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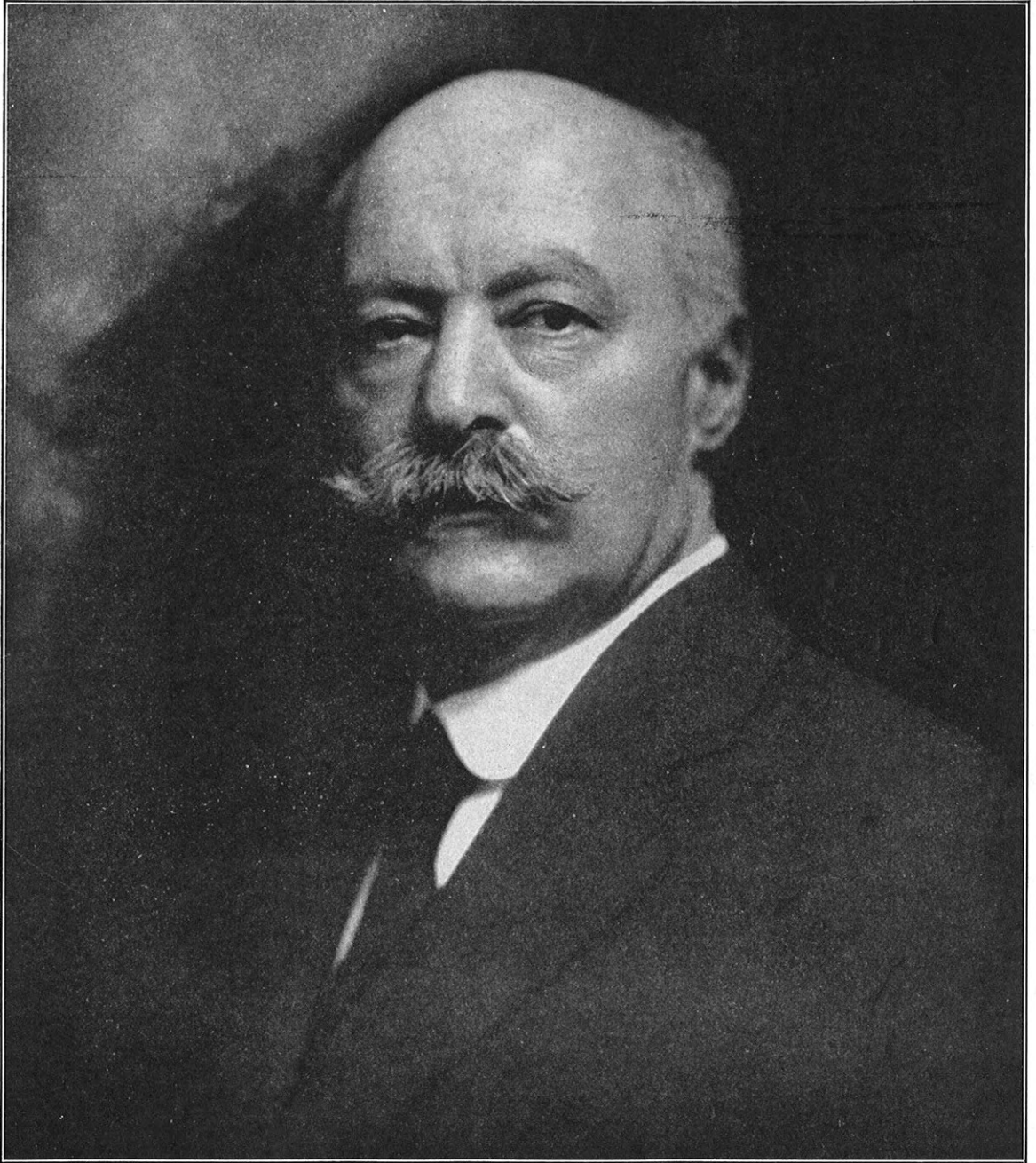
BIOGRAPHICAL MEMOIR SAMUEL JAMES MELTZER

1851-1920

BY

WILLIAM H. HOWELL

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S. J. Meltzer

SAMUEL JAMES MELTZER

By WILLIAM H. HOWELL

Samuel James Meltzer was born of Jewish parents on March 22, 1851, at Ponewjesh, in Curland, northwestern Russia. His parents were poor but belonged to the intellectual class. His father was a teacher, with an intense devotion to his religious faith. He undertook the early education of his son, but, as might be expected, the training was limited almost entirely to a study of Hebrew theological literature. The boy displayed early an eager desire for learning of all kinds, against his father's wishes and commands, with the result that the two came into conflict, the father attempting to limit his son's interests solely to those studies which would prepare him for the career of a rabbi, while the boy borrowed books from neighbors and friends which he was compelled to read in secret under the fear of punishment if discovered. There was constant friction between them and frequent occasions for the exercise of rigid discipline. After one severe punishment following upon this kind of disobedience the boy declared his freedom by leaving home and walking many miles to the house of an aunt in a distant village. Owing to the intercessions of his mother, who sympathized warmly with her son's love of learning, he was permitted to remain with his aunt for a while and subsequently was sent to a neighboring town where he lived in the temple, was taught by the rabbis, and got his meals from various families in the village. He was a scholar of such ability as to attract the general attention of the community, and it is recorded in the family traditions that at the early age of 16 he had learned all that the rabbis could impart to him. The learned men of the community came to him for help in the interpretation of difficult passages in the Talmud.

