COMMENTARY

Perspectives

What did Edward Jenner and John Tyndall have in common?

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Virtually every school child is familiar with the story of Edward Jenner (1749–1823) and his conquest of smallpox. Jenner, who practised medicine in the English countryside, which was continually ravaged by smallpox, observed that milkmaids and cowmen did not fall victim to the disease. Furthermore, he established that these individuals, in the course of their work, had all suffered from cowpox, a relatively mild, self-limited disorder. Based on these epidemiologic observations, Jenner concluded that cowpox somehow prevented the more serious disease, smallpox. He then set about to test his hypothesis by inoculating lymph derived from a dairymaid into a boy; 1 month later he inoculated the boy with smallpox. The child did not develop smallpox. Thus began the science of immunology.

Somewhat less familiar perhaps is the story of John Tyndall, the 19th century British physicist. In the course of experiments designed to investigate why the sky is blue, Tyndall demonstrated that a beam of light can be perceived only when the light waves strike particles in their pathway and are scattered. This phenomenon accounts for the fact that the light *beam* from a movie projector is visible in a dark theatre because it hits myriads of dust particles in the air and for the fact that the *beam* of an automobile headlight is usually visible only in foggy conditions when particles of moisture fill the air. A corollary of this concept is that air containing only pure gases and no particles behaves like a vacuum (such as outer space) and remains pitch black when traversed by a beam of light.

Soon after making his basic observations on the physics of light, Tyndall applied his discovery to prove that Louis Pasteur was correct in disclaiming the phenomenon of spontaneous generation. Pasteur claimed that germs did not generate spontaneously, although they could appear in liquid solutions in which even the most powerful microscopes could not detect pre-existing organisms. By applying his light-scattering technique, Tyndall established that organic liquids that had been previously boiled remained free of bacterial growth when exposed to “optically pure” air; but soon swarmed with bacteria when exposed to “optically impure” (i.e., dust-laden) air. Thus, Tyndall provided scientific proof for Pasteur’s theory that “spontaneous generation” resulted in fact from the contamination of culture media by bacteria in the air. These concepts played a key role in establishing the science of bacteriology.

At first glance it would appear that Edward Jenner and John Tyndall had little in common. Jenner, the physician, began with an *epidemiologic* observation (that milkmaids and cowmen did not suffer from smallpox), from which he then formulated a hypothesis. Although the basic science underlying his hypothesis was then unknown, he nevertheless tested the hypothesis in a *clinical trial* (albeit with an *n* of 1, and no preceding ethics review) and established its validity. In contrast, Tyndall, the physicist, made basic scientific discoveries related to the visibility of light waves, far removed from clinical medicine and certainly with no clinical application in mind. Yet, a short time later, he and Pasteur were able to apply his basic scientific discoveries to the solution of a biomedical question. Thus, despite all their differences, Jenner and Tyndall both contributed through their original research to the conquest of human illness and to the prevention of disease.

The examples of Jenner and Tyndall demonstrate that epidemiologic, clinical and basic research are all of inherent value in preventing disease and treating illness. The question arises, however, as to which of these approaches is more likely to produce direct clinical benefits for patients. In short, how do advances in clinical medicine really come about? This question is not merely of philosophical interest, but rather is important in ensuring the maximum payoff for the medical research dollar. Unfortunately most debates on the subject are based largely on anecdotal evidence because exceedingly few scientific studies that have addressed this question. The most comprehensive study is that of Comroe and Dripps[1] who set out to determine objectively and systematically how the great modern discoveries of medicine and surgery came about. Because of the size of the task, they limited their study to discoveries in cardiovascular and pulmonary medicine and surgery. Comroe and Dripps began by asking 90 cardiac and respiratory *clinicians* (both physicians and surgeons), who were otherwise not involved in the study, to list what they considered to be the most important *clinical* advances in their field between 1945 and 1975. Important clinical advances were defined as those that had saved or greatly prolonged lives, prevented disease, or substantially reduced suffering and disability. From the responses they received, Comroe and Dripps selected for study the 10 most frequently cited advances (open-heart surgery, medical treatment of hypertension, chemotherapy of tuberculosis and rheumatic fever, prevention of poliomyelitis, etc). They then screened over 6000 scientific reports relevant to these advances, from which they analyzed in detail what they considered were the 663 “key articles” that were essential in making 1 or more of the top 10 clinical advances possible. They were particularly interested in determining how many key articles leading to advances in clinical medicine described basic research studies, and how many described clinical or applied research. For this purpose they defined research as basic if it investigated the mechanisms by which living organisms function (rather than simply reporting descriptions and observations), regardless of whether the work involved healthy or sick humans, animals, tissues, cells or molecular elements.

The results of the Comroe and Dripps study are compelling. They found that 62% of the key articles leading to important *clinical* advances were clearly *basic* in type; 21% reported descriptive but critically important clinical observations; and 17% dealt with the development of new techniques, apparatus, operations or procedures. Of particular importance was the finding that 42% of all the key articles reported research done by scientists whose goal at the time was completely unrelated to the later clinical advance to which it contributed. Such research often came from disciplines with no particular relationship to clinical medicine, including physics, chemistry, botany, mathematics, zoology, engineering and agriculture.

Although the results of the Comroe and Dripps study were published a quarter-century ago, their findings lead to several conclusions that remain relevant today. Two conclusions are particularly important. First, major advances in clinical medicine are ultimately derived from a very broad range of scientific disciplines, including in particular, the basic biomedical sciences. Second, many important advances in clinical medicine have their origins in research whose objectives at the time it is performed are completely unrelated to a clinical problem. These conclusions are important in informing public policy debates on the future of health care and on the support of medical research. The conclusions also serve to remind us that “evidence-based” clinical medicine, which drives today’s health care delivery systems, often begins with “evidence” that originates in the most unlikely and unexpected places.

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Reference

1. Comroe JH Jr, Dripps RD. Scientific basis for the support of biomedical science. *Science* 1976;192(4235):105-11.

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