MEDICAL ODYSSEYS

The Different and Sometimes Unexpected Pathways to Twentieth-Century Medical Discoveries

Allen B. Weisse, M.D.

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This book is dedicated to all the great scientists who have been recognized for having advanced the frontiers of medical knowledge—and to all the equally dedicated and hardworking men and women beside them who have not.

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Introduction

How Do Discoveries Happen?

In 1984 I finished a book that mainly concerned great discoverers in medicine.* No sooner had I completed this project than I felt compelled to embark on another: one about important discoveries themselves and how so many different people under different circumstances have contributed to them. As I began to tell my friends and colleagues about *Medical Odysseys* and about how important medical discoveries are made, too often I found that this would provoke a knowing smile and a nod of the head with a response such as "Oh, I get it. It's about serendipity!"

That word, once a delightful neologism, has certainly lost its sheen through overusage. Serendip is the ancient name for Ceylon. In 1754, Horace Walpole, the fourth earl of Orford and a member of Parliament, coined the word in reference to a fairy tale about three princes of Serendip who frequently made unexpected discoveries, that is, by accident. The term lay relatively dormant for more than two hundred years when suddenly it seemed to break out like an epidemic. It could be found on everyone's lips and numerous café signs. It even managed to infect an entire singing group (The Serendipity Singers). We have not yet recovered, especially in discoursing about science.

**Conversations in Medicine* (New York: New York University Press, 1984).

Contrary to this belief in serendipity, major advances in science are often encumbered by a lot of bad luck along the way as well.

There is also hard work and perserverence.
There is inventive daring and even touches of genius.
There are kindly, supportive, and inspiring mentors.
There are obtuse, bureaucratic martinets in positions of authority.
There is ambition and competition.
There is ethics and morality.
There is trust and betrayal.
There is anger and remorse.
There is generosity of spirit and spiteful jealousy.
There is money and the lack of it.
There is danger to oneself and sometimes to one's patients.
There is politics.
There are wars, which not only create new health problems but often serve as an impetus to the solution of old ones.

One special aspect of medical discovery relates to how many ideas there are that we think of as new but which have been introduced before, though in less fertile ground where they failed to take root. It is what I like to call the Phoenix phenomenon. An idea appears, has its day, and dies. Then, years, perhaps decades, or even centuries later, like the mythological bird, it rises from its own ashes to soar again. So it is that we often look upon a concept as completely new and novel when, in reality, it is merely the resurrection of what has gone before and been forgotten.

I recall, during my early training, an attending physician who was acutely aware of this phenomenon, and therefore, whenever some muckamuck of the medical establishment was about to give a lecture on some new great medical advance, he would hurry to the library and start searching the early literature for clues. At the conclusion of such a talk, when questions from the audience were invited, he liked nothing better than to rise and say something like, "What you have shown is very interesting, but isn't that precisely what von Helsing and Köh-

ler reported in the *Deutche Medizinsche Wochenschrift* (German Medical Weekly) in 1878?"

Our reliance on what has gone before was probably best expressed by Sir Isaac Newton in a letter to Robert Hooke in 1675. "If I have seen further [than you and Descartes] it is by standing on the shoulders of giants."

As for the role of serendipity in science and just stumbling upon great discoveries by accident, the more mundane comment of virologist Thomas Rivers should be heeded. "You don't stumble unless you are walking. . . . There is no substitute for work in science."

The stories I have gathered in this book represent a wide range of subjects from various eras in the realm of medicine. Some have been told before, but incompletely, in my judgment. Some of the principals are gone, but, in many cases, I have been able to meet with these scientists personally, to probe for details of their discoveries, and to uncover their sources of motivation. These meetings, along with a good deal of correspondence, have provided, I believe, an important added dimension to the telling.

Dozens of books and hundreds of articles have been perused, but, to keep the narrative flowing, I have cited only major sources in the final section, Notes, for purposes of documentation and for those who might wish to read further.

