When I told my wife about coming to this meeting, she said, "Why?" And I said, "Because I'm a historical figure and that's what they think of me." (Laughter.) And she said, "I've been saying that about you for years." (Laughter.) What can I say? I've had some big birthdays in recent times. I have an illustrious family. I have two grandsons, one of whom is becoming a star for music at the Kennedy Center. He is a second-year college student and he won a contest for arranging and playing music. So, he is going to play in the Kennedy Center here in Washington. And I think that most of our immediate family is about to come for it, and we're having a family get-together. Anyway, I have a brief time to tell you stories. I thought what I shall do is to tell you a little bit about how this all started.
I was a second-year medical student at New York University, and the administration of the school decided that it would be better to have medical students training on the wards of Bellevue Hospital work all year round. We thought it was mostly because we did the lab work as students, the clinical lab work. When the students weren't there, the house staff had to do the tests, and they didn't like it. So, to make the house staff opportunities a little more attractive, they changed the schedule so the students had to do that. With the extra time that we would be spending in school, they permitted us to have electives, which meant that we could study with almost any department we wanted to work with. But this was my first opportunity to work with anything clinical, because, before that, we did all basic sciences. We looked for clinical research opportunities.

I was introduced to Dr. Felix Wroblewski, an internist caring for my uncle, who had been treated by him after surgery for cancer of pancreas, and he had done very well for my uncle. So, I had dinner with Felix Wroblewski and I asked him if he could help me get an opportunity to do some research. He was interested in trying something different at Sloan Kettering Institute where he worked, and he asked me, since he was not able to get me any other opportunity, whether I would like to spend the summer working with him.

As a second-year medical student at NYU in 1952, I was interested in finding a research project to work on. A cardiologist, Dr. Felix Wroblewski, suggested that I might search for a blood marker for acute myocardial infarction, thinking that damage to the heart muscle might release intracellular enzymes into the circulation. With a $200 grant, I started in summer 1952 to work on finding a suitable method to measure products of serum glutamic oxalacetic transaminase (SGOT; now AST). Using a paper chromatography method that took 3-4 days to do, I presented results in the spring of 1953.
I did, and one of the ideas he thought about at that time was developing a test, a chemical test, for diagnosing myocardial infarction. Now the question was: where do I start in this? I really had no idea. I knew a little about myocardial infarction from what I learned in the pathology course in the previous year, but that wasn't much. I looked up myocardial infarction in the famous Harrison textbook of medicine. The only information I could find there said that the laboratory was not involved in diagnosis of myocardial infarction. That was written by the man who was the editor and the major author of the standard textbook of hematology. So, I looked at it and was not able to find any guidance at all. Felix Wroblewski introduced me to the library of Sloan Kettering Institute. One of the textbooks that I found there was a book called Enzymology by Sumner and Northrop. It had a list, almost the kind of thing you might get from today's computers. But I sat with it one afternoon and saw a lot of enzymes listed. We had had some of that introduced to us in biochemistry, but not very much.
The enzymes were first named for the products produced:
- glutamic acid and oxalacetic acid, SGOT 
  (from α-ketoglutaric acid and aspartic acid);
- glutamic acid and pyruvic acid, SGPT 
  (from α-ketoglutaric acid and alanine);

Now they are named for the substrates, the amino acids that react with α-ketoglutarate, as
- aspartate aminotransferase, AST, and
- alanine aminotransferase, ALT

I spent some time reading that book and finally found on one page that there was an enzyme that was said to be richer in heart muscle than anything else, transaminase. And I said, I wonder if that would be a clue to what might be a good indicator? Wroblewski told me, "Just look up what the normal range is and set it up." So, I looked up the normal range, but nobody had mentioned about measuring transaminase in blood.

It turned out that somebody else had come later and said, "What is it that you think you're measuring here, because I have read in many places that there is no transaminase activity in blood?" So, I said, "I guess I didn't read the textbook that said there wasn't any there."

I tried to set up measuring transaminase. We had one problem that, when I tried to prepare this talk, was one that I never really emphasized in anything I had written about it. The main problem of what I had to work on was that we had no money. (Laughter.)

