

THINGS THAT AREN'T WHAT THEY SEEM

Lawrence I. Bonchek, M.D., F.A.C.C., F.A.C.S.

Editor in Chief



I. MORE ON CONFLICTS OF INTEREST

In two previous issues of the *Journal* this column has drawn attention to a plague afflicting the medical profession—Conflict of Interest (COI). The winter issue of 2010–11 discussed the paradoxical effect of the decision by the International Committee of Medical Journal Editors to require disclosure of conflicts of interest by all authors.¹ Though the policy was intended to discourage payments to medical investigators of large consulting and lecture fees, it seems to have had the opposite effect. The disclosures of such payments, which now routinely accompany scientific articles, have become so commonplace as to be part of the scenery, and the payments have been able to rise to exorbitant heights without arousing comment. “Hiding in plain sight” seems one way to describe this phenomenon. A more provocative descriptive phrase, “the banality of evil,” was used by Hannah Arendt to describe incomparably more despicable actions, but her point was similar: even the unspeakable actions of Nazi Germany’s leaders, when carried out routinely, could eventually seem so ordinary that they wore away the moral veneer of society.

When unprincipled acts become “that’s just how things are done,” and moral transgressions become part of everyday life, anyone who objects can feel as out of step as the boy in Hans Christian Andersen’s fairy tale who could not see the Emperor’s New Clothes. The daily newspapers bring an unending parade of stories about moral compromises that reflect greed—usually for money or power. Athletes who use drugs are everyday news, including—possibly—even that icon of determination and survival, one who holds a special interest for physicians because of his recovery from metastatic testicular cancer, Lance Armstrong. Though we do not yet know the truth about the

allegations against him, it is telling that we cannot immediately reject them as being absurd. After all, anything is possible.

In the current issue of the *Journal* we publish an essay in the form of a letter by Dr. Stefan P. Kruszewski on the COI theme. He focuses attention (and cites numerous well-documented examples) of conflicts among physician/researchers who extol specific drugs or medical products and receive payments from their producers. He also points out problems unique to meta-analyses: the fact that COIs in the original studies are rarely reported, a matter that was also discussed in the previous issue of this *Journal* in a Letter to the Editor from Dr. Alan Peterson.²

Even if these problems only reflect a fraying moral fabric of society in general, it is troubling that they are becoming manifest in a learned profession like ours, where the consequences are more far-reaching and potentially damaging than the simple problem of distorted outcomes in sports. In this column I am referring to the growing number of scientific studies being retracted, often long after publication, because their data have been found to be invalid, or—most disturbingly—often simply fabricated.

Data compiled for *The Wall Street Journal*³ reveal that the number of papers retracted by science research journals* soared from just 22 in 2001 to 339 in 2010. The current year is off to a flying start with 210 retractions in 7 months. Medical journals are not exempt, with the *New England Journal of Medicine* having three retractions in the first half of the last decade, and five in the last half. Meanwhile, retractions in the British journal *Lancet* rose from one to five in the same periods. The situation has deteriorated to the point that a website—“Retraction Watch”—has appeared to monitor the flow of retractions.

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Thompson Reuters news service compiled these statistics from its “Web of Science,” an index of 11,600 worldwide peer-reviewed journals of science.

In a particularly infamous case, *Lancet* withdrew a 1998 paper that linked MMR vaccine to autism.⁴ The author, Andrew Wakefield, was later revealed as a profiteer in league with class-action lawyers, and was stripped of his license to practice medicine in Britain for “professional misconduct.” Like all scientific investigation, medical research is an inverted pyramid in which multiple later studies are prompted by one or a few early ones. An erroneous medical study is particularly distressing not merely because considerable funds and effort are wasted if the foundational study is false. In the time it takes to expose the fallacies (more than a decade for MMR and autism), patients suffer the consequences of misinformation. In the case of MMR, children who did not receive vaccines were vulnerable to contracting Hib (Haemophilus influenzae type b), measles, and whooping cough. Further, though retractions of erroneous studies are eventually published, the misinformation lingers on. In the case of vaccines, where anxious and often litigious parents are spurred on by trial lawyers, it is almost impossible to expunge the myth.

The full sad story of this distortion of scientific inquiry is told for a lay audience in *The Panic Virus; A True Story of Medicine, Science, and Fear* by Seth Mnookin. As the Amazon review of that book points out, “the myth that vaccines somehow cause developmental disorders lives on. Despite the lack of corroborating evidence, it has been popularized by media personalities such as Oprah Winfrey and Jenny McCarthy and legitimized by journalists who claim that they are just being fair to “both sides” of an issue about which there is little debate. Meanwhile millions of dollars have been diverted from potential breakthroughs in autism research, families have spent their savings on ineffective “miracle cures,” and declining vaccination rates have led to outbreaks of deadly illnesses.”