At the age of 20, according to the custom of his people, a marriage was arranged for him with Olga T. Levitt, the daughter of a well-to-do merchant. The bride was only 16 years old. She was his devoted wife until the day of his death, during the periods of storm and stress when he was struggling hard to get his start in life, and during that longer period when he had attained to eminence and enjoyed the comforts and luxuries of life. After his marriage young Meltzer announced his fixed determination not to enter the ministry, a decision that caused both anger and sorrow to his father. He betook himself to Konigsberg and with the help of his wife's dowry essayed to become a business man. The business that he selected was the manufacture of soaps. But at the same time he seized the opportunity to enroll in the Real Gymnasium. The result was what might have been expected. The work of the gymnasium interested him, he gave more time and thought to his books than he did to his business, and the latter therefore was not a success. At the end of the year he recognized that business was not his calling. His greatest interest at that time and for some years was in philosophy, but he realized that along that path it might be difficult to earn a living for his family, so he decided to begin the study of medicine. His wife and children returned to her father's house, while he proceeded to Berlin and entered the university in the fall of 1876. He was a student of medicine for five years. The tentamen physicum was absolved in the spring of 1879 and the examen rigorosum in June, 1881. They were very lean years for him from a financial point of view. He was in fact desperately poor. He lived with a humble family in an attic room, spending as little as possible of his meager income on food and raiment, and as much as he could spare in payment for his medical courses at the university.

His love of philosophy was still strong within him, and one of the stories he told of this period was that he surreptitiously attended Professor Steinthal's lectures in this subject, sitting far back in the room for fear that he would be discovered as an interloper and turned out. But on one occasion, during a heated discussion of the meaning of a certain passage in Kant's Critique, his interest got the better of his fears and he suggested that if a certain comma was transposed the meaning would be made clear. This suggestion aroused the interest of the professor. He asked the young man to remain after the lecture, and as a result of the conference that ensued

Meltzer was invited to visit him at his home. This was the more or less accidental beginning of a beautiful and lasting friendship between the two men. However hard the physical conditions of life may have been during this period, there is no doubt that intellectually and spiritually they were gloriously enjoyed and utilized. He threw himself into his work with intense zeal, and taking advantage of his opportunities gave as much serious attention as time would permit to the cultural studies of art and music. In the medical school he sat under great masters—du Bois Reymond, Virchow, Helmholtz, Friedländer, and the like—but the teacher who exercised the greatest influence upon his life and came closest to him was Hugo Kronecker. Like Steintal in philosophy, Kronecker was impressed by the ability and industry of the young student in physiology. He became interested in him personally, invited him to his home, and finally became his warm personal friend as well as his guide and councilor in physiology. It was under Kronecker that he completed his inaugural dissertation for the degree of doctor of medicine. The dissertation was dedicated to Kronecker "in herzlicher Dankbarkeit," and in collaboration with this master and friend he completed some notable investigations, which will be referred to later on. The fact that this poverty-stricken young student enjoyed the personal friendship of two eminent professors in the university and was received into the intimacies of their family life throws an interesting light upon the conditions of university life at that time.

A trivial incident of this phase of his life, which Doctor Meltzer sometimes referred to, indicates quite clearly that the relationship between student and professor was not that of a poor dependent and well-to-do patron, but an intellectual companionship of two scholarly men not influenced by the mere externalities of life. Kronecker, knowing that Meltzer was so poor that he got insufficient food, once in the kindness of his heart sent him a ham, but it was refused with indignation, just as Dr. Sam Johnson, as related by Boswell, spurned the mistaken kindness of a friend in sending him a pair of shoes to replace his shabby footwear when a poor student at Oxford. After graduating in medicine Meltzer could have made his career as a scientific man in Germany. It is stated that he was offered several positions on the condition that he be baptized in the Christian faith. But such a step did not accord with his sturdy sincere character. His thoughts turned to America as the country that had the best form of government and promised the most freedom in speech and action. He did not have sufficient means to purchase his passage; he therefore shipped as surgeon on one of the trans-Atlantic liners and thus arrived in New York. He was provided with letters of introduction to leading men in scientific, medical, and musical circles, but it is not recorded that he obtained any material assistance through this agency. He applied himself to the practice of medicine in order to support himself and to obtain sufficient means to bring over his family. His efforts must have been unusually successful, since in the second year of his residence in New York, in 1885, he felt justified in sending for his family. He became subsequently a successful practitioner, owing no doubt mainly to his intrinsic ability as a physician, but partly also, in all probability, to the fact that he at once began to make himself known to members of the profession through his scientific publications.

Just as soon as his financial position made it at all possible he sought the opportunity to use the facilities then existing in New York to carry on investigative work. He found and utilized such opportunities in Welch's laboratory at Bellevue and in Curtis's and Prudden's laboratories at the College of Physicians and Surgeons. For many years his practice and his investigations were carried on simultaneously. He worked with that extraordinary intensity and devotion which characterized him throughout his life. All his spare time during the day and a large part of the night were given up to laboratory investigations or the reading of current scientific journals. The eagerness for knowledge that he had shown in his early youth and manhood remained with him throughout life. It was a passion with him that seemed to grow stronger as he grew older, so that almost from the beginning of his residence in this country there came from his pen an increasing stream of communications to medical and scientific journals that have served to establish his reputation as a scientific investigator of high rank. His productivity was remarkable. The list of his published papers includes over 240 titles, distributed among some 48 scientific journals of this country, Germany, and England. These

papers contain contributions to the subjects of physiology, pharmacology, pathology, and clinical medicine, in addition to a number of lectures and general addresses. It is a striking demonstration of the breadth of his interests and knowledge that he was recognized as a competent and indeed leading investigator in all of these subjects. Physiology was the subject in which he was most deeply interested and in which he had the most intensive training as an investigator, and his contributions to the other medical sciences were made mostly from the point of view of the physiologist. His practical knowledge of clinical medicine and his extensive and thorough acquaintance with its literature gave him the opportunity to realize how often the results of physiology, as a basal medical science, may be applied with profit to throw light upon the problems of all other branches of the subject.

