

# Malignant Hypercompliance

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"If we want things to stay as they are,  
things will have to change."

—Giuseppe Tomasi di Lampedusa,  
*The Leopard*<sup>1</sup>

AT the University of Wisconsin, Madison, Wisconsin, in the 1970s, a circulating nurse was designated to maintain a list of all malignant hyperthermia (MH) family surnames taped to the inside of the swinging doors to the operating suite to be cross-checked by everyone responsible for preoperatively evaluating a patient. Efforts to avoid trigger agents at all costs in those at heightened susceptibility by family history led to risky and often unpleasant alternative anesthetic regimens. Imagine, for example, induction and maintenance of anesthesia for an upper abdominal procedure in a difficult airway patient at risk for MH before introduction of fiber-optic laryngoscopy and nontrigger IV anesthetics. Lethality of the syndrome during the two decades that elapsed between its recognition and its suppression by dantrolene engendered waking nightmares in the care of probands who triggered in the absence of advanced warning.

In the current issue, Pollock *et al.*<sup>2</sup> provide a learned account of Keith Ellis's tenacious and articulated efforts to identify the site of action of dantrolene within the sarcolemma of skeletal muscle. Ellis's discovery motivated investigation of components of the excitation-contraction coupling triad as molecular candidates for MH pathogenesis in the face of alternative lipid, central nervous system, catechol, and other MH theories that prevailed until the 1990s.<sup>3,4</sup> As eloquently detailed by Pollock *et al.*, Ellis and his coworkers bent diverse experimental models to their purpose in testing dantrolene's potential sites of action, spanning the central nervous system to the periphery. With these data



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in hand, Ellis was primed for the cognitive leap in perceiving that dantrolene may have utility in the treatment of MH. He sought a collaborator able to perform a first trial of dantrolene in the swine model of MH and forwarded stocks to Gaisford Harrison. Rescue of seven of eight pigs from certain death by MH at Ellis's instigation has since saved thousands of lives and loosened one of anesthesiology's most terrifying shackles.<sup>5</sup> With Pollock *et al.* as guides, readers of Ellis's original manuscripts will be rewarded by familiarity with a chain of experiments that serves as a model of its kind.

In bringing Ellis's discoveries once again to light, Pollock *et al.*'s survey impels the reader to consider what technical advances of comparable magnitude may be identified in contemporary anesthesiology. The current editorial addresses why so little comes to mind. Looking

back, the period of Ellis's inquiries stands as a demarcation at the dawn of an incredible quickening in the practice of anesthesia in the two decades that were to follow (table 1). Conversely, innovations in anesthesia care from 1995 to the present have been less generous and of a different order, with a shift in focus from the introduction of disruptive technical advances in drugs and devices to the regulation of caregiver behaviors. What accounts for this shift? I suggest that the decline in innovation in anesthesia care over the past two decades may be traced to the specialty's envelopment by a culture of complacency coupled to a culture of compliance. It has been alleged that "By adhering to the six sigma approach, the anesthesia community has reduced mortality attributable directly to anesthesia so significantly that it is now almost

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Corresponding article on page 774.

Accepted for publication January 10, 2017. From the Department of Anesthesiology, School of Medicine and Public Health, University of Wisconsin, Madison, Wisconsin.

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**Table 1.** Innovations in Anesthesia Care**1975–1995**

Advanced cardiac life support, advanced trauma life support  
 Alfentanil  
 Anatomic ultrasound  
 Anesthesia simulation  
 Anesthesia technician  
 American Society for Testing and Materials color-coded drug labels  
 Atracurium, *cis*-atracurium  
 Blood filters  
 Blood scavenging, conservation  
 Body warmers  
 Calcium entry blockers  
 Capnometry  
 Caregiver infectious disease screening and vaccinations  
 Cardioplegia, safe cardiopulmonary bypass, extracorporeal membrane oxygenator  
 Catheter-based regional anesthesia  
 Cerebral oximetry  
 Chlorhexidine  
 CPAP, BiPAP, PEEP  
 Cerebrospinal fluid drains  
 Dantrolene  
 Desflurane  
 Dexmedetomidine  
 Esmolol, labetalol, carvedilol, selective  $\beta$  blockers  
 Exchange and wire-guided airway instrumentation  
 Exhaled anesthetic gas analysis  
 Fiber-optic video-assisted intubation  
 Fluid warmers  
 Fractionated and recombinant blood products  
 Gore-Tex gowns and barriers  
 High-efficiency particulate air and powered caregiver masks  
 High air exchange operating rooms  
 High-dose opioid anesthesia  
 Hypoallergenic gloves  
 Intraaortic balloon counter-pulsation  
 Invasive vascular monitors, arterial lines, pulmonary artery catheter  
 Isoflurane  
 Lipid treatment of local anesthetic toxicity  
 Low injury risk IV access  
 Midazolam, flumazenil  
 Milrinone  
 Needlestick protocols and prophylaxis  
 Noninvasive vascular monitors  
 Ondansetron  
 Nonsteroidal antiinflammatory injectables  
 Pain services  
 Pharmacogenetics of MH  
 Point of care operating room labs  
 Preanesthesia clinics  
 Processed electroencephalography  
 Programmable cardioverter  
 Programmable external drug infusion pump  
 Programmable implantable drug infusion pump  
 Programmable pacemaker  
 Programmable ventilator  
 Propofol