Hypertension guru Dr. Franz Messerli has pointed out the tenacity of error in the case of COOPERATE, a 2003 study of combined ARB and ACE therapy for hypertension, in which the combination was thought to be safer than either alone because it decreased proteinuria. After the study was retracted by *The Lancet* for multiple irregularities, Franz Messerli and colleagues emphasized the clinical implications of this unfortunate tale in the *European Heart Journal*.⁵

“In 2003 the COOPERATE trial seemed to confirm that dual RAS blockade was beneficial and that proteinuria reduction was synonymous with nephroprotection. This study had to be withdrawn recently attesting to the suspicion that the data looked too

good to be true. Moreover, the large prospective ONTARGET data argue against a nephroprotective effect of dual RAS blockade and together with renal findings from ACCOMPLISH, cast doubt on albuminuria/proteinuria being a reliable surrogate endpoint for renal outcome.” They concluded, “For the time being, given the adverse effects and lack of consistent survival benefits, the use of dual RAS blockade should be avoided unless ironclad data emerge to the contrary.” Despite this retraction, Messerli fears that it may take years before what he has termed a “fashionable trend” dies out, and physicians drop prescribing habits that were developed in response to the original study.

Though most retractions, by a margin of three to one, are the result of error, not fraud,⁶ the number of retractions caused by fraud is increasing much more rapidly.⁷ The Editor of *The Lancet*, Dr. Richard Horton, expressed the view in an interview with *The Wall St. Journal* that scientific journals and research institutions don’t have adequate systems to investigate misconduct, and called this problem “a scar on the moral body of science.”

But in fact, not all conflicts of interest are a sign of moral degradation. There is, after all, a potential COI inherent in the practice of medicine: in a fee-for-service system we benefit financially from advising a patient to come under our care. Surely most physicians are immune to that particular affliction except for the inevitable few bad apples, but there is another innocent yet powerful potential for a subconscious and unintentional COI: the fact that we must believe in the goodness of what we do or we could not get out of bed and go to work in the morning. For procedure-oriented specialists, it is natural to have the bias that procedures solve problems, and this necessary belief has the potential to unconsciously influence our recommendations.

When I was still practicing cardiothoracic surgery, I tried to explain this unavoidable bias to patients if I was advising them to undergo surgery. Not surprisingly, this well-intentioned confession only seemed to assure them of my objectivity, and did not dissuade them from proceeding with the proposed operation!

2. MORE ON MIND-BODY CONNECTIONS

Another subject that has received a lot of attention in these pages is the placebo effect,^{8,9} but even when this specific mind-body connection is acknowledged by physicians, they often ignore the full panoply of mind-body connections, and their wide-ranging implications.

In this issue Dr. Jennifer Kegel corrects that important omission by providing an introduction to the subject of Integrative Medicine. As she carefully explains, this often misunderstood approach must not be confused with holistic/alternative therapies, which often lack validation by peer-reviewed research and are rejected by mainstream medicine. Rather, as Dr. Kegel explains, Integrative Medicine is an *evidence-based* approach that addresses “the powerful interaction of every individual’s mind, body, and spirit . . . Integrative Medicine acknowledges the many resources a patient has.” These can enable and enhance, not replace, the traditional medical system. They include “the body’s innate capacity for healing, the support of family and friends, cultural or religious beliefs, and the ability to find meaning in illness and suffering.” Read her article and you will gain considerable insight into the power within us that affects our well-being.

This introductory article is the first of a series on this vital topic. I am sure you will find the sequels equally informative and stimulating.

ALSO IN THIS ISSUE

A variety of other interesting articles await your attention. Dr. Janet Larson of the A.I. DuPont Hospital for Children has provided a comprehensive review of the use of hypothermia for neuroprotection in the newborn. This approach is particularly timely in view of the widespread utilization of hypothermia in adults for neuroprotection after cardiac arrest.

Dr. Leigh Shuman continues his informative of discussion of PACS (Picture Archiving and Communication Systems) and how it is bringing about a revolution in radiology that impacts all physicians and patients; Dr. Michael Horst, Director of the LGH Research Institute, and his co-workers, provides a interesting analysis of Emergency Department utilization; and Dr. Alan Peterson explains why the latest study of salt and hypertension, which achieved such publicity in the lay press because it downplayed the relationship but is actually quite a flawed study, should be taken with “a grain of salt.” (The pun is his, not mine!)

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EDITOR'S NOTE

Seth Mnookin, author of *The Panic Virus*, will speak at Franklin & Marshall College's Mazer Gymnasium on October 6, 2011 at 11:30 AM.