The professional physiologist is usually out of touch with the problems of the practitioner, and hence he fails often to realize how useful the new results in his science may be to his coworkers on the practical side. Once in a while we have active practitioners who at the same time are competent investigators in one or other of the underlying medical sciences. Such men serve as liaison officers capable of bringing about rapidly a mutually beneficial exchange of knowledge, which otherwise would develop only slowly through many intermediate agencies. Weir Mitchell and Meltzer are perhaps the two most conspicuous examples in this country of this advantageous combination in one individual of practical and scientific knowledge in medicine. In Weir Mitchell's generation it was perhaps less difficult to play this dual rôle, since the medical sciences had not become such highly developed specialties. In Meltzer's generation the task was more difficult, and he was able to carry it through with success only because of his unremitting devotion, his remarkable capacity for work, and his excellent training in the theoretical and practical sides of medicine. While he made important contributions to the fundamental problems of physiology, it may be said with truth that his special field of work lay in the borderland between medical practice and medical science. He was in sympathetic touch with the workers in both fields, he published papers in the theoretical and the practical journals, and he enjoyed the acquaintance and confidence of the leaders on both sides. No one perhaps in the generation now passing was more influential in bringing about a sympathetic understanding and coordination between the laboratory worker and the practitioner. To the latter he preached without ceasing the importance and necessity of scientific investigation, and the former he kept continually reminding of the possible application of scientific results to the explanation or cure of disease. As a consequence of this somewhat unique position which he held in the medical profession of this country we find that he was an active member of many of the important medical societies, both clinical and scientific, and indeed he was immediately concerned in the formation of some, particularly those whose chief function was to bring the results of scientific investigation to bear upon the problems of the clinician. In further confirmation of this view, that he served in a special way to link up the practical and theoretical workers in medicine, attention may be called to the fact that at various times he served as president of the American Physiological Society, the Society for Experimental Biology and Medicine, the American Gastro-enterological Society, the American Society for the Advancement of Clinical Research, the Association of American Physicians, and the American Association for Thoracic Surgery. In this list are represented some of the societies that stand mainly for research, together with associations that are composed mainly of active clinicians. That he was elected to the presidency by the votes of his fellow members is a clear enough demonstration that he stood high in the esteem of both groups of workers in medicine. It is not probable that he will have a successor in this unique position. While his activities covered this large range, his training primarily was that of a physiologist. It was from this standpoint that he worked and investigated, and his contributions to this subject entitle him to be ranked among the foremost physiologists of his generation. It seems appropriate, therefore, to attempt to give a critical estimate of the major contributions at least that he made to physiology. His papers in this field are so numerous and cover such a variety of topics that it is not possible to bring them all under review.

His first appearance as an investigator is recorded in a brief note in the "Verhandlungen der Berliner physiologischen Gesellschaft," printed in the *Archiv für Physiologie*, 1880, page 299. The communication to the society made by Kronecker in behalf of Herr Cand. Med. Meltzer, was entitled, "Die Bedeutung des M. Mylohyoideus für den ersten Act der Schluckbewegung." Kronecker had become interested in the mechanism of the act of swallowing, and under his direction two of his students, Falk and Meltzer, were carrying on investigations which demonstrated that the older view, namely, that the bolus is carried down by a progressive peristaltic wave of the pharyngeal and œsophageal musculature, is not correct. In the first act of swallowing the bolus is shot into the œsophagus by a contraction of cross-striated muscles, and Meltzer's first paper gave a probable proof that the chief muscle concerned is the mylohyoid. At a later meeting of the society in the same year Kronecker gave a second fuller paper by Meltzer and himself, "Ueber die Vorgänge beim Schlucken," *Archiv für Physiologie*, 1880, page 446, in which the outlines of their theory of swallowing were presented. This work, which was continued through several years, was published in full first, in the *Monatsberichte der Königl. Akademie der Wissenschaften zu Berlin*, January 24, 1881, under the title "Ueber den Schluckmechanismus und dessen nervöse Hemmungen," and later in more complete form in the *Archiv für Physiologie*, supplementary volume, 1883, page 328, with the title "Der Schluckmechanismus, seine Erregung and seine Hemmung." In its essential features their theory of swallowing has been generally accepted in physiology. As stated above, the important new discovery that they made was that the act of swallowing is initiated by a sharp contraction of the mylohyoid and hyoglossi muscles. The effect of these contractions is to shoot the bolus of food, which lies upon the dorsum of the tongue, through the pharynx and for a certain distance, depending on the consistency of the material, into the œsophagus. The contraction of the constrictors of the pharynx and the peristaltic wave along the œsophagus follow later, and in the case of soft foods, at least, constitute a sort of movement in reserve. The whole act of swallowing was studied with great care and many interesting observations were made, partly from experiments upon animals and partly from experiments which Meltzer made upon himself. In later life he developed a very sensitive larynx, which he attributed to the irritations resulting from the long-continued observations made upon his own deglutition. Some of these experiments must have been exceedingly uncomfortable, as they involved the placing of rubber bags in the pharynx and at different levels in the œsophagus to obtain graphic records, by means of connected tambours, of the passage of the swallowed bolus. Those who knew Doctor Meltzer well will realize that the intense earnestness which he threw into all of his work might easily have led him, in these experiments, to overstep the bounds of prudence, if thereby he could obtain evidence for what he believed to be a true explanation of the process of swallowing.

In connection with this work upon the mechanism of swallowing Meltzer undertook, presumably upon Kronecker's advice, the study of a special phase of the action of the deglutition center as the subject for his doctor's thesis. The results were published in his inaugural dissertation for the doctorate in medicine and surgery under the title "Das Schluckcentrum, seine Irradiationen und die allgemeine Bedeutung derselben." This is dated August 12, 1882, and is dedicated to Kronecker "in herzlicher Dankbarkeit." It was published later, under a slightly different title, in the *Archiv für Physiologie*, 1883, page 209. It is a suggestive and interesting paper on account of the careful analysis which it contains of the far-reaching effects of the act of swallowing upon other centers of the nervous system. He shows that the swallowing reflex influences, by irradiation or overflow, the centers for respiration, the heart, the bloodvessels, the uterus, the erection of the penis, etc., thus making it probable that the act of irradiation, so evident in the case of this relatively unimportant and infrequent movement, is a general accompaniment of the activity of the centers of the nervous system. But the main significance of this paper is to be found in the fact that it suggested to him certain views regarding the importance of inhibition in the reactions of the central nervous system or indeed of living matter in general. Thus early in his career he acquired a point of view in regard to the rôle of inhibition in the life processes which greatly influenced his later work. The idea or theory is outlined in this first paper, but is developed in greater detail in subse-

