

thinking, despite the seductive elegance of Claude Bernard's ideas. Although the Meyer–Overton correlation has not been expunged from textbooks, and the biophysical concept of hydrophobicity remains important to anesthetic pharmacology, these ideas have been subsumed into a broader neurobiological framework. Research investigating unitary mechanisms or even alluding to these mechanisms in discussions of new experiments is diminishing. Are unitary hypotheses dead? Not quite. Many ideas central to unitary hypotheses have collapsed, and few scientists dig there, but some tunnels of knowledge in that area remain surrounded by hard material that resists excavation. Instead, research on mechanisms of anesthesia is emerging as a field of systems neurobiology, linked closely to research on mechanisms of consciousness.<sup>8–10</sup> Moreover, advances in our scientific understanding of general anesthesia are starting to translate into promising efforts to develop better general anesthetic drugs<sup>11</sup> and improved monitors for assessing depth of anesthesia.<sup>12</sup>

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(Accepted for publication December 18, 2012.)

## In Reply:

We were interested to read the letter from Sette *et al.*<sup>1</sup> regarding our editorial. We agree that the “Shoulders of Giants” analogy extends back into antiquity. Interestingly, one use of this aphorism in the history of the accumulation of knowledge is that it has been used throughout the ages to enable the opinions of early intellectual giants to be amended by subsequent generations, despite their perceived diminished stature.

A classic example is cited here from ancient Jewish rabbinic tradition. There is an accepted step-wise regression in rabbinic legal stature and authority with the passage of generations, but this may impair the forces of progression and innovation. In an elegant attempt to justify his departure from the legal opinions of his forebears, R. Isaiah di Trani (c. 1180–1250), the leading Italian Talmudist of his generation, wrote as follows<sup>2</sup>:

I applied to myself the parable of the philosophers ... The wisest of the philosophers was asked: “We admit that our predecessors were wiser than we. At the same time, we criticize their comments, often rejecting them and claiming that the truth rests with us. How is this possible?” The wise philosopher responded. “Who sees farther, a dwarf or a giant? Surely a giant for his eyes are situated at a higher level than those of a dwarf. But if the dwarf is placed on the shoulders of the giant, who sees further? Surely the dwarf, for now the eyes of the dwarf are situated at a higher level than those of the giant. So too, we are dwarfs, astride the shoulders of giants. We master their wisdom and move beyond it. Due to their wisdom we grow wise and are able to say all that we say, but not because we are greater than they. .... Wisdom is greater than the wise”.

This passage was cited by Leiman<sup>3</sup>, in an encyclopedic review of the aphorism “Shoulders of Giants” in rabbinic literature. He reported that R. Isaiah di Trani “openly acknowledged his literary debt to contemporary non-Jewish philosophers” (in this case to Bernard of Chartres), and went on to state that in the Talmudic context, “the aphorism was particularly ingenious and apt, for it paid tribute simultaneously to progression and regression... On the one hand, the earlier generations are depicted as giants and the later generations as dwarfs – a clear case of regression. On the other hand, the dwarfs see farther than the giants – clearly evidence for progression.”<sup>3</sup> We believe that the art and science of medicine rightly share some elements of this duality.

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(Accepted for publication December 18, 2012.)

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“Theories are ..... never to be absolutely believed.”

**Claude Bernard**

*In Reply:*

I thank Drs. Sette, Dorizzi, and Azzini for their foray into the history of the On the Shoulders of the Giants (OTSOG) aphorism and I appreciate their persistence in disseminating these fragments of insight to various audiences (compare their reference no. 5). Unfortunately, I find myself unable to follow them all the way back to Priscian, as the quote they provide (“grammatica ars ... perspicaciores”) seems to bear little rapport to the OTSOG aphorism. More importantly, as the semantics of aphorisms are determined by the setting, I prefer to strictly separate the use of this aphorism in the scientific from its (mis)-use in the religious–spiritual and especially political context. In science, as opposed to religion, the view provided by the shoulders of giants permits the observer to see beyond the horizon of ones’ forebears. In religion, the authority of the giants may thwart skeptical examination of the canonical view and enforces conformity. Therefore, compiling the use of the OTSOG aphorism in these largely mutually exclusive endeavors of mankind is somewhat misleading. I cannot comment on its use in politics by the luminaries referred to by Drs. Sette and Dorizzi as neither this letter nor their reference no. 5 provide the necessary context.

