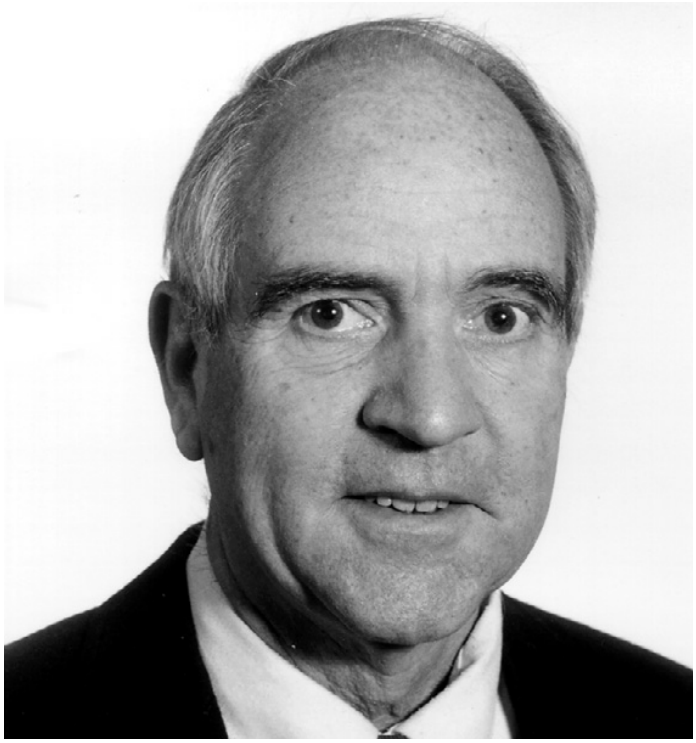
THE FACULTY OF MEDICINE
Harvard University

Ronald John Gibbons



Dr. Ronald Gibbons died in his home at Kittery Point, Maine on September 27th, 1996 while looking out on the waters of Portsmouth Harbor. Ron was an accomplished yachtsman with a talent for winning. He approached sailing and racing, and a host of hobbies - wine-making, cabinet work, photography, and gardening - with the same quiet energy, analytical skill, insight and commitment to excellence which marked his scientific career.

Dr. Gibbons attended Wagner College and received his Ph.D. in Microbiology from the University of Maryland in 1958. While at Maryland, he studied the microbiota of the bovine rumen, an experience which prepared him well to work with the anaerobic bacteria of the oral cavity and with mixed bacterial populations. His thesis at the University of Maryland was concerned with polysaccharide production by rumen bacteria. He subsequently demonstrated similar storage mechanisms in oral streptococci.

In Dr. Gibbons' early years at Forsyth Dental Center he was engaged in the study of experimental mixed anaerobic infections induced in guinea pigs by injections of subgingival bacterial populations from humans. Prominent and essential to these infections were strains of a species of black pigment-producing anaerobes (known then as *Bacteroides melaninogenicus*). Dr. Gibbons concentrated his efforts on these organisms and identified an essential growth factor provided by other components of these mixed infections. He showed that it could be replaced by menadione, a vitamin K analogue. He also demonstrated a requirement for heme and, based on these findings, was able to grow strains in pure culture. Subsequently he showed that these *Bacteroides* produce a true collagenase. This work opened up a field of study on the specificity of periodontal infections which has occupied many laboratories for the past 35 years and has had a major impact on the clinical management of periodontal disease.

On the strength of his earlier work, Professor John B. Macdonald, Director of Forsyth Dental Center at that time observed: "I felt certain that in bringing Ron Gibbons to Forsyth and Harvard, we had struck gold. His fine mind, his analytical skills and his ability to formulate and address the right question held out the promise of a truly distinguished career".