quent work. In the dissertation he calls attention to the fact that stimulation of certain afferent nerves, such as the superior laryngeal, the splanchnic, and the second branch of the trigeminal causes a contraction of the expiratory muscles and simultaneously an inhibition of the inspiratory muscles, while stimulation of the vagus nerve, on the other hand, causes a reflex contraction of the diaphragm and inspiratory muscle, together with an inhibition of the external oblique muscle of the abdomen, an expiratory muscle. For the muscles of respiration, therefore, the arrangement is such that reflex stimulation of the inspiratory muscles is accompanied by reflex inhibition of expiratory muscles and vice versa. He goes on to assume that a similar reasonable arrangement must exist in the case of antagonistic muscles in other parts of the body, for example, with the flexors and extensors of the limbs, if they are to act most efficiently in locomotion. Some ten years later Sherrington gave the necessary demonstration that this interrelation does hold with the muscular antagonists of the limbs; the contraction of an extensor is accompanied by a relaxation of its opposing flexor and vice versa. He designated this relationship under the term of "reciprocal innervation," without apparently being aware of Meltzer's similar views.

Meltzer meanwhile had been accumulating further data bearing upon his generalization. In his paper upon "The self-regulation of respiration," read before the American Physiological Society in 1889 and published in the *New York Medical Journal* and under a different title in the *Archiv für Physiologie*, he describes experiments intended to show that two kinds of afferent fibers exist in the vagus nerve, one exciting and the other inhibiting inspiratory movements. He used this view to modify the Hering-Breuer theory of the self-regulation of the respirations by assuming that the expansion of the lungs stimulates simultaneously both sets of fibers. The resultant effect, as in the case of the simultaneous stimulation of the motor and inhibitory fibers of the heart, is a dominance of the inhibitory action, thus arresting the inspiration and bringing on a passive expiration, but subsequently the excitatory effect, which, like that due to the accelerator fibers, has a long after action, comes into play and starts a new inspiration. In his first general paper on inhibition (*New York Medical Journal*, 1899) this idea of a combined action of opposing processes is extended by the citation of numerous instances taken from physiological literature and is expanded into a general theory which makes inhibition a universal property of living matter. "I entertain and defend the view that the phenomena of life are not simply the outcome of the single factor of excitation, but they are the result of a compromise between two antagonistic factors, the fundamental forces of life, excitation and inhibition." That is to say, whenever a tissue is stimulated two different processes are aroused, one leading to the functional activity and one to the suppression of this activity. As to the nature of these processes he does not speculate to any extent. He was not satisfied with the Hering-Gaskell conception, according to which excitation follows or is an expression of catabolic changes while inhibition is the accompaniment of processes of an anabolic or assimilative nature. He goes only so far as to assume that the two processes involve the potential and kinetic energies possessed by the system, and that while excitation facilitates the conversion of potential to kinetic energy, inhibition hinders or retards this conversion, the two processes being compared to the turning on and off of a stopcock. Nor was he satisfied with Sherrington's term of reciprocal innervation to describe the general relations he had in mind. Unfortunately, perhaps, he had not proposed any concrete designation in the beginning to express the interplay of these opposing processes, but later, stimulated no doubt by Sherrington's example, he did attempt to find a suitable descriptive phrase.

In his second general paper on inhibition (*Medical Record*, 1902, page 881), he suggests the term "law of crossed innervation," an expression used by von Basch and Ehrmann to describe the opposed activity of the longitudinal and crossed musculature of the intestines. Later still, in a paper in the *Archiv für Verdauungskrankheiten*, 1903, Volume IX, page 450, he modifies this to the "law of contrary innervation." But he did not succeed in establishing either of these variations upon Sherrington's nomenclature in current physiological literature. He no doubt felt, and very justly so, that he should have had some of the credit for establishing this general physiological law. His own plea for priority in the matter is given in a footnote to a paper

written in collaboration with his daughter, Mrs. Auer, "On the paradoxical pupil-dilation caused by adrenalin" (*American Journal of Physiology*, 1904, Vol. XI, page 40). He believed that this process of "contrary innervation" is practically universal in its action; it is "manifest in all the functions of the animal body." As was his custom with all of his theoretical conclusions, he attempted to apply this law to the explanation of some of the pathological phenomena that were presented to him in his practical work as a physician. As he expresses it, "a disturbance of this law is a factor of more or less importance in the pathogenesis of many disorders and diseases of the animal body," and he illustrates his meaning by a specific application to gastric and intestinal colic. If we could imagine that the orderly sequence of a peristaltic wave is disturbed so that the advancing wave of contraction meets a constricted instead of an inhibited area, then evidently conditions are present which may cause distension and give rise to the pains of colic. Other instances of a similar character, cardio spasms, biliary obstructions, etc., are cited to show that known pathological results may follow from a disturbance of or a disharmony in the normal process of contrary innervation. How far Doctor Meltzer was correct in these concrete applications of his theory it is not possible to say. Some of the cases he uses are undoubtedly amenable to other explanations; but in his general conception of the importance of the inhibitory processes in the functional activity of the organs he was in advance of most of his contemporaries, and he deserves credit for keeping this more or less hidden side of vital activity in the forefront of physiological discussions. The whole story is far from being told, and it may be that later work will demonstrate that he saw deeper into the processes of life than his fellow workers have done. Certainly so far as the effect upon himself was concerned it was a rewarding and stimulating theory. It played, as he expressed it, a dominating part in all of his researches. Thus his explanation of the mysterious condition of surgical shock, to which he held tenaciously in the face of all opposing criticisms, was that "the various injuries which are capable of bringing on shock do so by favoring the development of the inhibitory side of all the functions of the body," or to express it in a figurative way, the normal balance of the opposing processes is shifted toward the side of inhibition.

