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*Reflections*

# Advice for Young Investigators: Historical Perspectives on Scientific Research

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**Abstract.** Physicians attempting to carry out well-executed scientific investigations require an historical perspective; an awareness of our ignorance; an imagination unencumbered by scientific prejudices; originality, curiosity and imagination; patience and persistence in the face of frustration; adaptability and perseverance; a critical spirit of evaluation and willingness to question dogma; devotion to the search for truth; and an awareness of those responsibilities to individuals and to society which define the medical profession.

This paper explores, through the words of famous scientists, philosophers and authors, the process of scientific investigation and discusses those qualities that investigators can develop to become more insightful and successful researchers.

**Key words**: history of medicine, literature in medicine, medical research, philosophy of science, Rudolph Virchow, scientist-writers, young investigators

**Summary points.** Successful scientific research requires historical perspective, cooperation, patience, endurance, an open mind, flexibility, and devotion to the truth.

The writings of famous scientist-writers exhort investigators to develop these traits.

These writings also encourage us to remain true to the ethical principles that define our profession.

The example of Rudolph Virchow's life and philosophy is used to show how one can, through research, seek truth and justice for the all mankind, particularly the underserved.

In this paper, through the words of famous scientists, philosophers and authors, I wish to explore this process of scientific investigation and discuss those qualities we can develop to become more insightful and successful researchers.

A historical perspective should underlie any investigation. An appreciation of the work of others equips us to relate our findings to the existing body of knowledge, and helps foster a willingness to collaborate rather than compete. Cooperation helps us to avoid useless repetition, allows for larger, higher-powered studies, and may lead to previously unforeseen avenues of study. A historical perspective also can lead us to rediscover findings dismissed or forgotten which now possess particular relevance. Dr. Alphonse Raymond Dochez commented: "Many clues to the unknowns in medicine are locked in the library, waiting for someone to open the

right book at the right time" (Dochez, 1968). O'Shaughnessy's nineteenth century theory of treating cholera with fluid and electrolyte replacement, for instance, was not accorded its proper significance until the mechanism of the cholera toxin was worked out a few decades ago. Some early twentieth century textbooks even suggested such counterproductive therapies as phlebotomy and purging for severe cholera-induced diarrhea.

A sense of history also encourages us to humbly acknowledge the incompleteness of our knowledge. Medical scientist-author Lewis Thomas regards our ignorance about nature as "the major discovery of the last hundred years of biology" (Thomas, 1979). Hopefully, rather than stifle our creativity and paralyze our thought processes, the acknowledgment of this ignorance will stimulate our curiosity, excite us, challenge us, and encourage us to be open-minded. Scientist T. H. Huxley advised: "Sit down before a fact as a little child, be prepared to give up every preconceived notion, follow humbly wherever and to whatsoever abyss Nature leads, or you shall learn nothing" (Huxley, 1968). And Spallanzani warned:

> If [you] set out to prove something, [you are] no real scientist – [you] have to learn to follow where the facts lead – [you] have to learn to whip [your] prejudices (Spallanzani, 1952).

Unencumbered by scientific prejudices, your imagination is free to develop hypotheses and design experiments with which to test these hypotheses. Nobel laureate Joshua Lederberg's imagination allowed him to envision himself as a strand of DNA as he dreamed up experiments:

> I literally had to be able to think . . . "What would it be like if I were one of the chemical pieces of a bacterial chromosome"? And try to understand what my environment was, try to know where I was, try to know when I was supposed to function in a certain way, and so forth (Lederberg, 1968).

Lederberg's imagination gave his work originality; and it is originality, according to researcher-philosopher Maurice Arthus, that "[gives] scientific work its frankness, its grace, its elegance, [and] its warmth" (Arthus, 1943).

We test our original hypothesis, the product of curiosity and imagination, by meticulously designed experimentation, remembering that even the most carefully planned studies are subject to error. Lewis Thomas acknowledges that, in scientific research, "error is the mode", and ironically, that good research depends "on the human capacity for making decisions that are wrong" (Thomas, 1983). Well-designed studies are also subject to the vagaries of chance. Dealing with error and chance requires patience and the willingness to persist in the face of frustration. If we develop these traits, our investigations may lead to findings as important as those in which chance played a major role. For example, Alexander Fleming discovered penicillin after accidentally contaminating some bacterial culture plates; and, von Mering and Minkowski recognized the endocrine role of the pancreas after noticing flies swarming over the sugary urine of pancreatectomized dogs (Arthus, 1943). The adaptability and perseverance of these researchers

when confronted with the unexpected illustrates Pasteur's famous maxim that "Chance favours the prepared mind".

