

## An ASCI Tradition

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I will speak to you today about one of the traditions of our Society, one which tells how our breed of clinical investigators came into being; it may also give us reason to contemplate some of our responsibilities.

The subject of my address is the founder and first President of The American Society for Clinical Investigation, whose name may not be familiar, even to many members of our Society. His name was Samuel James Meltzer (Fig. 1 shows his picture). He was born in Russia in 1851. When he was 25 years old he left for Germany to study medicine.<sup>1</sup>

While he was a medical student, he did research on the mechanism of swallowing, using himself as the experimental subject. He observed that a single swallow would elicit a peristaltic contraction in the esophagus, but that repetitive swallowing, as in drinking, prevented any peristaltic activity until the last swallow. He was thus the first to describe normal esophageal function, and his experiments are classics in this field of research. But he didn't stop there. By carefully controlled experiments, Meltzer discovered that repetitive swallowing not only inhibited esophageal contraction, but also inhibited respiration, uterine contractions, and a variety of other body func-

<sup>1</sup> Personal information on Dr. Meltzer was obtained from references 1-11, which include (3-8) a Memorial Issue of *Proc. Soc. Exp. Biol. Med.* dedicated to Dr. Meltzer. Dr. Meltzer's complete bibliography is published in reference 1. The comments about Osler and MacKenzie are based on references 12-14. The state of medical science at the time of Meltzer's presidential address to The ASCI is taken from reference 14. References 15-19 are Meltzer's papers, from which direct quotations were taken. References 20-22 contain discouraging data on the ethics of some physicians.

tions. Surprisingly, he showed that 14 to 18 swallows of water, performed at 1-second intervals, also completely abolished erection (15).<sup>2</sup>

His conclusion from these studies was that repetitive swallowing causes a dispersion of inhibitory impulses from the swallowing center in the brain to other nervous centers. The concept that inhibitory processes constitute an essential phenomenon of life became a focal point of much of his future research.

In 1883, shortly after graduation from medical school, Meltzer emigrated to the United States and began the private practice of medicine in New York City. He was, according to various testimonials, an accomplished physician, and he published a number of papers on clinical subjects, including observations on subphrenic abscess, paratyphoid fever, pneumonia, and intestinal colic. But his main interest throughout his career was in the application of scientific methods to clinical medicine. "I belong," he said, "to those who believe that the knowledge of physiology is of special importance to clinical medicine."

And so, while continuing his practice, he resumed research in pathophysiology. The major areas in which he worked are as follows: (a) Mechanism of swallowing; (b) inhibitory influence of magnesium and antagonism by calcium; (c) adrenalin effects; (d) adaptation to environmental stress; (e) artificial resuscitation; and (f) anaphylaxis as a cause of bronchial asthma.

<sup>2</sup> The effect was observed to start after as few as eight swallows. Only one subject failed to respond to 18 swallows; in this one it took 45 swallows in 90 seconds to abolish erection. Swallowing the same amount of water in two swallows (instead of in 14 to 18) was not inhibitory. (Article translated by Dr. Guenter Krejs.)



FIGURE 1 Samuel J. Meltzer; picture reproduced with copyright permission from the Society for Experimental Biology and Medicine.

He was a careful investigator and conservative in drawing conclusions from his research, yet he always looked for practical applications. Magnesium was used successfully to treat tetanus, and his observation that magnesium inhibited the sphincter of Oddi was the basis for an important diagnostic test of biliary tract function.

Meltzer continued to practice medicine and do physiological research simultaneously up until 1904. Fig. 2 shows some of his progress up to that time. His productivity was enormous, the quality of his research was excellent, and he was elected to the National Academy of Sciences. His was a unique performance. To my knowledge, no one else has ever done so much basic clinical and physiological research while at the same time managing a busy medical practice. His contemporaries in this dual role of clinician and investigator must have been William Osler and James MacKenzie, but neither was an experimental scientist, and Osler was never in private practice.<sup>3</sup> Dur-

<sup>3</sup> Osler did have a busy consultation practice while at Johns Hopkins.

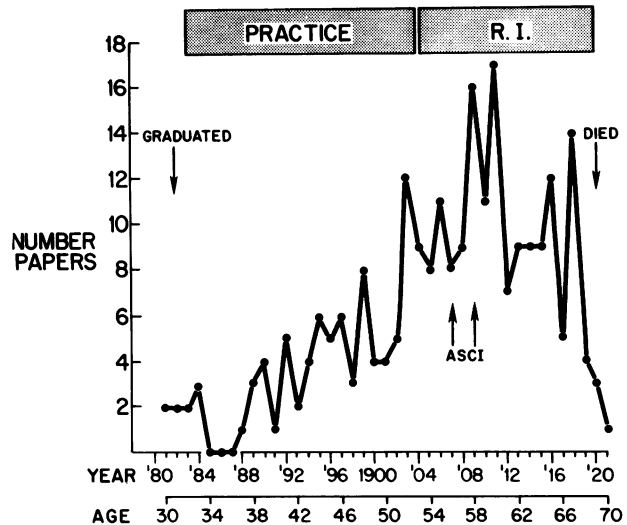


FIGURE 2 Publications of Samuel J. Meltzer. The horizontal axis shows the year and Meltzer's age, and the vertical axis is the number of his published papers per year. R.I. stands for Rockefeller Institute for Medical Research.

ing this time, Meltzer had no affiliation with any academic institution. His research was done at night, either in his home or in the physiology laboratory of friends at Columbia Hospital of Physicians & Surgeons. He paid for his equipment and supplies with money he earned during the day from his practice.

