Reflections on Cellular Physiology as a Catalytic Framework for Medicine

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These are the reflections of a retired physician who was introduced to cellular physiology in 1947 at the University of Pennsylvania. I majored in Zoology. I took the required major courses, which were interesting but not exciting. I was a premedical student at the time. Fortunately I was introduced to cellular physiology in 1947. The teacher was Professor Louis Heilbrunn, an amazing man dedicated to teaching and the love of his students. He had a number of graduate students at the time. The undergraduates were well integrated with these advanced students. We used his textbook of physiology and we were all proud of being his students. He gave us a new way of thinking about biology. It was exciting and we were treated as mature students.

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Beginnings

The material was quite different. Professor Heilbrunn wrote a book about the function of basic cellular levels of the living organism. We studied the then known cellular anatomy and chemistry. He had an interest in simpler organisms to understand adult human physiology. His summers were spent at Woods Hole Massachusetts on the Cape. He had an unusual interest in calcium metabolism of the cell to explain many functions. His hypothesis attempted to explain many of the observable facts about cell muscle contraction, retinal function, membrane function, cell division, and cell death.

When I entered medical school at the University of Vermont, we were taught gross anatomy and histology as the basis of medical science. This was a carryover from my pre-med courses in zoology. It was exciting; something that you had to know but it left a large gap in the study of medicine. We gradually got to the outskirts of cellular physiology with courses in biochemistry and general physiology.

In pharmacology, as taught then, there was no connection with cellular physiology. A large gap in my clinical years of medical school, I could clearly see the relationship with cellular physiology and diabetes as well as many endocrine diseases that could not be explained by gross anatomy alone.

During my fourth year, the cholesterol theory was being debated to explain coronary artery disease. The overwhelming consensus was rejection of the theory even though rabbit studies showed it true.

I went off to residency, where my goal was to practice internal medicine. I had one year of training in pathology and laboratory tests. I had a great teacher, Dr. Lester Goldman who was a hematologist. In 1953, he taught us well what were the known facts about platelets, white blood cells, and red blood cells at that time. We also learned about the relationship to disease and the function of these cells. The complexities were not known. The whole field of lymphocytes and immunity was not well understood.

During this period of time, the stress theory relationship to disease was in vogue, surely a cellular phenomenon. Our tools were limited: penicillin, tetracycline, digitalis, quinidine, warfarin, chlorothiazide, mercurial drugs, and some others.

Electrocardiography was an exciting field. This brought us back to cellular physiology potassium and cellular membranes. Absorption across the membrane to the cytoplasm and the reverse explained depolarization and repolarization as seen on the electrocardiogram (EKG). The EKG was very sensitive to potassium levels. Low or high levels had profound effect on the EKG.

Atrial conduction of the impulse to the ventricles was profoundly influenced by various pharmaceuticals such as atropine and beta blockers whose effect had to be on membrane polarization and repolarization of cells. There were various conduction pathway’s which bypassed the atrioventricular node, causing arrhythmias and EKG changes as another example of cellular defects or problems. A new field of electrophysiology started.

Medical Practice

With time as I was in practice, new complexities began to emerge.

The first I recall was in protein chemistry. The division of globulins into various categories was very complex and took time to learn. Then came antibodies and cell receptors that were positive or accelerated or cured disease.

Further amazing developments regarded lymphocytes. Beta and T-cells gave us further understanding of the immune system. Abnormalities in proteins shed light on another group of diseases that one had to understand, such as waldentrom macroglobulinemia and other problems like human immunodeficiency virus (HIV).

Then came the oncologist with his various chemical approaches which did not seem to make much sense and really showed very little improvement in most cancers with maybe the exception of Hodgkin’s disease.
With HIV, T-cells in beta-cell function was better understood. It really was revolutionary and changed the thinking of immunity.

I was interested in cardiology, and saw rather devastating results for coronary artery disease in my early years of practice. I remember seeing a thirty-six-year-old woman with markedly elevated cholesterol levels who died while pregnant of an acute myocardial infarction. This was a very frustrating time. Our tools of prevention and understanding certain facets of disease were limited. Then the cholesterol theory was validated and the intracellular mechanisms understood. The therapy of statins came into play with remarkable results: a reduction and delay of acute coronary. In practice a few patients had a reversal of atherosclerosis confirmed by the usual testing. This was all a result of understanding of the mechanisms of cholesterol metabolism by various cells.

All the progress that followed was due to the understanding of cellular metabolism. Stents and the other resolutions that followed are based on basic cellular physiology, cell growth, fibrosis and clotting.

Then came the exciting field of DNA and genomic medicine with gene suppressors, gene mutations, deletions, causes, and chromosome defects to explain disease.

Editor’s Note:
Dr. Arthur Perelman was invited to share his experience-based perspective of contributions by cellular physiology to integrating understanding from anatomy and physiology into guiding principles for medicine. His appreciation for the intellectually catalyzing significance of cellular physiology to medical practice is inspirational.

Acknowledgment
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