Thus with flexibility and persistence we complete our experiment. We then critically analyze our data and reevaluate our methods, questioning and verifying, when possible, every result. UCLA Dean Emeritus Sherman Mellinkoff stresses the importance of this process, writing, "It is better to be in doubt than to be in error" (Mellinkoff, 1987). Mellinkoff's aphorism echoes the advice of the fervently dedicated investigator Max Gottlieb in Sinclair Lewis' novel Arrowsmith: "The scientist is intensely religious, so religious that he will not accept quarter-truths because they are an insult to his faith" (Lewis, 1980). No researcher should be satisfied with quarter- or half-truths, nor should one ignore exceptions, however minor they might appear. While these exceptions might nullify one theory, they may open up new and more valuable areas of investigation. Charles Darwin's son, describing the key to his father's success, wrote:

> Everybody notices as a fact an exception when it is striking and frequent, but he had a special instinct for arresting an exception. A point apparently slight and unconnected with his present work is passed over by many a man almost unconsciously with some half-hearted explanation, which in fact is no explanation. It was just these things that he seized on to make a start from (Beveridge, 1968).

Paul Broca warned that "the least questioned assumptions are often the most questionable" (Broca, 1968). Darwin's achievements resulted from his willingness to question dogma, to actively seek the exception.

We should maintain this critical spirit of evaluation when reading textbooks and the medical literature. However, we must not confuse the critical spirit with the spirit of systematic opposition or the spirit of disparagement. Maurice Arthus wrote:

> The critical spirit seeks the truth and hates above all the error; it is an eminently sound spirit. The spirit of systematic opposition takes the opposite side of every proposition, of every conclusion without endeavoring to ascertain their worth. The spirit of disparagement searches for evil everywhere and if necessary invents it where it does not exist (Arthus, 1943).

We should examine our data and that of others critically but fairly, evaluating our results in light of other studies, giving each their due importance. Once confident in our conclusions, and eager to see them applied, we communicate our findings via the scientific literature and at scientific meetings. Student researchers should take special pride in their accomplishments in the laboratories and clinics, for they constitute the continuation of a long and honorable line. Many great scientists have made invaluable contributions to medicine while still students. Examples include: Vesalius' pre-graduation discoveries in anatomy, Claude Bernard's investigations of gastric juice, Ivan Pavlov's studies on the nerves of the pancreas and

pancreatic fistula, and the discovery of insulin by Charles H. Best and Frederick Banting (Marti-Ibañez, 1961).

As we develop our scientific talents, however, we must not become so immersed in our specialized projects that we abandon those responsibilities to individuals and to society which define the medical profession. Medical-humanistic Felix Marti-Ibanez described these as the four major objectives of medicine: "to promote health, to restore health, to prevent disease, and to rehabilitate the patient" (Marti-Ibañez, 1960).

The life of the famous pathologist Rudolph Virchow stands as a worthy example of how we can fulfill these goals. Best known for establishing the cell doctrine in pathology, Virchow also elucidated much of the pathophysiology of thrombosis, pulmonary embolism, leukocytosis, and leukemia. Yet Virchow's contributions to social medicine were equally valuable. He recognized, if a disease is an expression of individual life under unfavorable conditions, then epidemics must be indicative of disturbances of mass life. He argued that "typhus, cholera, tuberculosis, scurvy, some mental diseases, and cretinism" were among "those maladies that result from the unequal distribution of civilization's advantages" (Nuland, 1988). Virchow "asserted the moral un-neutrality of medicine" (Eisenberg, 1986). To him, physicians were "the natural advocates of the poor" (Virchow, 1986). He served them as a member of state and local government for over 30 years, and founded a journal entitled *Medical Reform*. Both in the legislature and through this periodical, he spoke out for public provision of medical care for the indigent, prohibition of child labor, universal education, and free and unlimited democracy. He instituted "programs for improving and sewage system, stricter food inspection, [and] revamping the old, ineffective hospital organization" (Nuland, 1988). He elevated standards "for the training of nurses [and set] new criteria of hygiene for the public schools" (Nuland, 1988). In these activities, Virchow employed his research skills to elucidate a community problem, then used his imagination and originality to come up with a workable solution. Following a critical review of his solution, and after a historical and polished analysis of its likelihood of success, he fought vigorously and courageously for its implementation. An example of Virchow's employing the scientific method to try to solve a social problem, i.e., racism, is his study of cross-cultural cranial capacities which helped to invalidate, albeit briefly, the pernicious myth of German racial purity.

Today, social inequities continue to cause much illness and death, both in the United States and worldwide (Donohoe, 2002). Major problems include hunger and malnutrition, inadequate housing, impaired access of the poor to medical care, and racial disparities in morbidity and mortality. Enormous military budgets not only deplete the funds available to combat such maladies, but also support the production and maintenance of powerful weapons which threaten our species with annihilation. Virchow encountered similar economic disparities in his own era, and spent much of his life arguing against the rise of Prussian and German militarism and for the general disarmament of Europe.

The talent that Rudolph Virchow brought to his social activism was grounded in his scientific approach to both laboratory problems and community maladies. Virchow saw research as a powerful tool not only to determine the pathophysiology of individual disease states, but also to elucidate the causes of major public health problems. His scientific successes should inspire us, and his social activism challenge us, to fulfill our obligation to improve conditions for all mankind.

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