



BRIGHAM AND WOMEN'S HOSPITAL

FRANK E. SPEIZER

Interviewed by Peter Tishler, MD, 2011

2011 interview with Frank E. Speizer, physician. The Edward H. Cass Distinguish Professor of Medicine at Harvard Medical School, the professor of environmental science at the Harvard School of Public Health, and most importantly the senior physician at the Brigham and Women's Hospital.

Frank, you joined the staff at the Brigham in 1977 and you have lived at the Brigham professionally ever since. What stands out in your experiences with the Brigham both positive and negative?

The Brigham is an interesting place. When I started, it was not called the Brigham. It was called the Affiliated Hospitals Center, and that was because it was a joining of several hospitals in the Longwood area. Having come from the Boston City Hospital with Ed Kass and his group when Harvard left the City Hospital, it was an interesting experience for me because I had never worked except as a house officer in a nonpublic supported community setting. Seeing what we would call "private patients" for the first time was a new experience for me.

It was a challenge initially because I'm not sure that the house staffs of the Boston City Hospital, for example, versus the Brigham, were equivalent in their thinking about how to deal with patients. Though they were of equal caliber in terms of their intellectual backgrounds, it wasn't clear that the same house officer with the same grades would function as well at one institution or the other. There clearly were different attitudes that were there toward patients. I actually found it difficult to attend at the Brigham mostly because of the attitudes of the house staff, which were so different from what they were at the City Hospital.

I elected early on not to do general medicine attending, but only to do specialty attending, where I felt more comfortable. I think that changed over time. I think the house officers became more aware, as society became more aware, that patients had to be treated differently than they were back in the mid '70s. From the research side, I

think the Channing Laboratory, which came as a unit to the Brigham, continued to function as it had at the City Hospital, in space that was not ideal. We actually moved into the old animal hospital on Longwood Avenue and did not have sufficient funds to renovate that space. We essentially took it over and began to use it.

Let's talk about the Channing. It came from Boston City Hospital to the Brigham in 1977, as you moved here. In fact, you were a co-director of the Channing for many years. Let me ask you some specific questions about the Channing. What has the Channing brought to the Brigham, in terms of both assets and liabilities?

Obviously I'm a biased observer. There were no liabilities. The Channing Laboratory actually stayed at the Boston City Hospital after Harvard moved out for about 3 years and that was because Ed Kass, the former director of the Channing Laboratory, had developed at the City Hospital a brand new building with approximately thirty to forty thousand square feet of space, which was not available anywhere in the Longwood area. Therefore it took some time before we could find space to move the Channing Laboratory.

It was Ed's creative thinking about how to do that which led to first Harvard Medical School's buying the old animal hospital building and then renting it to the Brigham, which we paid for out of our research overhead monies. It was Ed's idea to bring the Channing group to the Brigham. Most of the work that had been going on at the Brigham had to do generally with very sick patients, and treatment modalities that were being tested on the patient lying in bed. To Gene Braunwald's credit, I think, he began his own research efforts in the treatment of myocardial infarction, but also he recognized that Ed Kass was bringing with him a group of people who would be interested in looking at both outpatients as well as populations who would become patients potentially. Bringing that into the mainstream of clinical medicine was an important component that the Channing brought to the Brigham. We had separate space as I mentioned before in the old animal hospital and that space was sort of divided between infectious disease activities and the chronic disease epidemiology activities. Ed Kass was the first director who came over here and until he retired, he continued to run the unit. When he retired, Dennis Kasper and I took over as co-directors.

What has the Brigham done positively or negatively to assist or foster creativity at the Channing once it arrived?

When we arrived we had to integrate ourselves into the various clinical departments in order to do the clinical work that we wanted to do. For my particular case, since I participated in respiratory disease consulting, I would join the Respiratory Division to carry out that work. The people who worked in cardiovascular disease or infectious disease similarly joined other divisions. We were welcomed by those divisions and provided some additional clinical support to them. We received actually very little credit

for that activity from the clinical side. In fact, we ran a negative clinical balance in terms of the amount of monies that were brought into our division from the clinical monies.

On the other hand, we had the largest research budget in the department of medicine. We were contributing to the department and to the hospital through what was a substantial overhead contribution for the space that we had. To Gene Braunwald's credit again, he recognized that our space was inadequate and indeed worked very hard to find us the new space that we actually moved into in 1996. This new locus gave us more space as well as additional opportunities to grow in terms of the various research activities that were going on. It added a huge viral disease component under Elliot Kieff to our ongoing activities.

What was the source of the monies that the Channing brought with it? Was it endowment or was it NIH funding?

The endowment of the Channing Laboratory was really not very large. It included a modest amount of general endowment money through Harvard Medical School, and at the time there were one or two endowed chairs, the main one being the Channing chair, which was held by the director. About 95% of our funds came from NIH-funded grants, which obviously provided full overhead. These became a point of contention between ourselves and the administration of the hospital because we never felt that we received adequate recognition or support from the hospital for the amount of money that we were bringing in.

