I doubt that you or he will be happy with it, but hand-waving is not my specialty." And we were warned not to mess with his editing: "If you want to change the formatting, it is better to ask me to do it. It took a while to correct some errors you put in."

Not until two weeks before his death did he cut back on his editing: "I already have more grants and papers in the queue than my health will allow me to do. Thus, I cannot help you with your project."

And what will we do without Charley to advise, and edit? "Unfortunately there is no way that I can come up with something reasonable in the next two weeks, as I have to renew three grants—without Charley." And his influence remains: "I was thinking about Charley the other day—whenever I write something I conjure a mental image of Charley as a reader, and then I write it again."

CHARLEY THE HELP DESK

Charley came to computers late in life, but long before they were generally available. He spent long hours showing us, in his patient way, how to use them. Indeed, he was a member of the computer users's committee in every institute he visited (and sometimes the only member). He evaluated our local so-called computer experts: "What a bunch of stumble bums! They are much worse than UCSF or Roche."

Howard Etlinger (*Basel*) says it thus:

You might think it's strange, but till the mid-1980s I had hoped to go through my entire professional research life without using a computer. There were several reasons for this, and the takeover of the space ship by HAL, the computer in the movie "2001: A Space Odyssey," only reinforced my feelings. It all came crashing down where I worked when management decided that every scientist would get and USE a computer. Charley helped me learn how.

A few years later, Charley and I were in the Basel Institute for Immunology, talking about this and that, and, as I esteemed his thoughts, I asked him what he would

do if he knew he only had a short time left to live. You could say it was a rather theoretical question because it wasn't long before he became mortally ill.

Charley said, "I would do exactly what I'm doing now."

More than a decade later, I was in the Basel Institute for Immunology unsurprisingly having problems with a computer and asked Charley for his help. Charley was the pro when it came to solving computer problems and had often helped me in my endless losing strife with 0's and 1's. By then Charley was very ill and would die a couple of weeks later. In addition to having leukemia, his cataracts made it difficult for him to see. Despite this, he immediately stopped what he was doing to help me. He couldn't find the cursor on the monitor and asked where it was. As I sat there watching him, totally absorbed in solving MY computer problem, I thought to myself, "Jesus Christ, Charley, what the hell are you doing here working on someone else's trivial difficulty when your life is so clearly slipping away?"

Charley helped so many people in so many ways over the years; his help was one of the things you could count on. Hypocrites are not hen's teeth. But considering Charley's health, it would have been understandable if he hadn't helped me. Although Charley never would have said it, helping people without expecting anything in return came under "do(ing) exactly what I'm doing now." Still, I was astounded by Charley's fulfillment of his ancient answer.

And so the point that Charley gave me, right before my very eyes, is not to live with the knowledge of what you would do shortly before your death, but to live at all times doing precisely the thing that you would choose to do shortly before your death. Charley exemplified this pattern and would certainly have agreed with the late Jack Chiller, who in 1976 once said to me when I was a postdoc in his lab, "Aren't they crazy to actually pay us to do what we're doing?"

But Charley himself obtained great satisfaction at helping and mentoring: "I fixed a couple of bugs for Louis today, and now he is dancing with glee because he has used the program to localize a new gene he found in Boston to a chromosome."

LIFE MENTORING

Many of us used Charley not only as a mentor of science but also as a mentor in our lives. With *Una Chen* (*Giessen*) he encouraged her artistic side:

I picked up the brush painting again in 1995 when I lived alone in Cassis and painted a side profile of Charley in oil. He said with humor that this guy looked Chinese, but he kept the oil painting in his office. In 1999, I modeled Charley in beeswax melted in a pot on my kitchen stove. When I showed him the prototype, he smiled and said that the nose seemed a little bit too Jewish. Five days before his death, I showed him the finished terra-cotta model. He was almost blind by then and the room was dim, but he smiled and said, "He has the peace in him." I told him that it took two hard weeks of work, with three entire days sketching his profiles. Charley answered, "Una, you work hard two weeks and you have this piece. If you work two weeks in the lab, what do you get?"

Charley fought many of the Swiss battles for us Ausländers. He did our income tax and interpreted the many forms and requests from the Fremden Police (for interesting details, ask Polly Matzinger, NIH). Charley loved getting the better of the administrators: ". . . looks like the old dog squeezed the bureaucrats! A victory for our side!" As another Ausländer said, "I was often in trouble with the authorities and a lot of the time with my boss. Charley would advise, 'Deal with the head person-in-charge nicely, and this will take care of the rest of the crowd.' "

ACT V

Charley would on occasion assess his life: "I have heard complaints that I am/was not ambitious enough. Maybe so, but I also never needed to lobotomize myself with alcohol." Many of us have witnessed the activities of colleagues when they realize that they have not attained their Holy Grail. An example to all those he mentored and those who mentor: In his last week of life he sent off a paper that he called, "Son of Requiem." As Charley said:

You well know that being needed and doing things are very important. If I stop working, I will not last very long. When I went to the ER last night, I was not sure that they would not hold me there, and it was a source of some comfort that I got Son of Requiem out the door before leaving.

Jack von Borstel and John Cairns wrote in their obituary for Charley (von Borstel and Cairns 1999), "He chose to retreat into his role as unseen advisor," and so many stories of his mentoring have not been told. We gave you a flavor of the man, the man who mentored a generation of scientists.

If I had it to do all over again, I would not change. I prevented a lot of atrocities in my day. I have nothing to apologize for.

Charles M. Steinberg (September 1999)

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