(Continued)

**Table 1.** (Continued)

Pulse oximetry  
 Rapid transfusion pumps  
 Remifentanil  
 Rocuronium  
 Sensory and motor evoked potentials  
 Sevoflurane  
 Sufentanil  
 Supraglottic airway devices  
 Thromboelastogram  
 Transesophageal echocardiography  
 Tranexamic acid  
 Universal precautions  
 Vasopressin  
 Vecuronium  
 Ventilation alternatives (airway pressure release ventilation, prone, low stretch)  
 Ventricular assist devices

**1995 to present**

Affordable Care Act  
 Accountable Care Organizations  
 Checklists, hand-offs, huddles, timeouts, debriefings  
 Continuous quality improvement  
 Drug bar-code readers  
 Dantrolene suspension  
 Drug diversion protections  
 Electronic health record, meaningful use  
 Hand gel  
 Health Insurance Portability and Accountability Act  
 Maintenance of Certification in Anesthesiology Program  
 Managed care  
 Mandatory vaccination, e.g., influenza  
 Medicare Access and CHIP Reauthorization Act, Merit-based incentive payment system, Alternative Payment Models  
 Microprocessor-controlled anesthesia machine  
 Operating room security identification badges and locks  
 Patient Safety Network anonymous reporting  
 Perioperative surgical home  
 Pharmacogenetics of nitrous oxide toxicity  
 Sugammadex  
 Quantitative electromyogram monitors  
 Regional anatomic ultrasound  
 Resource-Based Relative Value Scale  
 Universal testing

BiPAP = bilevel positive airway pressure; CHIP = Children's Health Insurance Program; CPAP = continuous positive airway pressure; MH = malignant hyperthermia; PEEP = positive end-expiratory pressure.

impossible to measure.”<sup>6,7</sup> Such assertions have led many to believe that achieving a “six-sigma performance standard” (*i.e.*, a work product that is 99.99966% free of defects) leaves little or no margin for improvement in anesthesia care.<sup>8</sup> To the contrary, Lagasse<sup>9</sup> reports an all-cause perioperative mortality rate of 1 in 500, with anesthesia care contributing to 1 in 15,000 deaths within 48 h, a rate that has been stable over 20 yr. Similarly, two large investigations of anesthetic morbidity report severe and permanent damage arising in part from anesthetic management in 0.2 to 0.5% of surgeries, intermediate

severity outcomes including unplanned postoperative intensive care in 0.5 to 1.5% of procedures, and an incidence of minor anesthetic morbidities in 22% of patients, many of which comprise “near-miss” events in which immediate attention is required to forestall far more deleterious outcomes.<sup>10–12</sup>

Accordingly, there is little need for the profession to seek beyond its borders to identify numerous opportunities for improving the “sigma” of its “work product.” Up to 50% of elderly patients experience new-onset delirium and cognitive decrements in the postoperative interval.<sup>13</sup> Why aren’t preoperative cognitive assessments a standard of care? Up to 30% of those dying from cancer suffer intolerable levels of pain.<sup>14</sup> A preponderance of patients undergoing surgery arrive with vitamin insufficiencies.<sup>15</sup> Impacts of suboptimal vitamin levels on postoperative outcomes are easy to prevent, diagnose, and treat, but are ignored. The single largest variable we make no effort to measure or modulate in perioperative care is the body’s intense inflammatory response to the trauma of surgery. Are there no consequences of this inattention? Why aren’t preoperative genomic profiles performed as a routine?<sup>16</sup> Of more topical relevance, despite 40 yr of escalating sophistication in understanding the pathogenesis of MH, the profession still lacks a noninvasive way to identify the MH phenotype outside the operating room. Nor has the diagnosis and management of MH changed materially in the interval since the introduction of dantrolene, despite a persistent mortality in 1 to 4% of patients.