So, what I had to do was to have a minimum of expense. Very good. I had no salary and nothing else in the way of income, and my family was not wealthy. But I was paying my tuition well enough with the help of scholarships.
What happened? I saw that the transaminase, in particular, had a concentration in heart muscle that was higher than in most other places. When I spoke to one of the biochemistry friends that I had from the medical school, he said "If you want to measure an enzyme in blood, I think you ought to start with something to the liver." But Wroblewski and his senior at Memorial Sloan Kettering, Dr. John LaDue, told me that what the world really does not need is another liver test. (Laughter.)

And that was the way they taught it in those days. When I was invited to this meeting and saw the title and all that, it was amazing that you are all so smart about what was important and what wasn't important. But that is where I came on the scene back then.

I looked for methods that had been used by other people to measure transaminase and transaminase activity. There was one that used a Beckman spectrophotometer. I found out very quickly that nobody in Sloan Kettering would take a medical student who had been a student someplace else and entrust them with this very expensive instrument.

So I learned about the cost of things. When I looked at the price of a Beckman spectrophotometer, it was something like $2200, and there was no computer to put with it. There wasn't any such thing. For manually operated and interpreted equipment, you had to make do with no computers, no data reduction, or anything like that. The cost of a spectrophotometer was $2200 in
those days. The Oldsmobile that I wanted to buy also cost $2200, though I think it went up, in the next two years, to $2600. So, you can get some idea about how long ago this was.
Anyway, I found one paper by a graduate student and a professor from Texas, where they had a method for measuring transaminase distribution in different tissues, using paper chromatography. I hadn't heard about that, either. I had been a chemistry major, but my chemistry majoring in undergraduate school was something like four years, five years before. So, I looked at it and asked a couple of other people for advice. They said that they had a couple of people around who know about it, know how to do it. And I was introduced to the use of paper chromatography, which I presume that most of you either are very familiar with or can find somebody quickly who can tell you about it. It became a very useful tool. I ended up meeting the major inventor of chromatography who had won the Nobel Prize for it, A.J.P. Martin.

Anyway, what it involved was incubating whatever tissue you wanted to test with a small amount of material that you wanted to test -- for transaminases, with an amino acid like glutamic acid and a keto acid, to which it would give its nitrogen group. So, that was the transaminase idea. And it looked like I could borrow some of the reagents for the amino acids and buy some, because they finally gave me a small stipend. I think it was about $50, to start to buy some pipettes and do all that. The rest of it, I got the Bronx way of obtaining financial support. I stole it. (Laughter.)
As it chanced, the Professor of Pharmacology, Dr. Severo Ochoa heard the presentation and offered me a chance to work in his laboratory the following year. He allowed me to use his spectrophotometer, and provided useful advice. I had found that amino acids such as aspartate or alanine reacted with $\alpha$-ketoglutarate to yield glutamine and oxalacetic or pyruvic acid, as a measure of the enzyme activities of SGOT or SGPT (now AST or ALT). I worked on a method to measure them by spectrophotometric disappearance of DPNH (NADH) as the keto acids were reduced.

So, I had pipettes that I could get from different laboratories, particularly if I worked at night. It turned out that the Sloan Kettering Institute, for those of you who are familiar with it, used to have an entrance on 68th Street in Manhattan between First Avenue and York Avenue. It was a very classy, little office that you could use as an alternative entrance. The main entrance for the patients was on York Avenue, and the entrance to James Ewing Hospital, which was City Hospital at that time, was on the other main street.

But I used to go in and out at the entrance on 68th Street to Sloan Kettering Institute. It was a very solemn, little place with marble walls but no place where you could sit down. But you could walk through the two hospitals from there. There was a plaque on the wall that said, "Within these walls a few work unceasingly, that many may live." So, that struck me. That is very nice.

I found out that when I walked through the walls in evenings, I never saw anybody working at eight or nine o'clock at night. So, I figured if there were a few that worked unceasingly, there were damned few. And that was the end of that. (Laughter.)
Anyway, I set up a method by which I chemically separated amino acids. For my first experiment with a blood sample, I didn't have the sense to try to measure it with some liver extract or something like that. So, my first experiment with a blood sample, I separated the material by paper chromatography and looked at the appropriate spot for the second amino acid, which was probably aspartic, as I remember it. And when I looked at it, there was a faint increase in color in an anhydrant spot, more than there had been in the control that I ran right next to it without the incubation. So, it turned out I believed that it was there, but I couldn't figure out what you did to increase the sensitivity of the method.

