

# Translational Research and the Perioperative Phenotype

*University of Michigan*

I DO not believe in fate, but some things just make you wonder. In 1875, a senior resident completing his training in surgery at the University of Michigan presented his required senior thesis entitled: “Anaesthetics and their Use.” This 46-page neatly handwritten manuscript described the state-of-the-art of anesthesiology in impressive detail. What was surprising to me is that his name was Robert Tremper and he left Michigan to practice surgery in Los Angeles, California. One-hundred and fifteen years later, I left Los Angeles to become the fourth department chair of anesthesiology at the University of Michigan.

The University of Michigan Medical School advanced anesthesiology from a section of surgery to departmental status in 1949, making it one of the early academic departments of anesthesiology in the nation. Warren Wilmer, Jr, M.D., served as acting chair until Robert B. Sweet, M.D. (1917–1980), was appointed as the first permanent chair in 1952. Bob Sweet had completed a surgery residency program at Michigan prior going to Massachusetts General Hospital (Boston, Massachusetts) for his training in anesthesiology. He progressively developed an excellent clinical program to support a well-respected surgical department (they trained the Mayo Brothers in surgery). At that time, there were few formally trained anesthesiologists to recruit as faculty. In the 1920s, the Department of Surgery had a visiting exchange program for young surgeons with St. Bartholomew’s in London, United Kingdom. On behalf of Dr. Sweet, Frederick Collier, M.D. (1887–1964), the chair of surgery at Michigan,



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Ph.D. (1947–) who ultimately became the director of research. After Peter Cohen stepped down as chair in 1985, I was recruited and found not only an extremely supportive dean and hospital director, but an especially supportive chair of surgery, Dr. Lazar Greenfield, M.D. (of inferior vena cava filter fame). My decision to come to Ann Arbor was based primarily on the encouragement and support of these three individuals.

One of the reasons for selecting the University of Michigan to be highlighted in this issue is that we are a large U.S. public institution. Previous departments highlighted in the December issues were either private institutions or part of national health systems. Although public institutions receive state funding, the primary source of revenue is collections from professional fee billings. Most of the additional support received by departments in the United States is derived from their hospital, which is interested in clinical care, administrative duties, and the recruitment and training of residents. The common ground between the hospital director and the academic department chair is the desire for high-quality

asked his colleagues at St. Bartholomew’s whether there were any young anesthesiologists who might be interested in spending a year in the United States. Consequently, in 1956, Thomas Bolton, M.D., F.R.C.A. (1925–), and his wife came to spend a year in Ann Arbor supported in part by a scholarship provided by Senator Fulbright. Thomas Bolton enjoyed the year so much he encouraged others to follow him—a yearly tradition that has continued till today.

Dr. Sweet stepped down as chair in 1975 and a national search was initiated with the goal of finding an individual who would develop a more extensive research program. Dr. Peter J. Cohen, M.D., J.D. (1935–2010), became the second chair in 1976 and he recruited, among others, Paul Knight, M.D.,

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subspecialty anesthetic care. These subspecialty anesthesia teams are the focal point for development of subspecialty education, fellowships, and academic programs (frequently focused on clinical investigation). Therefore, it is important in the Chair's negotiation that the department receives a financial model that will provide a margin to support the academic mission. As part of my negotiation when I came to Michigan in 1991, I requested the resources to implement a perioperative anesthesia information management system (AIMS) to be used for clinical perioperative care, education, and ultimately outcomes research. It seemed inevitable at that time that AIMS would be a part of anesthesia practice and that early adoption and development of an information system could provide the faculty a clinical research database derived from the electronic anesthetic record. This was ultimately accomplished but not for nearly a decade.

By 2005, the time was right for our department. There were a large number of talented and enthusiastic residents in our program, and we had accumulated a significant financial academic reserve, so we started the process of recruiting at least one research-track faculty in every subspecialty area. The majority of these faculty members were recruited from our own residency and were largely self-identified. These were residents/fellows who clearly had the drive to conduct research even with little time to do so. All of them had areas of focused interest and were driven to succeed, displaying that critically important "fire in the belly." Even more rewarding is that they worked together synergistically. Along with the development of the perioperative information system in the early 2000s, we had recruited a strong group of information technology (IT) specialists to develop and manage our AIMS. They ultimately developed into an outcomes research IT query group. By 2010, the academic productivity was evident with multiple publications per month in a broad scope of our clinical discipline.

Two other programs were developed at this time, which helped coordinate our department's clinical research and stimulated collaboration with other academic programs throughout the country. In 2008, we had multiple faculty conducting outcomes query research simultaneously, which was encouraging but lacked coordination. In that year, we initiated the Anesthesiology Clinical Research Committee. This committee, which met every other week, had members from all the subspecialty groups, their research support personnel, statistical support, and a member of the IT research group. We made it a departmental requirement that all clinical research projects must be presented to this committee before being initiated. This process accomplished several goals. First, it ensured that the faculty had done their homework; they had focused the question, reviewed the literature, and comprehensively planned the methods and statistics. This also ensured that there was not internal competition or overlap between investigators. Finally, the discussion usually improved the study and often spawned new interesting

research questions. This committee has continued to the present, but now meets every week.