Mercury Finally "Makes It"

"I was the only man in San Francisco who could treat pulmonary edema properly. You gave 'em intravenous mercury and they told all their friends that you were a miracle worker."

—William Dock, M.D.

Given the numerous potent oral diuretics ("water pills") now available, it is difficult to appreciate the impact of the mercurial diuretics introduced in the 1920s and which, for the next thirty to forty years, were to prove the mainstay in the treatment of dropsy. Dropsy was the name long given to the clinical picture of patients who, owing to congestive heart failure or certain types of liver or kidney disease, begin to retain excessive amounts of fluid, their tissues and body cavities filling up with unwanted salt and water. The new forms of mercurials, injected intramuscularly or infused intravenously, provided for the first time an effective treatment of the edematous condition, alleviating the suffering and prolonging the lives of countless patients so treated.

Beyond the realm of medicine, mercury has always had a special hold on the human imagination. Mere mention of the word evokes a host of mythological, alchemical, cultural, and scientific connotations. Perhaps it is for this reason that mercury has held a particular fascination for historians and scholars.[1]

A book on alchemy by Allison Coudert begins with the story of a twelfth-century Chinese "health fanatic" who was offered the elixir of life by his physician. As a result, he died an ago-

nizing and slow death from mercury poisoning. In truth, much of the history of mercury, even to the present day, is associated with its toxicity and potentially lethal nature. Such aspects of its use, however, did not deter the ancient alchemists and their successors from extolling it as second only to gold itself. After all, each of the other metals had to be heated in order to liquidize, while mercury (quicksilver) was normally a liquid at room temperature.

For much of its history mercury has been associated with the treatment of syphilis. We now know that there is some scientific basis for this practice. Mercurial antiseptics have been shown to be bacteriostatic; that is, they will arrest the growth of a number of organisms. But often, following this initial inhibition, with insufficient concentrations of the chemical or inadequate periods of exposure the growth of these organisms will resume. Unfortunately, doses of mercury compounds potentially sufficient to overcome a syphilitic infection are also accompanied by severe toxic effects. The patient might survive the infection only to succumb to the treatment.

Although, in the modern world, penicillin and other safe antibiotics are very efficient against the syphilitic spirochete, at the end of the fifteenth century, when the disease was introduced into Europe, no such remedies were available. It broke out into ravaging epidemics in Europe after being carried there, perhaps, by Columbus's sailors returning from the New World.

Syphilis was named for the shepherd hero of the long poem written in 1530 by the physician Girolamo Fracastoro, who gives an account of the disease therein. The victims of syphilis in the fifteenth century and for many years thereafter turned to a number of nostrums. None of these was effective, with the possible exception of mercury, which probably did bring about a few cures without killing the patient by mercury poisoning.

The most notable of these success stories has been documented in the autobiography of the celebrated Florentine sculptor Benvenuto Cellini. In 1529 and in his twenty-ninth year, he had an extended dalliance with a servant girl-model,

following which he broke out in blisters all over his body—the secondary stage of the disease. (The primary chancre or sore may be overlooked in some cases and in others may not appear at all.)[2]

Good Italian that he was, Cellini recognized that it was the "French disease" he had contracted. (The French called it the Neapolitan or Italian disease; the English and Germans sided with the Italians; the Poles blamed the Germans, the Russians the Poles, the Dutch the Spanish, and the last named, probably closest to the truth, accused the Hispañolans, as the original residents of Haiti and the Dominican Republic were then known.) An indication that informed individuals were already wary of the toxic nature of mercurials is that Cellini attempted to avoid them. He began by "taking the wood," a solution of guaiac prepared from a wood resin, a harmless but totally useless remedy. When this had no effect, he tried leeches, with a similar lack of results. Only when he began to apply mercurial ointment in the form of plasters did the lesions begin to clear.

For some, the healing of lesions signals the end of the disease; for others, it means only that the infection has become dormant, going underground only to emerge at a later date in one of its multitudinous tertiary forms. Syphilis, in its final stage, can affect practically any organ, although it shows a predilection for the central nervous and cardiovascular systems.