I further suggest that anesthesiology has joined its sister specialties in a descent into a culture of compliance as evidenced by table 1. Compliance requires pathways, guidelines, and performance standards to be complied with, each taking years to formulate, disseminate, train, certify, monitor, reeducate, reward, and punish. Compliance and innovation are disdainful of one another. Compliers do not innovate. Innovators do not comply. Within a culture of innovation, choices to be made in patient care expand. Within a culture of compliance, choices constrict. A supine profession in a crisis of compliance becomes rigid, its reflexes fevered, its pulse thready and weak. T.H. White’s commandment “Everything not forbidden is compulsory” defines the asymptote of perioperative compliance that metastasizes without limit until halted by rebellion or desertion.<sup>17</sup> Innovation dampens the aspirations of the authorities of compliance. Extension of the dictates of compliance into the conduct of innovation including, for example, parade-of-horrors institutional review board demands, sum-of-all-fears Health Insurance Portability and Accountability Act mandates, apprehensive intellectual property and technology transfer policies and procedures, and guilty-until-proven innocent conflict of interest provisions are destructive and discouraging to investigators committed to making improvements in clinical care. Spread of the culture of compliance contagion to the heart of the culture of innovation (“Everything not compulsory is forbidden”) does not merely chill progress. It suffocates innovation in its crib.

What can be done? As a first step, I encourage you to generate your own version of my table 1, perhaps with distinct inclusion and exclusion criteria, threshold dates, and the like. Do you agree there’s been a break with the past? If so, do you believe that a culture of complacency and compliance accounts in part or in whole for the shift? If you do, is the shift acceptable to you? Many peers may have no issue with the status quo and trend. My listing above of performance deviations is idiosyncratic to my personal interests. If you believe that a contemporary culture of complacency and compliance in anesthesiology is unacceptable, I further encourage you generate your own list of long-felt, unmet needs. After that, “The most difficult thing is the decision to act, the rest is merely tenacity.”<sup>18</sup>

If, as I believe, the models of innovation that sustained us from 1975 to 1995 have failed us from 1995 to the present, then new models must be actively sought. First stops with a listing of needs in hand are the entrepreneurs and business schools of the twenty-first century that regard the discipline of innovation as a *sine qua non* to the conduct of a successful enterprise. In turn, new models of innovation rely on the profession’s capacity to identify, recruit, and foster talented individuals early in postgraduate training, and perhaps before, who are skilled in the quantitative methods necessary to collapse barriers between departments, schools, and institutions. Thereafter, during postgraduate anesthesiology training, a return to the past is belated:

Waters directed second year residents to undertake laboratory studies for a six-month period **to assimilate the principles and methodology of research, and learn the critical reading of studies and objective interpretation of the data.** “Waters instilled an inner fire in his residents.”<sup>19</sup>

C. Parsloe (Emphasis added)

As an added incentive, purchase Drs. Eger, Saidman, and Westhorpe’s superb *The Wondrous Story of Anesthesia*.<sup>20</sup> Chapters 10 through 13 amply chronicle the decline of technical innovations in anesthesia to a trickle over the preceding four decades but do not descry a clash between a culture of innovation and a culture of compliance as a cause. The text’s omission of Keith Ellis and his seminal contributions is remedied herein.

Although Harrison’s manuscript appeared in 1975, nearly 5 yr were to elapse before the role of dantrolene in human MH therapy was widely recognized. The first published report of human use by Friesen *et al.*<sup>21</sup> underscores core attributes of a culture of innovation. Dr. Jay Brodsky, the article’s senior author, dates his familiarity with dantrolene to a seminar he gave as a resident in which he reviewed Ellis’s work in MH swine (Brodsky, e-mail communication, November 7, 2016). There matters stood until 4 yr later when premature ventricular contractions and a heat-radiating carbon dioxide absorber were noted in the care of an otherwise healthy person undergoing knee arthroscopy and a diagnosis of MH was confirmed. Dr. Brodsky was aware that his pharmacy maintained a supply of dantrolene for treatment of spasticity in patients with cerebral palsy.

He relates: “My familiarity with the condition and the availability was completely serendipitous.” To the contrary, I suggest that serendipity played a minor role in saving the life of Dr. Brodsky’s patient. The experiences of Drs. Ellis and Brodsky provide clear evidence of a great innovator’s maxim, “Fortune favors the prepared mind.”<sup>22</sup> Ellis and Brodsky ranged widely and deeply in their curiosity and knowledge and were unconstrained by conventional wisdom or an ironclad standard of care. Would they have been able, or even willing, to act on the flashes of insight of their prepared minds in today’s culture of complacency and compliance?

## Competing Interests

The author is not supported by, nor maintains any financial interest in, any commercial activity that may be associated with the topic of this article.

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