In the 1960's, Dr. Gibbons became interested in the role of bacteria in the initiation and progression of dental caries. His first efforts in this area were based on the hypothesis that cariogenic bacteria might store polysaccharides that could be used both for the production of energy and for the production of acid between meals. The latter property was of concern in the pathogenesis of caries since it might prolong the period of tooth demineralization. It was shown that specific species of oral streptococci were able to store intracellular polysaccharides when provided with fermentable carbohydrates and that these polysaccharides would be utilized and lead to acid production when carbohydrates were depleted from the environment. Of greater interest to Dr. Gibbons, were the extracellular polysaccharides produced by bacteria. He demonstrated that streptococci such as *Streptococcus mutans* produce extracellular polysaccharides when provided with sucrose. These polysaccharides were shown to be important in the formation of copious amounts of dental plaque in animal model systems and essential to the production of the massive caries observed in such systems. He isolated strains of *S. mutans* from human dental plaque that caused caries when transmitted to germ-free rats, supporting the notion that this species might be critical to the production of dental caries in humans. More important to Dr. Gibbons was the mechanism by which this species caused caries. Why was this species cariogenic and similar streptococci less cariogenic? Among the additional properties revealed by Dr. Gibbons and others (in other laboratories) was the ability of the species to lower the pH to extremely low levels, the aciduric properties of the organism and most importantly, the production of extracellular polysaccharides. Working with investigators at NIDR, Dr. Gibbons demonstrated that inclusion of low molecular weight dextrans in the diet of experimental animals would diminish extracellular dextran formation and thus inhibit dental caries demonstrating the essential role of this virulence property in the pathogenesis of the disease.

The studies of dental caries and possible attachment mechanisms provided by dextrans led Dr. Gibbons into the area for which he is justifiably world famous. He reasoned that the first requirement for an organism to colonize any site in nature would be that it be able to attach to that site. Thus, the concept of the central role of adhesion in the pathogenesis of infectious disease was born. A legion of studies of adhesion as a virulence determinant in the broad biomedical area have been derived largely from Dr. Gibbons early studies of the attachment of streptococci to oral surfaces. The key point of his initial studies was the specificity of the processes involved. Dr. Gibbons demonstrated that different species of streptococci would attach preferentially to different oral surfaces. For example, *S. mutans* would attach preferentially to the tooth, *S. salivarius* to the tongue, while *S. sanguis* would attach to the tooth, tongue or cheek.

The mechanism of this specificity turned out to be the presence of specific adhesins on the surface of

different bacterial species which would attach to specific receptors on the surface of mammalian cells or pellicle-coated hard tissues. This specificity intrigued Dr. Gibbons, who carefully measured the relative adsorption of different species to different surfaces (e.g. to mammalian cells vs mineralized surfaces) and to purified substances attached to such surfaces. Further, he examined the inhibition of attachment by various substances such as sugars, amino acids, proteins etc. He observed that adhesion is often mediated by lectin-like interactions which could be blocked by specific sugar molecules. In collaboration with Dr. Donald Hay, he showed that different oral species would attach to different pure proteins present in saliva. They demonstrated the molecular basis of this attachment for selected species and demonstrated that the configuration of the receptor protein was critical in the binding process. They found that "hidden receptors" on proline-rich proteins, which they termed cryptitopes, would be exposed if the protein was adsorbed on a hard surface such as enamel. However, these receptors were hidden if the protein was free in salivary secretion. They reasoned that possession of an adhesin by a species that would bind to a salivary protein when it was attached to the tooth but not when it was free in saliva would favor its retention in the mouth by promoting colonization of the stable hard surface.

Ron has left a living legacy embodied in the many students, postdoctoral fellows, visiting professors and colleagues at Forsyth and Harvard who trained under or who collaborated with him. As stated by Richard Ellen Professor of Periodontology at the University of Toronto, Faculty of Dentistry: "Graduate students and postdoctoral fellows benefited enormously from his ideas, work ethic, broad reading habits, intuition and outstanding communication skills". Trainees were thrust early into the international network of worthy investigators in Oral Biology. Forsyth those days was a magnet for visiting scholars. Ron made sure that his students met them personally, and he involved the students with them both at home and on the road at conferences. He was a loyal and dedicated mentor whose guidance to his students extended beyond the restricted environment of the laboratory and into the somewhat more bewildering world of academia, funding agencies and the employment market.

There is no doubt about the tremendous value of Dr. Gibbons' scientific findings as they relate specifically to oral microbiology. Of equal or greater importance has been the impact of Dr. Gibbons' career on the field of dental research in general. He provided a symbol of excellence that was visible to researchers within as well as outside of his chosen field of work. The lines of research that he opened up, originally oriented toward periodontal disease, dental caries, and cellular adhesion, have provided fertile areas of research activity for investigators both inside and outside of dental research. He worked with and communicated extensively with scientists active in other areas of microbiology. These interactions have helped to spread the gospel that the oral cavity provides a premier model for the comparative study of a wide variety of biochemical phenomena significant to medicine and biology in general. His efforts have helped to expand the horizons of dental researchers beyond the boundaries of specific dental diseases and conversely have encouraged biomedical scientists in other fields to look to the mouth for some of their answers. His influence on dental research in this regard is perhaps his greatest legacy.

Respectfully Submitted,

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