You were an inventor of clinical epidemiology and of training programs in clinical epidemiology such as your program in chronic respiratory disease. How did this come about?

It is hard to say that I was an inventor of it. In fact, when I wrote something like that for Max Finland's tome on the Boston City Hospital, he told me that he was the inventor of clinical epidemiology.

The idea that I had was that I was interested in approaches to chronic disease. No one would live long enough to start to do those kinds of studies that would require assessment of risk factors from very early ages for diseases that would not occur for a very long time. So, the whole concept was to look at what I call recurrent wave design of short term, being 15 years of assessment of risk factors for disease development. In order to be able to do that, it requires a cadre of investigators who would overlap in time and age to be able to carry out studies over a long term. That meant one had to have a chronic disease training program to train people -- they just didn't do that kind of work. That was the basis of why we developed a training program.

From my perspective, I always felt that a clinical epidemiologist was essentially somebody who was a clinician who did epidemiologic work, just like a protein chemist

clinician who did protein chemistry in the laboratory and clinical work. I saw it no differently than that. That is the basis of the development of the chronic disease training program. It was a very successful program. I ran it for about 25 years, and we were initially the only program in the country that was doing respiratory disease epidemiology of that nature.

Even as a student in college, you did things which were epidemiologic. Who stimulated you to go down this path and who were your mentors?

I was very fortunate to have a number of mentors. My background was probably more in mathematics than in biology. As an undergraduate, I met a human geneticist, who was a visiting professor at Stanford where I was an undergraduate. He convinced me not to go directly to a PhD in genetics, but to go to medical school. He felt that, although he was from Chicago and could work there without any trouble, when he came to the west coast he could not get access to patients because he did not have an MD. He suggested going to medical school first, which I did.

In medical school I had the opportunity to work in a summer program in epidemiology and chronic respiratory disease assessment. I discovered that one could apply mathematics in a medical arena in a very heavy way, which I found that I could do and enjoyed doing. So I went down that avenue. After medical school I had the opportunity to serve my country as a research fellow at the Harvard School of Public Health in the Respiratory Physiology Department, where I got into air pollution research and discovered that I was more comfortable doing the epidemiology side of it than doing the physiology side of it. I had an important mentor there by the name of Jim Whittenberger, who was the chairman of the physiology department. He sent me actually through Charlie Davidson to the Boston City Hospital. There were important mentors obviously at the BCH, Ed Kass being one of them.

How about in England?

When I wanted to further expand my epidemiology education, Jim Whittenberger suggested that I do it in England. And I got to work with Richard Doll in England. Richard Doll was the primary person involved in discovering the relationship between smoking and lung cancer. It was in his laboratory that I got into the idea of studying oral contraceptives and breast cancer.

You founded or cofounded trailblazing population studies such as the Nurse's Health Study. What inspired you to set up these large populations and studies of them?

The Nurse's Health Study really grew out of my time in England, where I shared an office with Martin Vessey, an emeritus Professor of Epidemiology at Oxford now. He was assigned a task of assessing a series of reports on young, normally healthy women who were being reported as having pulmonary emboli or thrombophlebitis in their legs. In

the process of working with him through that, it became apparent that this was related to oral contraceptives. What was also apparent at the time was that although the oral contraceptives were quite potent and effective as a contraceptive, no one had considered the possibility of what would happen to literally hundreds of millions of women who were going to be put on this very potent drug, in terms of long-term effects.

I was sitting in the offices of Richard Doll, who had set up a study of smoking and lung cancer using British physicians, and it seemed obvious to me that one had to set up a similar kind of study in women to look at the long-term health effects of oral contraceptives. We initially tried to do this with physicians' wives. We were very successful in establishing some pilot studies to show that we could make those kinds of measurements in physicians' wives. We, in fact, received NIH funding to do such a study. However, by the time we received the funding, we discovered that a significant proportion of the physicians' wives' questionnaires had been filled out by their physician husbands, which was a disaster, essentially, and therefore we switched to nurses and that was the beginning of the Nurse's Health Study. That is how that study got off the ground.

This is an epic study that is still ongoing. How successful have these large population studies been an identifying and/or solving health-related problems?

There are two or three answers to that question. It is in fact a long-term study, now in its 36th year. It was the progenitor of a comparable study in men, which is ongoing since 1986, and a second round of younger nurses that began in 1989. The younger nurses were studied mainly because the opportunity of having taken oral contraceptives before one's first pregnancy was low in the first group, and therefore we had to start another round of younger nurses.

Along the way, several things happened. The oral contraceptive became a much lower-dose drug and therefore became far less potent in terms of its potential side effects. That in part, I think, can be attributed to the nurses, although industry is moving in that direction anyway. We have confirmed that those newer versions of oral contraceptives were not as hazardous as one thought they might be.

