Editor’s Preamble:

I have known Bob Jennings for more than 30 years. In the late 1970s, when I started working in the field of cardioprotection, he was already an icon because of his seminal contributions to our understanding of reperfusion injury and his classic studies of the transmural progression of cell death from endocardium to epicardium during coronary artery occlusion. More than 30 years later, my admiration for this man is as strong as it was at that time. This, in itself, is a remarkable statement about his stature.

What are the traits that I admire most in Jennings? First, he is one of the few investigators whose data I always believe. This is because I know the thoroughness of his work, the quality of his measurements, and the rigor of his approach. Invariably, he interprets his data parsimoniously. In his papers, you will not find premature conclusions based on insufficient evidence, nor extrapolations, exaggerations, unwarranted emphasis, or generalizations. He is the antihype. If one had to choose one word to describe his work, it would be solidity. Sadly, this is not a common virtue in today’s world of science, where so many rush to be the first even when the data are not sufficiently solid, in compliance with the abominable — but, alas, widely adhered to — principle that it is more important to be first than to be right.

Second, Jennings has remained remarkably focused on reperfusion injury and cardioprotection for more than 5 decades. As I often tell my colleagues, focus is one of the hallmarks of a great investigator. He has virtuously resisted the temptation to jump on the hottest bandwagon du jour. Unlike many others, he has not changed his interests in order to chase the latest fad.

Third, in the late 1980s, at the peak of the frenzy about reperfusion injury (when almost every week you could read another paper claiming that antioxidant therapies limit myocardial infarct size), Jennings had the virtue of publishing negative, but rigorous, studies that counteracted a torrent of positive reports, bringing reason and moderation to the field. When he found that antioxidants and antineutrophil interventions failed to reduce infarct size, he had the fortitude to complete this line of studies and publish them even though they were negative. I find this to be utterly admirable. The truth is just as important when it is negative as when it is positive.

My admiration for Jennings, however, transcends his scientific accomplishments, for I find his human qualities to be just as remarkable and refreshing as his scientific attributes. This is quite obvious to anyone who has interacted with him. He is what I consider a true gentleman — a man of total integrity and fairness. His unassuming, down-to-earth, simple style, coupled with his warm and engaging manners, make him a pleasure to interact with. One of his most striking features is that he never gets mad. Or maybe he does, but he manages not to show it. Even under very stressful conditions, even in situations that test one’s patience, I have never seen him lose his calm and his gentlemanly composure.

Jennings is one of those beautiful people who make the world move forward. The problem is that we don’t have enough of them. If there were more Jennings, how much better off we would be!

—Roberto Bolli
In the early 1950s, when Robert Jennings’ research career began, surviving a heart attack was far less likely than it is today. Back then, clinicians did not know when and how heart cells died after the onset of ischemia. Autopsy data indicated that heart cells survived many hours without an arterial blood supply, but a few researchers, including Jennings, suspected that the cells would die almost immediately. Jennings clarified these conflicting ideas by showing that some blood-starved heart cells died within 20-25 minutes of occlusion and could be saved if their blood supply was restored quickly enough. The time distinction between this reversible and irreversible ischemic injury was the subject of one of Jennings’s most famous papers. This work introduced the field to the concept of reperfusion therapy for heart attack victims, and thus ultimately to the development of thrombolytic drugs.

In further work with Keith Reimer, Jennings showed that following ischemia, a wave of necrosis spread across the heart as a function of time. Significant amounts of muscle could be salvaged even after 3 hours of ischemia.

Such paradigm-shifting work would be legacy enough, but later at Duke University, where Jennings was Chair of Pathology from 1975-1989, he shook up the cardiology field again. Together with his postdoc, Charles Murry, and Reimer, Jennings discovered that episodes of angina — reduced blood flow to the heart muscle — can actually precondition the heart to better cope with a future attack.

Besides these groundbreaking discoveries, Jennings has contributed 60 years worth of findings to our knowledge about myocardial infarction, ischemia, and reperfusion. It is surprising, then, that Jennings’ first foray into cardiology work on reversible ischemic injury was the subject of one of Jennings’s most famous papers. This work introduced the field to the concept of reperfusion therapy for heart attack victims, and thus ultimately to the development of thrombolytic drugs.

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Where Did You Grow Up?
I grew up in Bethlehem, Pennsylvania — an industrial town — home of Bethlehem steel works. My father was a professor of mechanical engineering at Lehigh University. Most of my student friends were sons of steel workers, with very low intentions of going to college. It was a town of workers’ families.

Then, when I was about 12, my father was offered a job at Northwestern University, where they were building a new technological institute. So we moved to Evanston, Illinois, which was a bedroom community for Chicago. It was an entirely different environment to Bethlehem — much more intellectual, and affluent.

How Did You Get Interested in Science?
I was sort of a lazy student in high school, but science interested me, so I did very well at it. I always liked to know how things worked.