In all of his experimental work Meltzer was very exact and objective in describing his results. In fact he entered into the minute details of his observations with a thoroughness that was probably derived from his German training. On the other hand, it is evident from what has been said of his views upon inhibition that he had a marked tendency to theorize or speculate upon the basis of his findings. He was not content to simply catalogue his observations and publish them as isolated facts which somehow would find their place in the growing structure of science. They were for him the subject of much reflection. He regarded them as revelations of the processes of the body which he must try to interpret, and his genuinely scientific mind was constantly seeking to formulate general theories to fit or to embrace the facts that were disclosed by his experiments. Nothing seemed to give him greater pleasure than to discuss these theoretical possibilities with his fellow workers, and from many conversations of this kind which it was my good fortune to enjoy I got always the impression of a mind constantly on the alert to understand and interpret his results and full of a certain eager expectancy of discoveries of importance. His theories and generalizations in turn supplied him with the interest and energy to devise new work, so that throughout his long career there was never any lack of problems to be attacked nor any diminution in enthusiasm for research. Young scientific workers are sometimes warned by their older associates against the dangers of speculation; and while this advice may be wise as regards the written word, there can be little doubt that an original and constructive mind must react in this way. Reflection and speculation are essential in keeping alive a spirit of investigation. When the proper time came Meltzer did not hesitate to announce his theoretical views in published papers or addresses. Some of them were effective in guiding and stimulating other workers beside himself, and some were so bold and far-reaching that only the future can determine whether they will be fruitful or barren. The work, for instance, which he began with Welch in 1884 upon the effect of mechanical vibration upon bacteria, red corpuscles, and other cells, and to which he returned from time to time in his laboratory investigations, led him to believe and announce that a certain rate

of vibration is one of the normal and essential conditions of life—like temperature, for example. Furthermore, he conceived that the rate of the heart beat is adjusted, on the one hand, to furnish the optimum vibratory condition for the cells of the organism, and, on the other, to give a mechanical vibration which is destructive toward foreign cells, such as invading bacteria. He considered that this constitutes one of the defensive mechanisms of the body, an idea which I fancy none of his fellow workers has adopted.

In one of the last, if not the very last paper that he wrote, a paper published only two months before his death, he announced a most interesting discovery, namely, that removal of both superior cervical ganglia in rabbits is followed by death in about 90 per cent of the cases. His experiments, as usual, are described with care and exactness, but he does not hesitate to speculate with some boldness upon the possible explanations of this remarkable result, and it is to be noted that the two chief hypotheses that he advanced are of a kind that probably do not at once commend themselves to his fellow physiologists. He suggests, in the first place, that these ganglia "contain a principle which is essential for the maintenance of life"—that is, they produce an essential internal secretion. In the second place, to account for the pulmonary lesions exhibited by the operated animals, he assumes that the ganglia normally send impulses to the respiratory centers through which the orderly play of the antagonistic (abductor and adductor) muscles of the larynx are controlled. In the absence of this controlling influence there is a disharmonious action of the muscles, a disorder of the law of contrary innervation, which, as in the case of section of both vagi, leads in some way, not clearly understood, to an infection of the lungs. These and like examples indicate clearly how experimental results tended to stimulate his imagination, as they must do with every worker whose soul is in his work. He held hard to his facts, and insisted that other workers should do the same; but on the basis of these facts his intense and eager mind sought to discover the larger principles that control the life of the organism. Some of his theoretical speculations were more fortunate in finding a prompt acceptance and application among his fellow workers. Thus, in his Harvey lecture, 1906, on "The factors of safety in animal structure and animal economy," he made a most happy application of this term, used in engineering, to describe the reserve powers exhibited by the mechanisms of the body. While the general conception that he developed had no doubt occurred to others, no one before him, so far as I know, had clearly visualized the great importance of these reserves in the adaptation of the organism to the changing conditions of its environment. The apt phrase that he selected to designate this property found an immediate acceptance in scientific medical circles the world over. One meets the expression now constantly in current literature, accompanied usually by a grateful acknowledgment to the author who first suggested its use. The mere term itself, "factor of safety," has proved most useful as a convenient and suggestive form of expression, but much more valuable than this is the emphasis it has given to a great general biological law expressing the way in which an organism is adapted to meet environmental stresses.

In his paper on "Bronchial asthma as a phenomenon of anaphylaxis" (Journal of American Medical Association, September 17, 1910) Meltzer made a theoretical suggestion as to the nature or cause of true bronchial asthma which not only attracted wide attention in medical circles, but has proved to be a real assistance in the understanding and treatment of a troublesome disease.

The most important of his contributions in later years are contained in three series of researches: One dealing with the action of adrenalin upon the blood vessels and the muscles of the iris; one with the inhibitory action of magnesium sulphate and the antagonistic effects of calcium salts; and one with his method of artificial respiration by pharyngeal and intratracheal insufflation. The first series consists of eight or nine papers, mostly in collaboration with his daughter. They showed in this work that the temporary action of adrenalin upon the blood vessels may be converted into a long-lasting effect, in the case of the ear vessels, if these vessels are first denervated by section of the vaso-motor fibers in the sympathetic and the third cervical nerve. A more striking result still was obtained for the iris. In the mammal subcutaneous injections of adrenalin in moderate doses have no effect upon the size of the pupil, but if the

superior cervical ganglion is first excised, then, after a certain interval, subcutaneous injections bring on a marked and long-lasting dilatation. His explanation of these phenomena was made in terms of his theory of inhibition. Whether or not his views in regard to the relations of the cervical ganglion to pupillary dilatation will stand the test of future experimental work, it is to be noted that the observation itself constitutes a significant instance of a kind of independent physiological activity on the part of a peripheral ganglion. The bearing of these facts upon the prevalent conception of the rapid destruction of epinephrin in the tissues was brought out especially in a paper with Auer, in which it was shown that if adrenalin is injected into a ligated limb and an hour or so afterward the ligature is removed the dilatation of the pupil quickly follows, thus demonstrating that for this long period the adrenalin had remained unaffected by the tissues. It is interesting to note that he made a second confirmatory contribution to this phase of the adrenalin effect in the last year of his life, in work done again with Auer and not published until after his death. Two incidental results that came out of this series of experiments have proved to be of value in physiological work. One was the discovery that the isolated eye of the frog shows dilatation of the pupil when exposed to small concentrations of adrenalin. A convenient biological reagent was thus furnished for the detection of minute amounts of adrenalin in the body liquids. The other was the fact that absorption takes place much more rapidly in intramuscular than in subcutaneous injections. The marked physiological effects of adrenalin furnished a positive indication of the rapidity of absorption, and the discovery that injections made intramuscularly are absorbed with great promptness has since been utilized to advantage by other workers.

