

ATVB Named Lecture Reviews—Insight Into ATVB Authors

ATVB Named Lecture Reviews—2013 George Lyman Duff Memorial Lecture

Insight Into the Author: Edward A. Fisher, MD, MPH, PhD, Department of Medicine (Cardiology), the Marc and Ruti Bell Program in Vascular Biology, and the Center for the Prevention of Cardiovascular Disease, New York University School of Medicine



Why did you choose the profession of scientific investigation?

Neither of my parents had anything to do with science. My father worked in a pawnshop, and my mother had a vocational high school diploma in sewing. I think my initial interest in science was pretty much instinctive: isn't everyone curious as a child? This was reinforced by excellent science teachers in the New York City public school system, especially at my high school, the Bronx High School of Science. My parents worked hard to give my brother and me educational opportunities they never had, and it turns out we both used these to become scientists, he a physical chemist. Why I chose metabolism as a field is based in part from my clinical experiences when I was a pediatrics resident at Duke. We had a chief of metabolism, Jim Sidbury, who was very inspiring. We talked at length about some of the patients with metabolic disorders, and he encouraged me to get the hard science training needed to understand biochemical mechanisms, to make more accurate diagnoses, and to improve treatments. He also pointed me to a joint graduate program at MIT and the Harvard-affiliated hospitals in metabolism, and in one of my first year courses, I attended a lecture by Jan Breslow on lipoproteins, which led to my joining his lab.

Who have been your role model(s) in your scientific and professional life?

I already mentioned two mentors, Jim Sidbury and Jan Breslow, who also became role models as highly successful physician-scientists in the area of metabolic disease. When I became an assistant professor of biochemistry at the Medical College of Pennsylvania, Julian Marsh, another outstanding physician-scientist, was very supportive personally and professionally, and his guidance helped me to establish my lab and to choose among potential independent projects. He also emphasized how important it was to "follow your nose"- to go where the data took you. Jan's fabulously successful application of the latest concepts and technologies to the questions he was interested in also encouraged me to follow Julian's advice. It is a good thing, then, that I have a long nose! As a more senior faculty member, I still learn from mentors—for example, by observing Valentin Fuster when I was at Mount Sinai, I was reminded that as hard as you think you are working, you can work harder.

What have been important influences on your professional life?

My parents, despite their lack of sophistication in science, valued knowledge and meritocracy, which became incorporated into my professional DNA. I did, however, disappoint them by not becoming a radiologist. My father tried to encourage this path by one day dragging home a set of golf clubs from the pawnshop because, he told me, radiologists played golf on their afternoons off.

As I noted earlier, I had many superb science and math teachers, especially in high school. Many of them had advanced degrees (including PhDs), but came of age during the Depression, could not get research positions, and were more than happy to get teaching jobs. I think by fostering the scientific interests of the likes of me, they were hoping some of us would ultimately take advantage of the opportunities they never had.

Many scientists I have interacted with over the years, even over a distance, also have taught me a number of important lessons, both positive and negative. After all, as important as it is to learn what to do, it is equally important to learn what not to do. Actually, it is not just from scientists from which you can glean these lessons—every Sunday I read the interview with a successful business person in the NY Times, and they cover a lot of topics germane to all of us in science, or in most professions, for that matter.

What are your scientific inspirations?

Nature has a richer imagination than we have, and all scientists are both challenged and inspired by this. Figuring anything out is a true accomplishment and a wonderful goal in itself. This is reflected in the guiding principle of the great biologist and thinker Jacques Monod, who said, "Je cherche à comprendre"—"I am trying to understand." Questions of the trainees in my lab and the students in the courses I teach are frequent reminders of the gaps in my knowledge, and stimulate more thinking/learning. Beyond the intellectual satisfaction, of course, I wouldn't mind if what we discover has some practical benefit. After all, I was partly inspired to

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undertake an investigative career after exposure to some of nature's experiments—the children with metabolic disorders. Now that I am 60+, I also am inspired by those older than me doing first-rate research, of which, I am happy to say, there are many!

How have mentors contributed to your professional development?

I covered a little of this in Answer 2. The contributions include the scientific training obtained under each. What I learned under the tutelage of Jan Breslow, Gary Felsenfeld (post-doctoral advisor), and Gunter Blobel (sabbatical host) provided essential underpinnings. After all, technical/conceptual proficiency is essential for an independent investigative career, much as mastery of notes, scales, and timing is required for a career in music. Beyond that, are their contributions that are harder to identify explicitly, and are gleaned mainly by observing how these superb scientists supervised trainees, interacted with colleagues, formulated hypotheses, and made decisions, especially when results suggested multiple avenues forward, or worse, failure, which to varying degrees, is a constant companion in science. Not all of my mentors contributing to my professional development, however, were scientists. In particular, my illiterate grandmother, who lived with us, was a font of wisdom about how to deal with life in general, and had the additional skill of making each of her 17 grandchildren feel that he or she was her favorite! My father-in-law, a high school graduate who became a very successful businessman, radiated energizing positivity, and I regretted not knowing him longer.

If you knew then what you know now, would you do anything different?

I would still be a physician-scientist, but given the prolonged periods of funding tightness (in my career, not just the current drought, but also the period before Bill Clinton raised the NIH budget), I might have stayed on at the NIH after my post-doctoral fellowship. Though the NIH intramural program is not without its own problems, it has been largely insulated from the severe funding pressure that the extramural investigators have had to deal with. I might also have chosen different parents, so that they would have had a smarter child, who would grow up to get selected for a Howard Hughes position.

