



The "Omes" Are Coming!



By David J. Gibson, MD

The Ome era will demand real bench based scientists, not the clinical study stamp collecting that masquerades as scientific training in our medical schools today.

I HAVE AN ENDURING INTEREST in the way disrupting technology changes the course of history. Accordingly, I have been reading Roy Adkins' masterpiece "Nelson's Trafalgar." On Monday, October 21, 1805, the French battle-ship *Fougueux* fired the first shot shortly after noon at the nearest British ship, the *Royal Sovereign*. The battle of Trafalgar was on!

The shots from this broadside all fell short. Trafalgar was the beginning of the end of the Napoleonic era. Since Trafalgar there has been an uninterrupted decline in the influence and authority of the French.

Trafalgar represented the zenith in the technology of sailing ships. However, these vessels could not point higher than 80-degrees off the wind; they were slow and took an inordinate amount of time to tack. Trafalgar was the last great naval battle using sailing vessels. Within 60 years, the first iron battle ship with steam engines was introduced to the fleet.

The Imperative to Change

Dislocating technology occurred in Pearl Harbor. Until then, the battleship was the cornerstone of the U.S. Navy. The advanced deployment of aircraft using a carrier base ended the battleship era forever.

Dislocating technology also has played a major role in medicine. Antibiotics were introduced during World War II and medicine changed for the better. In 1955, Jonas E. Salk began immunizing children at Pittsburgh's Arsenal Elementary School. The rest is history.

Dislocating technology is defined as being so manifestly better that the prior generation of technology cannot possibly compete. You would have to be troglodytic to miss the power of disruptive technology as a change agent in history.

A dramatic new example is about to unfold. The Omes are coming! Omes collectively represent the genome, proteome, epigenome, transcriptome and metabolome.¹ In aggregate, the "omes" define an individual's biology at the gene, protein and metabolic level. In the near future, Ome technology will redefine how we finance health care, how we define the role of the physician and the business model for how we manufacture pharmaceuticals.

Our health care system during the antibiotic era has been structured around "blockbuster" therapy. During this era, most physicians treated most similarly diagnosed patients with drugs and devices without any knowledge of which patient would benefit. Physicians now rely on evidence-based protocols to make therapeutic decisions. We construct complex three-dimensional grids based on the consensus of hundreds of barely conclusive studies

to define truth. We then populate these hundreds of resulting cells to determine the appropriate "best practice" therapy for complex diseases like metabolic syndrome.²

We have known the reliability of these protocols is flimsy at best, as has been demonstrated in the case of stents used to treat coronary artery disease, but grid-based protocols have been the best tools available. In the Ome era, treatment grids based on clinical trials will be remembered as hopelessly primitive. Clinical trial-based decision-making will be remembered as a quaint relic, similar to the use of leeches.

Few of our patients know there is a concept called "numbers needed to treat," or NNT.³ This is an estimate of how many patients use a drug or treatment compared to how many benefit from it. For treatments considered "effective," the NNT is typically between 30 and 80.

That is, 30 to 80 people have to use a specific drug or device before one person will actually benefit. Doctors and researchers simply do not know which individuals will respond to what. Therefore, we treat as many people as possible in an attempt to benefit as many people as possible. This has generated monumental inefficiencies within the industry.⁴

The implantable cardioverter defibrillator is a classic example. This device senses a life-threatening abnormality in the heart's electrical rhythm and rapidly delivers a shock to restore normal rhythm. The problem - out of every 100 patients who get this device permanently implanted, only 12 to 15 ever need it and receive the appropriate electrical discharge. The remaining 85 percent or more have a device that costs more than \$50,000 to implant, carries a risk of infection and may "fire" inappropriately. More than 200,000 such devices are implanted in this country every year.

On the pharmaceutical side, statins are among the world's top-selling blockbuster drugs, with more than \$15 billion per year in prescriptions. However, for every 100 patients who take a statin, only 8 to 10 derive any real benefit in terms of reducing the risk of heart attack, stroke or death. The remaining 90 percent or so are taking an expensive medicine - at a cost of \$3 to \$4 per day - with potential side effects. They gain the psychological comfort of a reduced cholesterol level but no real health value.

The second most commonly prescribed medicine in our country is Plavix, taken to avoid blood clots. About 30 percent of patients do not respond to the common dosage and as a result are left vulnerable to developing potentially lethal blood clots.

These outcomes are both rational and predictable. We do not test medicines in the same way that we prescribe them. Most medicines in common use have never been tested in the elderly population, whose metabolism and kidney function is dramatically reduced with age. In addition, most clinical drug trials are performed in low-risk populations that do not reflect the real world, where patients often have multiple co-morbidities and drug clearance compromised.