The work upon the inhibitory and anesthetic effects of magnesium salts gave rise to no less than 25 papers, most of them published in collaboration with one or another of his associates, but chiefly with Doctor Auer. The peculiar inhibitory action of magnesium sulphate had attracted his attention as far back as 1899, and he reported upon it incidentally in a communication to the American Physiological Society. But in 1904-5, influenced again by his general conception of the importance of the inhibitory processes, he took up with Auer a careful physiological study of its action. The results were most interesting and important. When given subcutaneously in certain doses the magnesium sulphate produces a condition of complete unconsciousness and muscular paralysis or relaxation, which is reversible, in the sense that when the animal is given proper care it recovers. Later he was able to show that out of this condition of profound depression or inhibition the animal may be restored to complete consciousness and motility with miraculous suddenness by the intravascular injection of small amounts of calcium chloride. No one who was fortunate enough to see this demonstration as given by Doctor Meltzer will forget its dramatic effect upon his audience. A healthy vigorous rabbit was brought quickly to a condition of complete immobility and apparent death by the magnesium sulphate and then even more suddenly raised from the dead and restored to its normal tranquil existence by the injection of some calcium chloride. Meltzer and his collaborators investigated various phases of this action of magnesium sulphate, and all of the results obtained tended to strengthen in his mind the conviction that in magnesium he had discovered the element in the body that is especially concerned in the processes of inhibition. The antagonistic action of the calcium, although exhibited in such a striking way, was not in his opinion specific. His own experiments in connection with the results reported by other observers led him to the general view that calcium serves to balance the abnormal activity of the other kations, potassium, sodium, and magnesium, whether this abnormal action is in the direction of excitation or of inhibition. Modern work upon the physiological significance of the inorganic constituents of the body fluids which was begun in Ludwig's laboratory, but was given its main impetus by the striking contributions of Ringer, had concerned itself chiefly with the salts of potassium, sodium, and calcium, which alone seemed to be sufficient to maintain normal conditions of irritability. Meltzer's work has shown that magnesium also has its place in this ancient balance of powers through which the functional activity of protoplasm is controlled. One can understand that in arriving at these results he must have felt that he was approximating at least a demonstration of the correctness of his general conception of the role of inhibition in functional activity. In this,

as in all of his experimental work, Meltzer was eager to give his results a practical application to the art of medicine. The possibilities of the use of magnesium salts as an anesthetic agent in surgical operations were tested with some success on human beings and more important still, their efficacy in controlling the spasms of tetanus has been attempted and gives promise of being useful under certain conditions. One outcome of this work which he did not foresee, but which has been exceedingly useful to the diagnostician, is its application to the procedure of obtaining specimens of bladder bile for bacteriological examination. By the local application of solutions of magnesium sulphate to Vater's papilla in the duodenum the sphincter of the bile duct is inhibited so that bile is emptied into the intestine and can be aspirated off for examination.

His last extensive series of researches dealt with anesthetization and artificial respiration through pharyngeal and intratracheal insufflation. Something like 28 papers, most of them in collaboration with pupils or assistants, were devoted to this subject. His interest in this topic seems to have been stimulated by the fact that in his use of magnesium sulphate for anesthetic purposes the chief danger lay in the inhibition of the activity of the respiratory center. To meet this difficulty he undertook a study of the methods of artificial respiration. The initial paper in 1909 by Meltzer and Auer described a method of artificial respiration by continuous insufflation of the lungs through a tracheal catheter. It was found that by this means not only could an animal be kept alive without the action of the respiratory movements to fill and empty the lungs, but that it furnished also a convenient and efficient method for anesthetization. The use of this method in animal experimentation, and especially its use in human surgery of the thorax and facial region, was apparent, and on many occasions Meltzer sought to make known its advantages and to ask for an adequate trial of its merits at the hands of practical surgeons. The method has found some acceptance, and the application of the principle involved will no doubt be extended in the future as the technique of thoracic surgery improves. It was in recognition of the importance of this work that the American Association for Thoracic Surgery asked him, a physician and laboratory worker, to serve as their first president. It was natural that this work should have led him to consider the whole matter of artificial respiration in its relations to resuscitation after accidents of various sorts. His general paper in the Medical Record for 1917, giving a history and critical analysis of the methods of resuscitation, is an interesting and valuable contribution. He gives experimental data to prove that his device of intratracheal insufflation is the most efficient method of artificial respiration both for man and animals. But he realized that it is a method which requires special knowledge and training for its successful execution, and his broadening acquaintance with and interest in the practical aspects of resuscitation led him to experiment with the less efficient and less safe method of pharyngeal insufflation. He was a member of the three national commissions on resuscitation and served as chairman of the third commission. In connection with the duties of this service he devised a simple portable form of apparatus for pharyngeal insufflation which can be used with very little previous instruction, and he demonstrated, with entire success I believe, that this form of apparatus is much more efficient than any of the so-called manual methods of resuscitation, or than any of the special machines for this purpose, pulmotors and lung motors, which have been exploited commercially during the past few years. It was, I imagine, a sore disappointment to him that he was not able to convince his colleagues on the third commission that this apparatus met all the requirements for industrial and military use. It is probably the simplest and best instrument yet devised for artificial respiration as applied to man, and in institutions or industrial establishments where the need for artificial respiration may arise frequently and where special individuals may be instructed in its use it can be employed to great advantage. But it does require some little amount of training to use it properly. The average uninstructed man or woman can not be trusted to apply it intelligently, and for this reason the commission felt constrained to recommend the adoption of a manual method as the form of first aid which may be used most successfully under ordinary conditions.