What wisdom do you impart on new investigators?

I do not want to engage in too many platitudes (work hard, have faith in yourself, blah-blah). The reality, as anyone reading this knows, is that the prolonged funding deficiency makes it tough on investigators at all career stages. For the new investigators, at least they have (or should have) start-up packages. With this cash in your pocket, it will be tempting to expand a lab quickly, but this risks having too many projects and people to direct, jeopardizing the timely completion of top-quality research publications, which are crucial to prove to the world (eg, study sections) that you are on your way. Establishing a “track record” as an independent scientist before the time period for early stage investigator NIH “bonuses” expires will make your first R01 application that much more competitive. My hope for all new investigators is that someday they will say, as I do, “If I knew how well I would eventually do, I would not have worried as much when I was an assistant professor.”

Another piece of advice is something I heard from Jan Breslow. He said the standard for a successful career is that for whatever problem you work on, the understanding of it changes based on your discoveries. I think this sets a very appropriate and achievable goal, and has more lasting value than some of the “trappings” of science many of us aspire to.

If you were not a scientist, which profession would you pick?

That is a deceptively tough question. During those inevitable nadirs that occur during a career in which the odds are stacked against you, I have asked myself this, and could think of nothing else! So, I would get back up, dust myself off, and try harder. I am also a physician, but early on realized that a predominately investigative career was a better fit, though I enjoy patient contact and still do a limited amount of clinical work in preventive cardiology.

Which direction do you envisage your science taking?

To motivate myself, I always imagine that my best work is still ahead of me. Of course, the trivial possibility is that this is because what I have done so far is rubbish, but I prefer the more positive view—though some of the studies have been terrific and have answered a number of questions, they raise even more important and interesting ones, tantalizing in reach with new insights and technologies. I mentioned some of these questions in each section of the Duff Lecture—the cell biology of VLDL assembly and secretion, the regression of atherosclerosis, and “theranostic” nanoparticles—and I expect they will keep me busy for the foreseeable future.

What are your nonscientific activities?

I am married and have 4 children, 3 of whom are human, the other being a dog. As corny as it sounds, I love being with them—and with the kids grown up—occasions when we get together, like the recent Thanksgiving, are that much more special. The upside of the kids being grown up is that my wife and I get to take more trips together and we really enjoy traveling. In fact, she tells our friends that the reason she married me was that I was a good traveling companion! Other activities—there is the music mania (see below), and whiskies/wine (especially in the company of friends), and walks with a pipe and our dog.

What sports do you follow?

As a Bronx native, I HAD to root for the Yankees when I was growing up. I was not totally faithful, however, and went to the opening day of the first season of the NY Mets, skipping school with my buddies. I was also a rabid Knicks fan as a kid, but it has been a long time since they have been a team to get excited about. Maybe this year (I say this every fall).

Having lived in NY, Boston, Philly, and DC, I adapted by rooting for the local teams in all the major sports, and now I do not get caught up in how any of them are doing during most of the season, but like to watch the playoffs/championships, and if one of them makes it, I root for them. If multiple ones do, then I have a problem.

What are your favorite books, movies, music (pick one or all)?

My dear friend and fellow former editor-in-chief of *ATVB*, Mark Taubman, and I are music fanatics. We share hard drives with over 8,000 albums on them—consisting of music of every genre, and I mean every. We have influenced each other over the years. For example, Mark had little awareness of jazz and I only knew the “hit” operas, like *La Boheme* and *Traviata*. Now he knows as much about the jazz greats as I do, and I am a big fan of some of the more obscure operas. Movies: I embarrass my brother-in-law all of the time with my ignorance—he is a Hollywood mogul, and when he introduces me to actors and actresses, I rarely know who they are. But I did love *Annie Hall*, which is probably a Baby Boomer thing. To this day, if I find it on TV while surfing channels, I always stop to watch. Books: Over the past few years, I have tried to fill-in the classics I never read. My high school teachers would be proud—I have really enjoyed Austen, Flaubert, Balzac, and others. I also read short stories—Raymond Carver, Flannery O’Connor, Alice Munro are a few authors that come to mind. Oh yeah, Agatha Christie, especially the Poirot stories, which were first encountered in the TV versions to which my wife and I became addicted after we lived in England.

What are your favorite foods and are they heart healthy?

I used to believe in knowing your enemy, and just loved eating all sorts of heart unhealthy foods—especially good hot dogs, which were legion in the NY area. When I was asked in 1995 to join the AHA Nutrition Committee, one of their most publically influential ones, given that the dietary guidelines are written by its members, my wife thought this was very funny. In fact, she found a cartoon showing a hot dog vendor in NY with a disclosure sign next to his cart that said, “The fact that you want one of these means you really couldn’t care less about nutrition” and had it framed next to my invitation letter to join the committee. When I decided to get serious about my creeping weight gain a few years ago, I made a number of heart healthy diet modifications. More salads, more fish, rice cakes instead of bread, etc. Even the occasional hot dog I have is 97% fat free. Not only did I pleasantly surprise myself that I had the discipline to make and maintain these changes, other people were impressed—the local AHA affiliate gave me a “Lifestyle Change Award”!

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