Mechanisms in Anesthesia and Analgesia

Convention, Crisis, and the Shoulders of Giants

"If I have seen further it is by standing on ye sholders of Giants."

—Isaac Newton (in a letter to Robert Hooke, February 15, 1676).

"'…there are different anesthetic agents but only one anesthetized state.'"

IN this issue of ANESTHESIOLOGY, Perouansky has written a scholarly historical study of the intellectual evolution of scientific thought in the late 19th and early-mid 20th centuries, as scientists grappled with the concept of anesthesia.[1] In his essay, Perouansky identifies two closely associated paradigms developed by Claude Bernard: "that all life is defined by the susceptibility to anesthesia" and "that all anesthesia can be reduced to the same essence … there are different anesthetic agents but only one anesthetized state." Although the thought of anesthetized plant life may make the first paradigm seem alien to current thinking, the second paradigm is still used, as evidenced by the interchangeability of different classes of anesthetic drugs used in current studies of both anesthesia mechanisms and anesthesia toxicity.

The use of the term "paradigm" in his review makes explicit reference to "The Structure of Scientific Revolutions" by Thomas Kuhn,[2] one of the most influential and controversial essays of scientific philosophy in the 20th century, and which is currently marking its 50th anniversary. According to Kuhn, scientific progress within any given specialty is not merely the consequence of the progressive accumulation of individual observations and theoretical contributions, but rather occurs in alternating periods of convention and crisis. During periods of convention, called by Kuhn "normal science," existing paradigms are based on previous scientific advances, and research "force(s) nature into the preformed and relatively inflexible box that the paradigm supplies." According to Kuhn, findings that cannot be explained within the paradigm are neither sought nor readily accepted. However, when normal science can no longer evade or explain these anomalous observations, a period of "crisis" or "scientific revolution" occurs, which Kuhn describes as "the tradition-shattering complements to the tradition-bound activity of normal science." Such scientific revolutions require a reevaluation of previous theories and observations. Once a new paradigm has been developed, the process of normal science will again attempt to incorporate within it subsequent anomalous observations.

Furnished with these insights, it is interesting to contrast the large numbers of different scientific hypotheses proposed to explain mechanisms of anesthesia in the late 19th century with the current situation, where large numbers of different research groups are conducting research within a common paradigm. It is certain that Kuhn would call ours a period of normal science. He would probably have stated that the publication by Franks and Lieb on the effect of anesthetic drugs on protein receptors[3] initiated a paradigm shift – a protein theory supplanting the previous lipoid theory of anesthesia.[4,5] To quote from Perouansky: "Within a matter of years, with the lipid theories retreating and scientific attention redirected, an increasing number of inconsistencies in the lipid theories, heretofore mostly neglected, were observed. Predictably, once the tide had turned in their favor, an avalanche of publications 'verifying' the protein theory followed." This development precisely fits the Kuhnian model of the "mopping up operations" that occur in normal science after a paradigm shift.

A fundamental component of Kuhn's thesis was that the principles of scientific revolution apply equally well to all areas of scientific endeavor. Kuhnian progress may be expected, and is indeed observed, in other areas of our specialty. For example, the neuron doctrine, championed by Santiago Ramón y Cajal, applied cell theory to the nervous system to state that the neuron is its structural and functional elemental unit.[6] This paradigm, still in use, replaced the earlier reticular theory, proposed by Joseph von Gerlach and supported by Camillo Golgi,[6] which stated that dendritic processes form continuous rather than discrete

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connections and which inferred that the basic structure of the nervous system was a reticulum-like neural plexus. Ramón y Cajal's paradigm shift incorporated anomalous observations made previously by William Hiss, August Forel, and Fridtof Nansen,[6] and was primarily based on histologic techniques developed by Golgi himself.[7] Although both Golgi and Ramón y Cajal observed the discrete terminals of dendrites rather than the neural reticulum predicted by the reticular theory, only Ramón y Cajal made the inference that "nerve currents are transmitted from one [neural] element to the other as a consequence of a sort of induction or influence from a distance,"[8] a hypothesis made long before the formal discovery of synaptic transmission. Despite observing these dendritic terminals, Golgi rejected the neuron doctrine[9] and remained one of the reticular theory's most ardent supporters. Similarly, Ramón y Cajal observed the presence of dendritic spines[10] and recognized their significance as key neuronal sites for synaptic plasticity,[11] although this was not demonstrated until transmission electron microscopy[12] and multiphoton microscopy[13] some 60 and 100 yr later. Yet in classic Kuhnian fashion, these dendritic spines had also been observed previously by Albert von Kölliker, Alexander Dogiel, and by Golgi, but these anomalous observations were dismissed as fixation artifacts or as silver precipitates and the dendritic spines were expurgated from their histologic drawings.‡

One of the controversies surrounding Kuhn's work has been the uncertain definition of "paradigm." Perouansky makes the novel assertion that both the lipoid paradigm of Meyer–Overton[4,5] and the subsequent protein-receptor paradigm of Franks–Lieb[3] both fit within the unified paradigm of anesthesia suggested by Bernard, namely that "there are different anesthetic agents but only one anesthetized state." Clearly, the more indefinite a paradigm, the less it is likely to be able to predict subsequent observations or to be challenged by them. But can an approach that neither suggests a mechanism of action nor makes predictions for subsequent observations really qualify as a paradigm? Kuhn identified two characteristics to define paradigm: that it is sufficiently unprecedented as to attract adherents from the previous paradigm, and that it is sufficiently open-ended as to leave many unanswered questions for normal science to resolve. Possibly a more useful definition is that the paradigm is a "specific collection of questions, viewpoints and models"[14] that characterizes a scientific agenda and determines what challenges exist and within which set of rules they may be solved.

