Interviews with

JOHN CLEMENTS M.D.

THE STORY OF PULMONARY SURFACTANT AND BASIC SCIENCE IN THE CARDIOVASCULAR RESEARCH INSTITUTE

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INTERVIEW HISTORY

At the Army Chemical Center there would be one or two people working with me and that's the way it would have been for fifty years. But here, [in the CVRI] I was transplanted from a small research lab to a growing unit that had an equal dedication to training as it had to research. So I was thrown into that milieu and surrounded by research fellows. That made it possible to develop the interest in a number of parallel ways. ...Now we could do lipid chemistry, now we could do protein chemistry, now we could look into metabolism, now we could look at questions of regulation, the histology of the system, the morphology of the system. So a group of people could then develop over the years with common interests in the surfactant system, but bringing a variety of experimental disciplines to bear.

John Clements, M.D.

Born the youngest of four children on the windiest day of 1923 in Auburn, New York, Dr. John Clements’ mother saw portent in his birthday weather. In this interview, Dr. Clements admits that “some people say I’ve been windy ever since,” setting the tone for this lighthearted, but meticulous account of his research career. A youthful desire to become a chemical engineer led him into Cornell in 1941, where he attended under a New York State Regent's Scholarship and flourished in Cornell's strong instructional program in chemistry, which he regarded as "immense fun." War intervened while he was still an undergraduate and he entered Cornell Medical College, volunteering for the accelerated Army Specialized Training Program and emerging with an MD in 1947. He recalls that about halfway through medical school he saw that in clinical medicine "there was an uncertainty factor that did not appeal to me. I felt that a lot of what was done was repetitive... very routine and that people did things because that's the way it had always been done....that was not my turn of mind. I was really filled with curiosity about things." Consequently he began a research assistantship at Cornell without taking an internship.

In the face of the doctor draft of the early 1950s Dr. Clements volunteered to serve in the medical division of the Army Chemical Center in Edgewood, Maryland where he hoped to work in the biochemical division with his old mentor, William Summersen. His commanding officer had other ideas, however, and informed him upon his arrival at Edgewood that "you're a physiologist from now on!" These words proved to be prophetic and the young investigator soon found himself in a full rubber gas mask and protective clothing doing respiratory measurements and learning to understand the physiology and toxicology of chemical warfare agents. He describes his surge of interest in pulmonary physiology, particularly the problem of surface tension in the lungs, as "the starting point for essentially all of my subsequent career."

In this interview, Dr. Clements reveals the existence of a small group of investigators vitally interested in lung physiology and linked by a series of military research contracts in the early postwar years. In his role as military officer in charge of these projects he describes himself as a “neophyte” who discussed research with “titans” like Julius Comroe at Penn and Jim Whittenberger, Jere Mead and E. P. Radford at Harvard.
Moreover, because of his position, he knew the important work in the field before it was published. He goes on to describe the early formulation of the lung surfactant question, stated simply, "if the surface tension did change with the size of the lung...there would have to be something in there to do it." When he and collaborator Elwyn Brown began to work on the problem, the change in surface tension of the lung had only been indirectly inferred. His first breakthrough was to demonstrate the presence of a surfactant directly, using actual lung extract and the Langmuir-Wilhelmy Balance to measure its effect on lung mechanics. He recalls his disappointment when the journal *Science* turned down this pathbreaking paper, finally published in 1957 without peer review in *Proceedings of the Society of Experimental Biology and Medicine*. Nevertheless, his colleagues received his work with enthusiasm, and in late 1957 Harvard pediatrician Mary Ellen Avery visited Dr. Clements’ lab and began to explore the link between lung surfactant and the clinical picture of respiratory distress in the newborn, then known as hyaline membrane disease.

Once the clinical relevance of surfactant was recognized, the field moved from its “monastic” to its “secular” phase and clinical researchers flocked to the field. In 1959 Dr. Clements came to the new Cardiovascular Research Institute upon invitation from Julius Comroe and there found an exciting interdisciplinary approach to basic research, a “lively place with a lot of communication.” He recalls his faith in Julius Comroe’s “absolute integrity” as Comroe anticipated his needs, providing him with technicians, research fellows, and laboratory space as his research program grew. In 1964 he received an Americana Heart Association Career Investigator Award: thirty years of support for “work on interfacial phenomena in biological systems with current emphasis on the pulmonary surfaces.” This interview reveals Clements’ persistent ability to move between chemistry and biophysics and relate to physiological clinical concerns, demonstrating his gift for interdisciplinary collaboration which flourished in the UCSF setting of the Cardiovascular Research Institute. It covers several decades of research in alveolar mechanics and the study of the composition and biological properties of surfactant, and the exploration of its potential as human therapy. He shows in fine detail how Comroe's leadership and NIH grants, especially Program Projects and Specialized Centers of Research shaped the CVRI over the years and allowed it to flourish economically along research project lines.

These interviews offer a more personal perspective that supplements the many other written accounts of the lung surfactant story. One of the first of these was Julius Comroe's 1976 essay, "Premature Science and Immature Lungs," written for *Retrospectroscope* as an example of the importance of both basic science and clinical research. More recent treatments of the story are those written by Dr. Clements: "Lung surface tension and surfactant: the early years," in The American Physiological Society series *People and Ideas* and his most recent account, "Lung Surfactant: A Personal Perspective." in the *Annual Review of Physiology* (1997): 59:1-21. Many of these written essays recount a linear and logical march to discovery; indeed Dr. Clements narrative represents a single-minded pursuit of lung surfactant studies that eventually had huge ramifications for clinical practice. As he fills in the story he himself cautions "when you ask the memory to reconstruct daily events from forty years ago, you've got to be appropriately cautious," a useful caveat for creators and readers of oral histories alike.
The account he presents in this interview is an important adjunct to more reductionist versions of the "discovery" of lung surfactant. Here, Dr. Clements places the development Exosurf into the context of the larger area of surfactant studies, referring to his successful product as "a pimple on the pumpkin." He fills in the important personal details, from his dream-inspired experiments adding cetyl alcohol to DPPC and its serendipitous patenting, through to development of the product “Exosurf” involving an important partnership with Burroughs-Wellcome that allowed them to complete clinical trials and gain FDA approval in record time. An account of subsequent data on surfactant use may be found in his article with Francis R. Poulain, “Pulmonary Surfactant Therapy, Western Journal of Medicine, (January, 1995): 162:43-50.

These conversations took place in Dr. Clements' office on the thirteenth floor of Moffit-Long Hospital and he has lightly edited the transcripts for accuracy. Augmenting the written records of the CVRI and lung surfactant research, he provides the reader with a personal, detailed account demonstrating the importance of informal networking, grant support and a favorable institutional milieu for conducting basic research. Observing the future of surfactant studies, he cautions that in the era of the molecular revolution, genetic methods and the analysis of cellular activities should be tempered with consideration of the proper context of organ and system physiology. The interviews reveal firsthand his investigative wit, optimism, and curiosity and the forces that shaped this classic story of basic research applied successfully to clinical medicine within the postwar academic medical center.
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