Lazy?
For example, I never really thought algebra was very useful. But when I got more into science I realized that it was very useful, so I had to relearn it because I hadn’t paid enough attention in high school classes.

You Must Have Caught Up Quickly Because You Went Off to College a Year Early
That’s right. It was right in the middle of World War II. I went to college at the age of 16 because my father thought I would be better off in the military with a bit of college education under my belt.

You Chose Chemistry at University?
Yes. My father was an engineer and a good mathematician, so I considered engineering as a specialty. But I had already developed an interest in chemistry, so I thought I would major in chemistry and then decide between chemistry and engineering later on.

What Swayed You to Medicine?
First it became clear to me that I liked chemistry a lot, so I made the decision not to become an engineer. After about 18 months of college, I decided I wanted to become an organic chemist. I even did a small research project on the chlorination of dioxane.

But with the war still going on, my father suggested that I might be better off if I went into medicine. He thought it would be better to be a medical officer than an infantryman with knowledge of organic chemistry.

So I applied to medical school and was admitted in Sept of 1945, just as the war ended. But I was never sorry I made this decision.

Your Internship Was at Passavant Memorial Hospital?
Yes. It was one of the University Hospitals of Northwestern. It had a great faculty. It was also right across the street from the medical school where I was still doing some research. So every once in a while I could escape and see how my research was going.

It wasn’t easy because being an intern was a full time job. Your free time was your own, but unfortunately it was only between midnight and 5 AM.

You Had Time to Meet Your Future Wife, Though
Yes. Linda was a student nurse at Passavant. We met in 1949 and we got married in 1952.

In June of 1950 the Korean War started. Over the next several months it became clear that it was going to be a big war and they were going to need a lot of doctors. I didn’t want to go into the Army, so I volunteered for the Navy. In June 1951, I reported for duty at Great Lake Naval Hospital. That’s essentially where I became a pathologist.

Why Did You Choose the Navy Over The Army?
I thought it might be more likely that I would get to sleep in a bed most nights, instead of the ground. This was not based on any experience or fact — just an impression I had. As it turned out, many physicians that I reported for duty with were
sent to action in Korea. But I was lucky — I’ve had a lot of luck in my career — the Navy made me a pathologist.

That was a funny story. When I reported for duty, the executive officer welcomed me with the usual Navy expression, “welcome aboard,” which was a little silly since we were on dry land. Anyway, we were talking for a few minutes and then he said, “And what kind of a department have you worked in?” I said, “A pathology department.” He waved his finger at me and said, “You’re a pathologist.” I said, “That’s not true, Sir.” — all I had ever worked on were rats and rabbits. He said, “Don’t tell me what’s true and what’s not true. You’re a pathologist.”

I reported for duty in the laboratory, but the commanding officer had gone on leave because the executive officer had told him he was going to send along a couple of pathologists. I had a master’s degree in pathology, the other young man had about a year of training, and together we were put in charge for 30 days! It was a very busy laboratory serving 4000 patients, with 120 technicians. I became a cigarette smoker because whenever a medical officer asked me a question I would light a cigarette while I thought of what the answer might be. After those 30 days I was pretty much a pathologist.

So, 2 wars had a big impact on my career. World War II put me into medicine and the Korean War put me into pathology.

After the Navy You Went Back to Northwestern? Yes. William Wartman, the Chair of the Pathology Department, offered me a job as an instructor. There was no clinical service work to do, which meant I could do full-time research, except for when teaching.

I started work in July 1953, but I had been almost ruined by the Navy. I had been working from 8 AM to 4 PM and no one ever mentioned or was interested in research questions. When I returned to Northwestern I was back in an atmosphere of research. I had to step up and decide what I wanted to work on. It took me a while.

I had already done some research on the kidney, and then I became interested in cell death. I decided that I wanted to find out what caused cells to die when you cut off their arterial blood supply — ischemia. My first choice was to study the cells of the proximal tubule in kidney.

I approached Wartman, who had funded me up to this point in time and told him I wanted to do this major experiment on ischemic cell death in rat kidney. He said he didn’t have enough money to support that. But here I was lucky again. He said that he did have a small grant from the Chicago Heart Association to study acute myocardial infarction in the dog. The heart worked out to be an ideal model. The kidney is a very complicated structure. But the heart is pretty much all myocytes, with just fibrous tissue support containing vessels and nerves. It was far simpler and the results were easier to interpret.

And a Bit More Clinically Relevant? Right. Although to begin with, the cardiologists didn’t care a bit about what I was doing.

Why Not? They were interested in clinical measurements, like electrocardiography and hemodynamics. I may have been using the heart, but I was doing cell biology.

The American Heart Association had started a journal called Circulation Research, in which it was very difficult to get papers on metabolism published. We tried anyway. We wrote a paper on the metabolism of ischemic cardiac muscle in reversible and irreversible ischemic heart injury (Kaltenbach and Jennings’), and in 1959 sent it to the editor of Circ. Res. — a physiologist named Wiggers.