I think we've laid the groundwork and for a lot of the behavioral and lifestyle factors that relate to a wide variety of chronic diseases. Although we initially started out studying breast cancer and other female reproductive cancers and cardiovascular disease, the study is now widely looking at a wide variety of chronic diseases -- everything from diabetes to adrenal diseases to cognitive function in the elderly.

I think the study has had a large impact on understanding health, lifestyle and behavioral risk factors. It has become a training ground for a wide variety of investigators mostly interested in epidemiology. Many of them come from clinical

medicine, adding what I would call additional clinical epidemiologists to the academic community. With the activities related to the nutritional aspects of a study in 1980, Walt Willett and his group have contributed significantly to our understanding of dietary and nutritional factors as related to disease. The most recent guidelines for food pyramids is evidence of how his work has changed that field.

With regard to these population studies and specifically the Nurse's Health Study, has the Brigham facilitated their execution?

Yes I believe it has. In a number of ways, academically first, chronic disease epidemiology has a mainstream component of the department of medicine, and this has led to some very bright people coming into medicine and being able to work and advance in the field. I credit Gene Braunwald with a lot of that, although I think I had to train him a little bit as to how these people fit in. A wide variety of divisions within the Department of Medicine and perhaps other departments within the Brigham have taken on people who do what I call standup or population-based research. We even have now carried this through with professors of medicine who are PhD statisticians. This is a new phenomenon on the academic side; and it has been in part supported by the hospital itself, recognizing the appropriateness and need for these people.

Have your trainees or mentees contributed to the research and training environment and knowledge at the Brigham and if so, how?

Yes, I believe that the trainees that have come through the program have contributed significantly to fostering the thinking about how a chronic disease affects both the patients who are in the hospital and how they got there. When I first started attending, I had to show that I could get the patient out of pulmonary edema, if that's what the case was. Once I could demonstrate that to the house officers, then the question could be turned around to say, "Where did this patient come from? Where is this patient going? What's going to happen to the health care of this person, and how can we incorporate it into the lifestyle?" We're recognizing that the hospital stay of a patient is a very tiny part of his/her lifecycle and so one has to deal on a broader base. Teaching that to the house staff is something that was important to do and it was important from everyone's perspective to begin to think more about those issues.

And so these large population studies and the people who trained in them and then went onto other facets of work at the Brigham brought this with them and the knowledge that they accrued from these studies.

I think so. I wish that more of them were active as senior clinicians than there are. However, many of them still do participate in clinical activities, and that exposure is important for both the house staff and even the faculty.

One of the primary major things that has accrued is studies of women. Are these studies spinoffs of what you were teaching and mentoring people about?

Yes I believe people who developed the women's health studies came out of their training from the Nurse's Health Study.

Has clinical epidemiology become a progressively more influential discipline both at the Brigham and nationally? You've answered that a bit, but perhaps you could expand on it.

Another aspect of my activities, because my interest in respiratory disease, has been related to air pollution research. We did develop a cohort study of air pollution, called The Harvard Six City Study. In that study we found a number of things related to air pollution exposures and mostly particle exposures that have had a major impact on the national scene in terms of the Clean Air Act and the establishment of national air quality standards. This Harvard Six City Study is the most quoted piece of work and perhaps the most important piece of work underlying the establishment of the current national air quality standards for particulates. Again, the people who trained in these programs have gone on to become leaders in the field, at a number of different institutions.

What changes in clinical epidemiology do you predict for the future?

For many years I have worried about the fact that as computing became easier and easier, it has become almost too easy to come up with a hypothesis and test it. This has gone to some extreme. In fact, the GWAS approach is basically not testing hypotheses; it is basically using technology to come up with ideas. I believe it is going to eventually be shown that it is not working as well as people would like it to work. One of the research phenomena many more people are able to do is what I call secondary data analysis rather than primary data collection, because primary data collection is very expensive. However, I think we have to worry about the field if we don't have the opportunity to collect primary data. One has to think about ways in which with the new systems that are available can be used to access primary data. This may include the electronic medical record. It may be possible to organize those records in such a way that one could consider them to be primary. I think, more importantly, that clinical epidemiologists have to get involved in how those clinical records are designed and data are collected. That keep them in the forefront of the field.

What do you foresee for the Brigham specifically, and medicine in general, for the future?

I'd have to say success. Because of the rich environment that we have and the successes that we've had at the Brigham and in medicine in general, one can recognize the importance of having the biostatisticians and PhD epidemiologists on staff. With this, we should continue to be successful not only in coming up with ideas that might be learned at the bedside, but also in translating ideas into outstanding research hypotheses that

can be studied by a multidisciplinary team. I think that the future is going to include much more multidisciplinary work.