This is where the Ome disruptive technology will be transformative. Medicine and the American economy simply cannot tolerate the inefficiency that our collective ignorance has generated to the present. We are now at the brink of an exciting discovery phase for biomedical research - one that will radically reboot medicine with new software. In the years ahead, we will tailor a specific therapy or prevention to a particular biologic vulnerability or need, one human being at a time.

With the introduction of the Ome era in medicine, what will be the dislocating effect on the current financing and delivery system within health care? There are implications for health insurance companies, physicians and pharmaceutical corporations.

Health Insurance Companies

Health insurance is based upon not knowing basic facts about the insured. Thus, large numbers of people not likely to generate medical cost are grouped with those who will.

Those without chronic conditions or even the genetic predisposition for disease may have a catastrophic event that will require financial support from a third party, but most of the coverage they purchase today is a waste of their money. Thus, buying only high deductible coverage is economically rational for most people.

As we move into the Ome era where the ignorance on which health insurance relies has been displaced, the current group model is not likely to survive. We will need to rethink the entire concept of financing health care in the future.

The Physician Paradigm

In 1906, following the proprietary drug scandals chronicled by *Harpers Magazine*, the development of the Division of Chemistry followed by the Bureau of Chemistry gave birth to the modern era of the Food and Drug Administration. With passage of the Federal Food and Drugs Act, physicians were entrusted with the sole franchise to diagnose and treat disease. Prior to this time, many health care practitioners, including pharmacists, filled this role.

This paradigm, in which the physician is at the apex of decision-making in health care, is about to disappear. Diagnosing and treating individual patients in the Ome era will require a much broader and better trained group of professionals. This team will include geneticists, statisticians, physical chemists, biochemists, physicists and specialty pharmacists to name only a few. In short, the Ome era will demand real bench-based scientists, not the clinical study stamp collecting that masquerades as scientific training in our medical schools today.

Pharmaceutical Manufacturing

The pharmaceutical industry is hopelessly wedded to the blockbuster-based business model. When Pfizer announced that it was halting clinical testing of its new cholesterol drug, torcetrapib, the company's market value fell by \$21 billion overnight; 10,000 job cuts followed. The ongoing promise of nearly \$3 billion in annual sales vanished when Merck pulled Vioxx (rofecoxib) from the shelves, and the company's market value fell by \$25 billion. For decades, blockbuster drugs have nourished big pharma. That era is over.

The Ome era demands orphan drugs manufactured for individual patients. The pharmaceutical manufacturing industry has demonstrated a complete inability to deliver to the market biopharmaceutical based drugs. These drugs are but a way station on the way to the orphan agents the Ome era will demand.

I doubt any of the current manufacturers will survive the coming transition to the Ome era. We will need new companies with radically different business models that are divorced from current investor expectations in the future.

It is easier to lead a parade than turn it around. No group or industry has ever been able to impede disruptive technology. WWII battle ship admirals tried and failed. Physicians who denied the germ theory of disease tried and failed.

A recent example involves the music industry. From 2001 to 2003 the industry pursued the single dumbest strategy possible in the digital age. It tried to stop the progress of technology and deny users access to a new download technology (peer-to-peer file sharing). The industry attacked and crushed Napster, which officially had more than 26 million users, but may in fact have had twice that many. This was accomplished by criminalizing the industry's own customers. From our current vantage point, this effort failed.

The question we face in the health care industry is how will we adapt to the Ome era? Resisting or even inhibiting the transformative effect of this technology is not an option. The CMA's annual political warfare before the legislature each year over scope of practice is about to become a quaint historic relic.

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1. The *genome* is the full set of chromosomes; all the inheritable traits of an organism. The *proteome* is the set of proteins expressed by the genetic material of an organism under a given set of environmental conditions. The *epigenome* controls the differential expression of genes in specific cells. The transcriptome is the set of all messenger RNA (mRNA) molecules, or "transcripts", produced in one or a population of cells. *Metabolome* refers to the complete set of small-molecule metabolites (such as metabolic intermediates, hormones and other signaling molecules, and secondary metabolites) to be found within a biological sample, such as a single organism.
2. *Int J Clin Pract Suppl.* 2003 Mar;(134):3-9.
3. <http://www.shef.ac.uk/scharr/ir/nnt.html>
4. Some of the following data is excerpted from Dr. Eric J. Topol's Op-Ed article, "A medical treatment all your own," in the *Los Angeles Times* on 03-28-07.

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