We had already done the reperfusion experiments that defined reversible and irreversible injury, but I hadn’t written it up. I referenced it as a paper in preparation in reference #1 of the metabolism paper. So, when we sent the paper to Wiggers he just wrote straight back with no editorial comments other than the statement: “I’ll publish your paper after you publish reference number one.”

So that’s how the reversible versus irreversible paper got published. I’m very grateful to Dr. Wiggers.

A Few Years Later You Went on Sabbatical in London. How Was That? That was fun. At Northwestern we had all kinds of postdocs and fellows in the department from Europe and Australia, and they learned a lot about themselves and about science in the US. I thought travel might offer me the same. I went to the Middlesex Hospital Medical School. However, I never got to do any research because there was so much paper work involved in getting licensed to use animals.

Still, I learned an enormous amount. I saw how another society lives. It was a very valuable experience. It broadened me a great deal. I also managed to write up a couple of papers on work that I had done at Northwestern, so I didn’t waste time. Plus I learned about tutorial teaching and a little electron microscopy.

Your Family Came With You? Yes. Linda and I had five children by this time. One was only about 15 months old. We couldn’t find a place to live in London so we lived in a village called Trottiscliffe, in Kent. Our older children went to the village school and my one daughter developed a horrible Kent accent. It got so bad that I could hardly understand her. We had been back in the US about two weeks when the mother of one of her playmates reported to Linda, “Mary no longer talks funny.”

You Came Back to Northwestern . . . Right, but I didn’t take back a lot of the jobs that I had had. That’s one of the principle advantages of sabbatical leave. If you’re doing a lot of work and you go on sabbatical, someone has to do it while you’re gone. So you let them keep doing it when you get back!

Soon You Took on Big Responsibilities, Though. You Became Chair . . . Yes. That was about 1969. Wartman had taught me a lot. He had a big influence on my career. He didn’t suffer fools well, however, and there was this one hospital administrator that he
thought was a total fool. I knew that he had exchanged words
with this administrator and I was afraid that he might just up
and leave. He did! He moved to the University of Virginia,
Charlottesville.
I didn’t really want to be Chairman – the department was
in decline because of a shortage of funds and administration
of a clinical and research department at Northwestern Uni-
versity was very complicated — but I said I’d do it for five
years on the understanding that I could start a practice plan
and provide the clinical services to the adjacent hospitals that
were staffed by the department. I hoped that this would yield
enough clinical income to support everybody. I did get a plan
in operation and the department was rescued.
Five years later, Duke was looking for a new Chairman and
they wrote to me inquiring whether I might be interested.
Duke had a much simpler administrative structure than
Northwestern, just one Chief, one Hospital and one medical
school. So I knew I wouldn’t have all the administrative
rigmarole that I had at Northwestern. In addition, Duke was
more focused on Cardiology.

And You’ve Been There Ever Since . . .
I’m semi-retired now. I never wrote up all the experiments we
did, so I’m writing up the last one of those now. I don’t know
exactly what I’ll do in my office after that. I still do some
work for the National Heart Lung and Blood Institute, I still
give the occasional talk, but I’m not working anywhere near
as hard as I used to.

How Hard Did You Work as a Young Researcher?
60-plus hours a week, but I was very interested in what I was
doing.

Was It Like Pursuing a Hobby Rather Than Doing a Job?
Yes, that’s exactly right. I enjoyed what I was doing and I
didn’t really want to do anything else.
I had to be the Chair so that I could get the research
environment the way I wanted, but I did the Chairman tasks
as quickly and efficiently as I could. My idea was to try and
administrate myself out of a job. I would give people major
tasks to do and if they did them well, then they had a new job.
So I managed to spend about half of my time doing research.

Were You Actually Working at the Bench Until You Closed the Lab?
Yes, I got to do that for my whole career. I closed my
laboratory in 2000. I was sorry I did so actually. The worst
thing was, if I went to a meeting and heard someone present
something interesting that was related to our experimental
goals, I would think of just the experiment to do, but then
couldn’t. That was very depressing. But as you get older
that’s a problem you have to face up to!

Any Advice for Young Scientists?
Ask an important question — one that the NIH can apply to
a clinical problem, such as hypertension, myocardial infarc-
tion, genetic diseases, so on.

Then, design your experiments carefully. There are 2 types
of experiments, one-ended and two-ended. With a one-ended
experiment, you can only move forward if the answer is the
one that you want. Sometimes you have to do such experi-
ments, but it is better to ask a question in such a way that
having learned the answer you can go in either direction.

Avoid experiments investigating small changes in biologic
systems. Stick with big changes and you are more likely to be
successful.

Also, don’t fool yourself. If you become emotionally
involved in the project then you should blind yourself so that
you can objectively interpret the results.

Lastly, be good and be lucky!

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Robert Jennings: A Labor of Love in the Laboratory
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