Finally, it dawned on me that, if it is an enzyme reaction, maybe I could do it better by incubating the possible enzyme with the reagents for a longer time period. I did it overnight. I found out that most people liked the overnight incubations because it meant you set something up at five o'clock, went home, and 16 hours later you came to work at 9:00 in the morning.

And sure enough, there was a nice, big, blue spot detected by the anhydrant, showing that there was transaminase activity in normal blood. And I started working on it. I bought a fish tank with the help of my father, and we did most of the work, made a contraption to hold butter dishes, and we did mass production chromatography. I was able to measure transaminase in blood.

### TABLE V

<table>
<thead>
<tr>
<th>Clinical diagnosis</th>
<th>SGOT</th>
<th>SGPT</th>
<th>HGOT</th>
<th>HGPT</th>
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</thead>
<tbody>
<tr>
<td>Carcinoma of lung</td>
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<td>0.41</td>
<td>8.86</td>
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<tr>
<td>Lymphoma</td>
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<td>0.53</td>
<td>6.35</td>
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<tr>
<td>Rhabdomyosarcoma</td>
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<td>1.60</td>
<td>9.13</td>
<td>7.46</td>
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<tr>
<td>Acute hepatitis</td>
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<td>1.75</td>
<td>7.20</td>
<td>10.40</td>
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<tr>
<td>Portal cirrhosis</td>
<td>0.49</td>
<td>0.38</td>
<td>3.10</td>
<td>1.40</td>
</tr>
<tr>
<td>Acute myocardial infarction</td>
<td>2.02</td>
<td>1.76</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>1.16</td>
<td>0.81</td>
<td>5.00</td>
<td>2.20</td>
</tr>
</tbody>
</table>
For this meeting, all I would add was that I measured the enzyme that was rich in heart muscle. There was a second one. It was uncertain whether it was the same enzyme as was measured with glutamic oxaloacetic transaminase, or one called glutamic pyruvic transaminase.

I bought some alanine and tried it, and, sure enough, it gave almost the same kind of activity in the blood. So, I started to measure both alanine and glutamic transaminases in all my specimens, done at the same time.
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In one of my last papers published in 1997, I compared the use of SGOT (AST) with some newer biomarkers for cardiac injury that were more specific, and concluded that troponin (TnT) was much better.

Troponin-T as a Serum Marker for Myocardial Infarction
Vadiraja V. Murthy and Arthur Karmen
Albert Einstein College of Medicine, The Bronx, New York

... but ALT has become the workhorse for assay of acute liver injury.

I got no enthusiasm from either Dr. Wroblewski he didn't discourage me from it, but no enthusiasm or from the Chief of the Department. Again, he repeated the story that I apparently he had grown up with, that everybody agreed that there was no need for another liver function test.

And it turned out that I would attend this meeting today, and I ought to probably stop my discussion about this with the dictum that they gave me about how the world really didn't need another liver function test, something they all subscribed to. They said they were not going to allow me to use this in the report that I made on my work "Because we know that nobody needs another liver function test, another liver indicator."

I guess that I've told you enough stories. (Laughter.) I have prepared an abstract that tells some of this, and you can read about it.
I went on to do an internship and medical residency at Bellevue Hospital and NYU, then to NIH for research on gas chromatography and lots of other projects. I did not get back to look again at transaminase for cardiac injury for a long while, but finally did so in 1997.

I ended up with a long career, not as illustrious as I might have liked, looking back, but it worked out pretty well. I retired as the Chairman of the Department of Laboratory Medicine at Albert Einstein College of Medicine and the lead director at several hospitals, which is not the way you might want to do it, if you planned for it.

I learned about taxi services. I learned how to speak Spanish mostly and occasionally Russian, from some of our patients. I would not give up the opportunity to do that for anything. I have a grandson that wants to be a physician, and I am rooting him on.

I am getting a signal from my friend Senior. He is pointing at his watch and going like that (pointing to his head -- Laughter) So, either I'm talking too long or I'm somewhat insane. Usually, insanity is this way (indicating -- Laughter)

Thank you. (Applause)