In 1904, he gave up practice to become head of the Department of Physiology and Pharmacology at the newly formed Rockefeller Institute for Medical Research. He founded The ASCI in 1907, and became its first president in 1909.

Meltzer's founding presidential address to this Society was given at the New Willard Hotel in Washington, D. C. His speech was heard by only 16 people. Fortunately, it was also published in the *Journal of the American Medical Association* (16). At this point I will give a condensed version of some of his remarks on that occasion. (I have rearranged the order in which some of the things were said in order to make a long speech more concise). As I repeat his words, remember that they were given at a time when the science of medical research carried out by physicians in the United States was based almost entirely upon the correlation of bedside observations and autopsy findings (14).

I wish to discuss the problem of clinical medicine as a science. I am of the opinion that clinical medicine, as it exists now, is made up of two constituents; one part has all the elements of a pure science and ought to be coordinated to the other pure sciences of medicine, and the other part is the real practice of medicine, an applied science which has many elements of an art. At present, both parts are so closely interwoven that they present the appearance of a natural unit,

the splitting of which into two parts might appear to some as an impossible and undesirable process. However, a considerable degree of separation of the science from its practice is highly desirable, because the requirements of science and practice are in a certain sense mutually antagonistic.

Permit me to say that my advocacy of the separation of a clinical science from its practice is not activated by any disregard for the practice of medicine. On the contrary, I entertain a strong conviction that the efficiency of practice should be the supreme object in medicine. At the same time, I feel sure that the efficiency of that practice will be best attained when the search for the knowledge which the practice has to use should be carried out in the same manner and by the same methods as are employed in the search for knowledge in other branches of intellectual activity. In other words, clinical research should be raised to a department of clinical science and separated from practical interests. It will be the practice not less than the science of medicine which will benefit by such a separation.

Who should be the men to carry on research in this field and what should be their qualifications? First, it is essential that they have had a bringing up within medicine, their senses must have been filled up with thinking, worrying and brooding over practical and theoretical problems of clinical medicine. Second, they must have a training fitting them to carry out investigations in conformity with the requirements existing in all pure sciences. They must also have carried on various investigations in one or more of these pure sciences, so as to become familiar with careful scientific methods and imbued with a scientific spirit. They will thus acquire the habits and the tastes of the investigator, the scientist, which may then stick to them for life.

And, third, after all these preparations, they must select clinical research as the main field of their scientific activity. Clinical science will not thrive through chance investigations by friendly neighbors from the adjoining practical and scientific domains. Such volunteer service is most certainly very welcome. But the acclamation, cultivation and maintenance of a field of pure science of clinical medicine cannot be accomplished by chance services from volunteers; for such a purpose, we need the service of a standing army of regulars.

In Meltzer's address he called for American physicians to apply scientific principles towards the solution of clinical problems and argued for the establishment of an "army of regulars" to carry out clinical research. It is interesting to note that Meltzer was 58 years old when he gave that speech, 13 years beyond the age of active membership by current requirements of our Constitution.

For the last 15 years of his life Meltzer suffered from diabetes. He managed his illness by staying on a carbohydrate-free diet, but he had poor eyesight and reading was difficult. During the last 2 years of his life, he was physically feeble. In spite of these handicaps, his greatest pleasures were his own clinical research and taking an active part in medical gatherings such as this.

Many of the things that Meltzer said and did during his long life are worth recalling today. Here is a quotation from his presidential address to The Association of American Physicians in 1915 (17): "Some older members complain that the papers presented at the meetings are getting above their heads. While this may be a fact, it cannot be made the basis of complaint—the science of medicine is progressing."

So you see, it's an old problem. But Meltzer always heard and probably understood every paper presented to our meeting. In fact, the first minute book of our Society reveals that he discussed two papers at the 1920 meeting, which took place only 6 months before he died. Fig. 3 shows the title of one of these papers, with the notation under it that Meltzer was the first discussant.

Here is Meltzer's advice to his fellow investigators (16): "The men whom you now see sitting on the bank left behind while the boat of progress swiftly glides away . . . were themselves in their youth passengers of similar boats and cut faces at others who were left behind. Be generous to them, but do not repeat their mistakes. The secret is: Never leave the boat."

The boat of progress was that branch of medicine most likely to yield advances in medical research. Meltzer thought that the boat of progress in 1909 was physiology, and he was, I believe, warning his audience not to be left behind as they continued merely to correlate bedside and autopsy observations. The message is pertinent today; each of us should examine our scientific discipline, to be sure it is capable of taking us where we want to go.

The following indicates Meltzer's appeal to his friend Graham Lusk, as his illness was progressing (6): "If my good friends at the Rockefeller Institute . . . insist that I leave my laboratory there, I want to know if you will not permit me to work in your laboratory."