Within the scientific framework, the exchange between Newton and Hooke remains, therefore, the relevant yardstick for the OTSOG aphorism. Importantly, however, one of the provocative novelties in Kuhn’s understanding of scientific progress is exactly the opposite of what the OTSOG aphorism commonly implies. Only “normal” science is cumulative and the tribute of “standing on your predecessors shoulders” makes literal sense. Revolutions and their associated paradigm shifts, however, are not. This paradoxical insight is what made Kuhn’s work brilliantly iconoclastic. I admit that the use of the OTSOG aphorism is problematic in the context of my review, including my own use of it, as OTSOG also paved the way into dead-ends as noticed by Thomas Butler more than half a century ago.<sup>1</sup> In fact, I intended its use only as an expression of my profound respect for all those scientists (including Claude Bernard) who, even when erring, contributed to the advancement of mankind’s quest for knowledge.

I appreciate Dr. Forman’s thoughts on my article. His mining-metaphor contains multiple appropriate analogies,

whether or not it captures the essence of a specific historian’s interpretation of the history of science. Dr. Forman recognizes my vagueness with respect to identifying a paradigm shift within anesthetic research. Indeed, I am skeptical of the commonplace notion that the move to proteins as anesthetic targets represented a new paradigm. Prior to the “accidental” and short-lived hegemony of lipid theories, a multitude of opinions about the nature of the anesthetic target (including proteins) coexisted under the umbrella of the “unified” paradigm. Only the temporary dominance of lipids and imperfect memory made the ascendance of proteins appear to be a paradigm-changing event. It is tempting to speculate that, had Nick Franks and the late Bill Lieb been able to publish their 1984 paper in the early 60s, it would have had a profound influence on the direction of research (possibly precluding the lipid era altogether) but it would not have been seen as a paradigm shift. At least not in the meaning commonly attributed to Kuhn and embraced by me. A key characteristic of paradigm shift in its rigorous interpretation is “incommensurability” between paradigms. Incommensurability implies that workers in different paradigms will not be able to fully communicate with each other because of the fundamentality of the differences in their frames of reference. In my opinion, the acceptance of the protein hypothesis did not generate such a disruption in the flow of anesthetic mechanisms research, certainly not an alternative to Bernard’s unified theory. I do acknowledge, however, that one may take license in attributing a specific meaning to the term paradigm, as an analysis of Thomas Kuhn’s own usage of “paradigm” famously yielded more than 20 different meanings within his own highly acclaimed book.<sup>2</sup>

Anyhow, the “paradigmatic” categorization of research itself is neither uniformly applicable nor universally accepted. Imre Lakatos<sup>3</sup> uses the notion of research program, whereas Larry Laudan<sup>4</sup> introduced the concept of research traditions. As opposed to a paradigm, more than one program or tradition are expected to coexist simultaneously in a given field of research. In my opinion, if a paradigm shift-like change occurred in our lifetime, it happened in the wake of the work of Ira Rampil<sup>5</sup> and Joe Antognini<sup>6</sup> on the importance of the spinal cord as locus of anesthetic-induced immobility: suddenly the unitary anesthetic state, with its continuous “depth” as indexed by immobility was fragmented into multiple components each with its own anatomic locus and mechanism. The unitary anesthetic state became an anesthetic syndrome and the notion of one universal anesthetic mechanism became obsolete. However, I do not want to belabor the analogy too much—biological sciences do not fit as neatly into Kuhnian paradigms as physics and chemistry do.<sup>7</sup>

I agree with Dr. Forman that unitary theories are not dead, although recently their focus has been narrowed to the most publicity-gathering component of general anesthesia: hypnosis disguised in its more attractive package of (un)consciousness. In this field, phantasies-disguised-as-theories