It will be evident even from this incomplete review that Doctor Meltzer's work constituted an important contribution to physiological science, and, as has been stated above, his contact with the practice of medicine and his frequent use of medical journals for his publications

enabled him to influence directly the thought and tendencies in medical circles. That he was a strong factor in the development of American medicine is recognized freely and gratefully by his contemporaries. It happens sometimes that men may pose as authorities in medical science among practitioners although they have little honor among the workers in science, or vice versa, but it was Doctor Meltzer's deserved good fortune to be most highly respected and honored by both the practitioners and the laboratory workers. While this reputation rested primarily upon the character of his investigative work, his personal influence was augmented greatly by his constant active participation in the meetings of the numerous societies to which he belonged. He believed strongly in the benefits to be derived from personal contact among workers, and he was especially interested in getting together the men who were doing scientific work in clinical medicine. He was the founder and first president of the Society for Experimental Biology and Medicine, and at the memorial meeting held by this society shortly after his death the speakers all emphasized the great importance of his personality in developing this important center of scientific activity. It was at his invitation that in 1903 the workers in the biological sciences who were resident in New York met to form an organization whose express purpose was to stimulate experimental work in biology and medicine. He gave to this society such devoted personal service and identified himself so completely with its activities that for a long period it was commonly designated as the "Meltzer Verein." In like manner he was the founder and first president, 1909, of the "Society of Clinical Investigation," the main purpose of which was to bring together the men, mostly young men, who were engaged in investigations bearing upon internal medicine. His fellow members give unanimous testimony to the influence that he exerted upon this group of men, and to the inspiration that they derived from the fine and high ideals that he impressed upon the society through his addresses and his example. He served also as president of the Association of American Physicians, the American Association for Thoracic Surgery, the American Gastroenterological Society, the Federation of American Biological Societies, and the American Physiological Society, and was in addition a faithful and active member in many of the other national societies, such as the Society of Biological Chemists, the Society of Pharmacology and Experimental Therapeutics, the Society for Experimental Pathology, the American Philosophical Society, the National Academy of Sciences, etc.

In most of these societies his membership was far from being simply nominal. He attended the meetings, he read papers and took an active part in the discussions and the business sessions. In all of them it may be said that he was a prominent member, influential in his contribution and personally known to the other active members. This fact in itself, when we consider the range of subjects covered and remember that these societies are composed of specialists and trained investigators, enables us to understand how his influence was so widespread. He came into contact, as a colleague, with the workers in all branches of medical sciences. He knew the kind of work that each was doing, so that to a really remarkable extent he was in sympathetic touch with the progress being made in all departments. To maintain this relationship meant of course that he kept himself informed in the current literature of all these various branches of medicine. He was in fact an indefatigable student in all sides of modern medicine. Members of his family inform me that he subscribed to some 35 medical and scientific periodicals and read them all faithfully in spite of the fact that very poor eyesight made his reading slow and difficult. But he had a retentive memory and was quick to grasp the essentials of a paper and, besides, the effort necessary to keep pace with medical and scientific progress was not for him a task, it was his greatest pleasure. It was this sustained and absorbed devotion that made it possible for him to participate actively and creditably in so many fields of medical research. He was really well informed on many sides, and this broad knowledge, supported, as it was, by an excellent memory for details, enabled him to appear to great advantage in society meetings in the discussions of papers. It would seem as though he was prepared to make some contribution to almost any paper that was presented, although the subject might be far outside his special fields of work. Some phase of the subject would appeal to him or remind him of things that he had read or that he knew from his own experience. Whatever it was, even if somewhat remote or trivial, he was likely to speak it out, as a sort of expression of interest, or to stir up

further discussion. He got the same kind of pleasure in listening to the presentation of scientific papers that he did from following the literature, so that he was an ideal society member, punctilious in attendance and in following the program, an absorbed listener, and willing and able to help in the discussion.

As physiology was his first love so the American Physiological Society was probably the organization in which he was most interested. He was elected to membership in this society at its Philadelphia meeting in December, 1888. From that time until his death he was perhaps its most faithful member in attendance, in the presentation of papers, in participation in the discussions, and in promoting social intercourse among the membership. It was evident that he enjoyed thoroughly these gatherings with his fellow workers. He believed in their importance as a means of promoting the advance of physiological science, and he gave the best that was in him to make the meetings profitable and to maintain the high standards of the society as an organization devoted primarily to the encouragement of research. It is a great good fortune for any society to have a member of this type, one who attends its meetings not from a sense of duty or for reasons of personal advancement, but because he thoroughly enjoys and believes in them. It may be said that Doctor Meltzer listened eagerly to every paper presented and had something to say about most of them. What he said was not always important, but it showed his interest. No one was more appreciative of good or new work and no one was more frank in expressing doubt or criticism when the work was not to his taste. Meltzer was not a good speaker. In spite of his long residence in this country he spoke with a marked accent and was far from being fluent or happy in his choice of words. But he was always sincere and earnest and in the discussions at least made his points so that they could not be misunderstood. In the presentation of his own papers, however, he was not particularly skillful. It was something of a strain to follow him closely, and very frequently he elaborated details at such length that the main points they were intended to demonstrate or illustrate were lost or obscured. But the constant interest that he manifested in all that was going on was singularly effective in the long run. One such member, provided he is free from suspicion of self-seeking, can contribute powerfully to the vitality and interest of an organization. Doctor Meltzer was just as much interested in the business meetings of the society as he was in the scientific sessions. The members of the society as a rule were not greatly concerned in such matters as the choice of officers. As is the case probably in most of such scientific societies, they voted for whatever ticket was presented or was nominated in open meeting. But Doctor Meltzer, because of his genuine belief in the influence of the organization upon the advancement of physiological research, took such matters very much to heart. He had quite decided opinions and expressed them with entire frankness. He looked upon the presidency of the society as an honor and recognition and was anxious that it should go to the men who in his opinion were most deserving. It so happened therefore that for a number of years he was a sort of king-maker. When he thought that a president had served long enough he said so plainly in the open meeting and proposed the name of his successor. And because he had given thought to the matter and was obviously sincere and disinterested, he usually carried the meeting with him. When in the course of time the honor of the presidency came to him it was evident that he appreciated it greatly, and he magnified as much as possible the importance of the office. He was in fact a bit autocratic in exercising its functions, but all of his actions were obviously meant to promote the efficiency and importance of the society. One of his reforms caused some consternation when it was first sprung upon the society. Like other presiding officers he was very anxious to finish the program in good time and for this purpose he brought with him an alarm clock which could be set to ring for any given interval. When a member arose to give a paper for which 15 minutes had been allowed on the program, Doctor Meltzer very carefully wound and set the clock and promptly at the appointed moment the alarm went off. This in itself was sufficient to bring most speakers to a precipitous and, usually, incoherent conclusion. Less sensitive members who made an effort to proceed after the noise was over found that the audience was not with them, the faces of the members reflected their somewhat amused conviction that the speaker's time had struck and it was his duty to sit down. Some of the members