Another event in 2008 positioned our department for collaboration nationwide and worldwide. At a meeting of a group of academic anesthesiology chairs, I proposed a collaborative effort in outcomes research to develop a common clinical research database derived from the AIMS. Eleven department chairs agreed that they would support a faculty member to come to Ann Arbor to draft the bylaws of a national data sharing organization for perioperative research, the Multicenter Perioperative Outcomes Group (MPOG). At that time, we were fortunate to have Sachin Kheterpal, M.D., M.B.A., as a recent graduate who had just joined our faculty. Sachin had been the lead developer of our AIMS when he was a principal of a small medical software company in the late 1990s. He had already conducted some excellent work in large database research as a resident and was clearly the individual to be the research director of MPOG. In August 2008, we held a meeting in Ann Arbor with anesthesia and surgical representatives from 11 academic centers. In this meeting, the ground rules were determined that our department in Ann Arbor would be the technical home for MPOG, that the membership "fee" would be 10,000 cases contributed into the common database and the commitment of IT support to enable the transfer of data. It was also agreed that the database would be vendor agnostic (it could receive data from anyone of the major AIMS) and that a research proposal from any site could request data from the entire database. Over the next 4 yr, MPOG developed the institutional ethics approvals, data use agreements, and an umbrella ethics approval at Michigan to enable this type of deidentified patient data sharing. MPOG has grown beyond the United States, including Dutch, German, and Israeli sites; and discussions are underway with the European Society of Anaesthesiology to develop a sister organization (EuPOG). Today, there are monthly perioperative clinical research committee webex meetings in which sites across the United States and Europe participate to evaluate protocols. This system has been set-up analogous to our department's Anesthesiology Clinical Research Committee meetings. Sachin Kheterpal has been the driving force of MPOG and has been recognized for his academic accomplishments with the 2013 American Society of Anesthesiologists Presidential Scholar Award.

A description of our department's accelerating research productivity over the last decade would not be complete without acknowledging what I describe as my most impressive "walk-on" faculty candidate. A description of how George Mashour, M.D., Ph.D., came to our institution was presented in *ANESTHESIOLOGY* as part of his receiving the Presidential Scholar Award in 2011. His translational research program spans the gamut from theoretical modeling of neural networks to experimental neurobiology to conducting the largest prospective clinical trial in our field's history (22,000 prospectively, randomized, consented patients

evaluating the bispectral index monitor). At the same time, he has been extremely collaborative within our department and with other departments, especially with Michael Avidan, M.B.B.Ch., F.C.A., from Washington University in St. Louis, Missouri (the department highlighted in the December, 2011 issue of *ANESTHESIOLOGY*). George arrived as a fellow in neuroanesthesia in 2007, just as Sachin Kheterpal was finishing his residency. These two individuals, working with the other five young research-track faculty, produced a critical mass of intellect, enthusiasm, and collaboration that is rare in academic medicine. The time was right, the resources were available, and all I had to do was let nature take its course. Mentioning these junior faculty should not diminish the efforts of the entire department and of some very academically productive senior researchers who built the academic foundations of the department and provided inspiration and mentorship for the junior faculty.

As I started in this editorial, I am not a believer in fate, but some things just make you wonder. I came to Michigan at a time when the institution was determined to build a first-class academic Department of Anesthesiology. The financial structure agreed upon along with the extremely favorable market environment during the 1990s enabled the department to develop an academic financial reserve. When the faculty shortages of the early 2000s were upon us, the department's long-standing collaboration with the United Kingdom enabled us to maintain clinical and educational services with visiting British faculty holding positions for the academic faculty to arrive over the next 5 yr. And finally, seven young faculty arrived, all with fire in the belly, and drive not only for their own success but for that of the department. Academic productivity has become contagious.

Finally, I am very grateful for the recognition that our department has received in the last few years; I was honored to be the Rovenstine Lecturer in 2010, George Mashour was the American Society of Anesthesiologists Presidential Scholar in 2011, Ralph Lydic, Ph.D., received the Excellence in Research Award in 2012, and in 2013 Sachin Kheterpal has been awarded the American Society of Anesthesiologists

Presidential Scholar Award, and this special issue in *ANESTHESIOLOGY*. My final advice and experience would not be earth shattering: build solid clinical and educational programs, ensure you have a financial model where you are earning more than you are spending, and recognize and recruit faculty who self-identify by their talent, enthusiasm, and collaboration.

In conclusion, I would like to thank Jim Eisenach and the editorial board of *Anesthesiology* for highlighting our department in this issue. As described in this editorial, over the last decade, our department has focused much of its effort on developing the capability for our department and faculty to conduct large clinical database outcomes studies that supplement the traditional clinical trials and bench research. This was the goal, for most of the faculty's primary interests were in clinical and outcomes research. We ultimately hope these large clinical databases (phenotype) will partner with large biorepositories (genotype) to enable us to determine how our patients are similar and are different, and direct our clinical decision making accordingly.

The primary function of a Chair is to develop faculty and allow them to fulfill their greatest ambitions. The database development, IT, and statistical infrastructure are tools to enable faculty to answer important questions. We believe that this type of research fulfills a crucial segment of the research continuum in finding and focusing important questions. It also has the advantage that it can be conducted by departments with inquisitive clinicians but without access to a large laboratory. I hope in this respect that this editorial has provided stimulus for the faculty in many departments to engage in this effort.

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