It is not clear whether paradigms "shackle" scientific thinking, as Perouansky argues, or enables it. Some have criticized the perceived "herd mentality,"[15] although this may merely reflect the fact that normal science has become progressively and overwhelmingly collaborative. Kuhn argues that these restrictive paradigms are "essential for the development of science. By focusing attention upon a small range of relatively esoteric problems, the paradigm forces scientists to investigate some part of nature in a detail and depth that would otherwise be unimaginable. And normal science possesses a built-in mechanism that ensures the relaxation of the restrictions that bound research whenever the paradigm from which they derive ceases to function effectively. At that point scientists begin to behave differently, and the nature of their research problems changes. In the interim, however, during the period when the paradigm is successful, the profession will have solved problems that its members could scarcely have imagined and would never have undertaken without commitment to the paradigm. And at least part of that achievement always proves to be permanent."

When breakthroughs do occur, they may do so in leaps, but these leaps are from the shoulders of the giants that preceded them. These leaps are often made by knight's-move progress, partly forward but partly sideways. To quote a recent review[16]: "(p)erhaps the most radical thrust of Kuhn's analysis … was that science might not be progressing toward a truer representation of the world, but might simply be moving away from previous representations." In most cases the paradigm-breakers were actively engaged in normal science but were able to appreciate a deeper significance of anomalous and serendipitous findings. As Louis Pasteur, another giant and a contemporary of Claude Bernard, wrote: "In the fields of observation, chance favors only the prepared mind."[17] When breakthroughs in understanding occur, are these more because of the crisis induced by the paradigm-breaking giant, or because of the consolidating effect of normal science that follows? What should be the implications for research funding? We doubt that this critical appraisal of past scientific endeavor was intended to provide the answers to these questions. However, Perouansky's eloquent account does serve as an opportunity to pause and reflect on lessons learned from the successes and failures of our intellectual forebears and provides an azimuth for researchers involved in normal science and the herd with which we run, or stumble.

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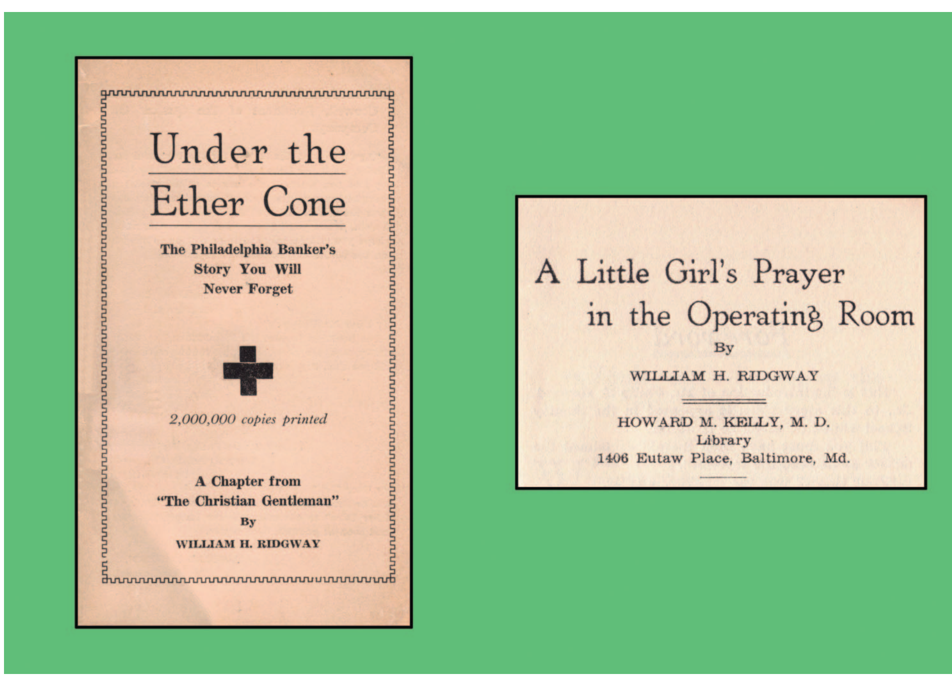
Ridgway's *Under the Ether Cone*



From his 1937 book *The Christian Gentleman,* author William H. Ridgway extracted one chapter as a pamphlet titled *Under the Ether Cone: A Little Girl's Prayer in the Operating Room*. In that pamphlet, Ridgway relates the story of a young girl informed in the operating room by her surgeon that she would go to sleep before he would begin working. "Why, doctor!" cried the girl. "I never think of going to sleep without first saying my prayers on my knees by the side of my bed." After kneeling in prayer, "she went under the ether cone" with a "sweet and peaceful smile upon her face." It is easy to understand why the pious Dr. Howard Kelly was interested in this story (*right*). The retired Johns Hopkins professor was infamous for startling anesthesia and nursing personnel by dropping to his knees to pray just before conducting surgery. (Copyright © the American Society of Anesthesiologists, Inc.)

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