Some have argued that it is natural for clinical investigators to give up research and leave it to younger men—but that's an idea that runs contrary to everything Meltzer stood for. Fig. 4 shows the title of a paper that Meltzer presented to the National Meeting of this Society in 1917, when he was 66 years old. Others

Dr. Cohen & Levy: "Digitalis studies: Beneficial effect of digitalis on the normally beating heart. Certain difference in the action of strophanthum & digitalis in patients".  
Discussed by Drs: Meltzer, Hamneger & Cohen & Dr. Robinson Stand & Levy

FIGURE 3 Notes from the First Minute Book of the ASCI, 1920 meeting. Meltzer discussed paper no. 3 (shown in this figure) and no. 4. The meeting took place only 6 months before Meltzer's death.

*Dr. S. J. Meltzer: "Demonstration of a Simple Apparatus for Administration of Oxygen under Pressure, with Remarks on the Efficiency of the Procedure."  
Discussed by Mrs. Cole and Emerson.*

FIGURE 4 Notes from the First Minute Book of the ASCI, 1917 meeting. This is the last paper that Meltzer presented to the national meeting.

might argue that a life-long research career such as Meltzer's was possible in 1909, but not today. Fig. 5 shows, however, that at least one current ASCI member has continued to keep pace with Meltzer up through 1977. Actually, if you study this man's pattern carefully, you will see that he is due for a major upsurge during the next 5 years. By showing this comparison, I certainly do not mean to overemphasize the number of a man's publications. In both instances, these represent good science, and it is the pattern of the work and not the number that is important. Although there are many ways to serve medicine as we grow older, a continuing effort in clinical investigation, as exhibited by these two men, must certainly be the best, insofar as the goals of this Society are concerned.

In 1915, Meltzer published a paper in *Science* (18) entitled "The deplorable contrast between intranational and international ethics and the mission of medical science and medical men." In this paper, Dr. Meltzer agonized over the immorality of people and their nations. However, he also said: "But there is one most inspiring exception to this sorrowful rule. It is . . . the behavior of medical men. . . ."

To Meltzer, medical people were something special—they were a better group of people than biologists, biochemists, lawyers, etc. And he developed this idea in a convincing fashion. He even formed an "Organization of Medical Brotherhood" (19) in hopes of improving the ethics of others.

Based on everything I have read about Meltzer, I think he would be terribly saddened by the evidence suggesting that many of the clinical faculty in medical schools today will not accept a personal involvement in the care of the sick without direct financial incentive (20), and that physicians not infrequently falsify data during the course of the clinical evaluation of new drugs (21, 22). If he were here today, I believe Meltzer would argue that medical scientists should take a leadership role in *actively* teaching our students and house staff the ethical, unselfish, and sympathetic attitude that can make a doctor so special. In today's environment, that can only be taught by the same people who teach medical science—otherwise it has a hollow ring and won't be learned.

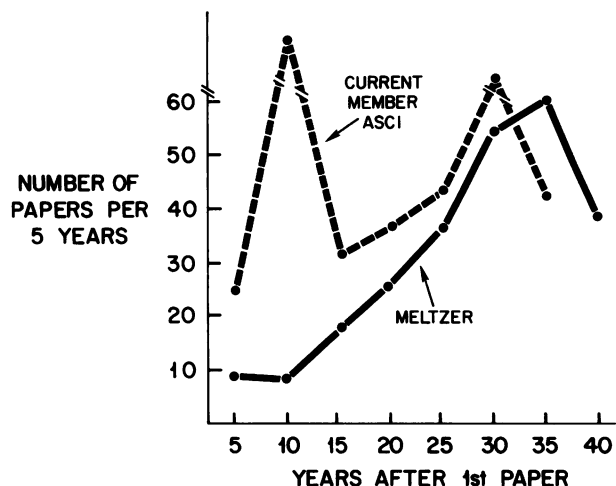


FIGURE 5 Research productivity of Meltzer, compared to a current ASCI member. The horizontal axis shows the number of years after the first paper was published, and the vertical axis shows the number of papers per 5-year period.

So, you have seen that our academic forefather was born in Russia, educated by the German masters, tempered by private practice in New York City, and then influenced by The Rockefeller Institute for Medical Research. It think that clinical investigators have a hero in Samuel James Meltzer. His life is an inspiration. The first goal of The Society he founded has been accomplished—the establishment of an "army of regulars" to conduct clinical research for the benefit of medical practice.<sup>4</sup> Moreover, his Society continues to serve two important functions: first, this national meeting, which attempts to counteract and resist the bad tendency towards isolation of medical science along clinical subspecialty lines; and second, the publication of a journal that I believe elevates the editorial standards of all medical publications. But the very success of the first Meltzer goal has placed medical education in the hands of clinical investigators, and thus has given to clinical scientists the responsibility of maintaining, or regaining, the status of the medical man or medical woman that Meltzer esteemed.

#### ACKNOWLEDGMENT

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<sup>4</sup> It should be noted that our Society was founded on the principle that clinical investigators, just as much as other physicians, care for the patient.

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