That this was the case with Cellini can be inferred from his increasingly bizarre behavior some time following the disappearance of his skin leasions. A careful reading of his erratic life-style during this period has suggested that the brain might have been involved, resulting in the psychiatric picture of "paresis."

It was during this time of his life that Cellini was involved in real estate dealings with some unscrupulous manipulators who, perhaps, had recognized the signs of mental illness in Cellini and decided to help it along. They invited Cellini to a sumptuous dinner including a dish in which the meat sauce had been heavily laced with mercurials. Cellini became aware of this when, soon after, he was seized with severe abdominal

cramps followed by a bloody diarrhea typical of acute mercury poisoning. A physician friend confirmed the diagnosis, but, providentially, the sculptor survived this attempt on his life.

Because Cellini lived until the age of seventy-one, it can be assumed that the poisoning also served to eliminate the infection in his brain. This whole episode is memorialized in Cellini's breathtaking larger-than-life bronze sculpture of the period, *Perseus with the Head of Medusa.* At the base of the statue, helping support the mythological hero and his trophy, Cellini placed a figure of the god Mercury flanked by representations of the multibreasted venereal goddess.

Despite the adverse effects of mercury on Cellini and others similarly intoxicated by its injudicious use, it continued to be prescribed for lack of any other effective drugs for syphilis. Another factor in its popularity was its continued magical aura thanks to the pervasive influence of alchemical thinking.

Only one light appeared during the intellectual miasma of the period. It was in the person of Theophrastus Philippus Aureolus Bombastus von Hohenheim (1493–1541), and he was all of that.[3] With the exception of lust—he was never known to have slept with a woman—he had his share of the seven deadly sins. He was guilty of inordinate pride; he was a glutton and a drunkard; he had a violent temper and almost continually boiled with anger. He also happened to be a genius.

Born in Switzerland, the son of a physician, he later took the nickname Paracelsus, perhaps to signify his stature as equal to that of a celebrated Roman physician of the first-century A.D., Celsus. It is by this name that he is best remembered today. Although steeped in much of the hocus pocus characteristic of his time, Paracelsus was frequently able to shed many misconceptions in the interests of reason and the provision of good care to his patients.

In his own practice, he erased the artificial separation between "physician" and "surgeon," much to the benefit of those to whom he ministered so effectively. He was the first to describe clearly silicosis and tuberculosis in miners and dub

them, in essence, occupational diseases. His views on mental illness were remarkably modern, and he described hysteria and other mental illnesses with clarity and compassion.

His conservative management of wounds and ulcers allowed for natural healing, free from the harmful interventions commonly employed by his contemporaries. Conceptually, he largely dispensed with the prevalent humoral theories about disease, seeking specific causes and specific remedies. He also clearly recognized endemic goiter for what it was: the result of inadequate minerals in the local drinking water where it was prevalent.

Not least among his accomplishments was the preparation of more rational dosages of the various chemicals that others frequently administered in toxic amounts, bringing therapeutics an important step closer to modern chemistry from alchemy. His preparation of mercury in the form of calomel (mercurous chloride) was a favored one during his own time and that of his disciples. And right into the twentieth century calomel was an ingredient of such concoctions as Guys pills, from the London hospital of the same name, which may have been used with some success despite problems with absorption and side effects.

About all this, Paracelsus later wrote and lectured in German or his Swiss-German dialect rather than Latin, much to the chagrin of the sages of the day.

It was through extensive travel that Paracelsus claimed to have perfected his knowledge. As a youth, he roamed through Scandinavia, Eastern and Southern Europe, as well as the Middle East. Although this was a common practice for eager students of that time, in Paracelsus's case one has to wonder whether his frequent change of address was encouraged by his own difficult personality.

Upon his return to Villach, Switzerland, at the age of thirty-three, he demonstrated his attitude toward the venerated teachings of previous demigods of medical practice by burning their books in front of the university in 1527. Other aspects of his personal behavior did not make such affronteries any easier to bear. Morbidly fat, he never bathed. He engaged