in fact were so much interested in observing the reactions of the absorbed speaker when the alarm broke upon him that I fear their attention was seriously diverted from the substance of his remarks. But Doctor Meltzer, whose sense of humor was not highly developed, took the whole matter very solemnly and conscientiously and ran his program off on schedule time.

In the meetings of the National Academy of Sciences Doctor Meltzer exhibited the same faithfulness in attendance and the same keen desire to participate fully in all the activities of the society. From the time of his election he made it a point to attend all of the spring meetings in Washington and most of the fall meetings in addition. Very frequently he was down on the program for a paper. Sometimes his papers were on quite technical subjects, and it is probable that most of the members present were not able to follow him satisfactorily. His method of presentation, as was stated before, was not well suited for a general audience; he did not possess the art of lucid expression, which depends chiefly no doubt on the ability of the speaker to appreciate the state of mind of his audience in relation to the subject under discussion. His own interest and enthusiasm made him overlook the fact that those whose minds are primarily occupied in other directions need to be led up to a new subject through an introductory incline of explanatory statements. His method was rather to plunge at once in medias res. This, together with his faulty pronunciation of English, made his papers difficult to follow, especially when given, as they usually were, in the large hall of the National Museum with its annoying reverberations. Meltzer himself was impressed with the dignity of this gathering of eminent scientists, and he was much more impressed by the importance and dignity of his subject. Whenever, therefore, he had any new results to communicate he felt it incumbent upon him to bring them forward. This was his idea of what such a gathering of scientists was for—to present and discuss new facts and theories. In the same sense he was an excellent listener to the papers of other members; not at all from any sense of duty but because of his genuine and enthusiastic interest in the advancement of scientific knowledge of all kinds. He was faithful also in his attendance upon the business meetings of the academy. When it came to the election of new members no one was more alert in insisting that the highest standards of scholarship should be applied. Eminence of other kinds he respected, but in his opinion membership in the academy should go only to those who are distinguished for their contributions to science; and when a candidate in his opinion did not measure up to this standard, when there was no evidence of scientific productivity of a high order, he was very frank in expressing his conviction that the candidate should not receive election. The directness with which he expressed himself in such matters was sometimes a bit startling, but no one could fail to appreciate his sincerity and to recognize that he was guided in what he said by what he conceived to be the principles involved.

Meltzer was eminent as a physician and as a scientist. Whether or not he can be called a great scientist depends upon the meaning attached to the word. Properly speaking that designation belongs only to those few workers who by reason of exceptional intellectual ability or by good fortune have added something of such outstanding importance to scientific knowledge that it marks a distinct advance, or constitutes an epoch-making discovery, influencing in a large way the subsequent development of some line of scientific inquiry. Meltzer was not so fortunate as to make a contribution of this kind, but he was a consistent, tireless, and devoted worker in science, holding always to the highest ideals, which he preached and exemplified at all times. He was never faint-hearted nor skeptical about the value of scientific methods and scientific ideals as applied to medicine. When he first came to America medical education and medical standards were at a low level, compared with what had gone before as well as with what has since developed, and this unhappy state of affairs must have made a deep impression upon him. He seems to have set himself the task of improving these conditions. He was a clinician and it was on the clinical side that conditions were the worst. In the scientific branches of medicine a new spirit had arisen. Laboratories of physiology and pathology were being established, and it was recognized for these subjects that special training is required and that men who give themselves to such work are a class apart from the general practitioner. But in clinical medicine the scientific spirit had not penetrated deeply. Meltzer believed with

all his heart that the future of medicine depends upon the applications of science to diagnosis and treatment. He had a perfectly clear vision of the good results to be expected in medical practice from the application of laboratory methods to the study of the normal and pathological physiology of the organism. But this was not the opinion of the great body of practicing physicians at that time. There was marked criticism of the elaborate laboratory methods that were coming into vogue and which seemed at first sight to be so far away from the pressing problems of disease. Meltzer, however, was thoroughly au courant with the modern point of view and he was at all times the vigorous defender and propagandist of experimental methods in medicine. In a very real way he became a prominent and influential representative of scientific medicine. Through his writings and his numerous societies he was constantly in evidence as an advocate of the importance of research, and, as was natural, his influence was felt first upon the younger men. The older men were more or less set in their ways, but the younger, better trained men who were then entering medicine were the hopeful element to be considered. Many of these who have since become prominent have expressed their appreciation of the stimulating effect of Meltzer's sympathy and criticism. The fact that he was recognized as an able practitioner, as well as a successful laboratory worker, gave him a position of advantage which he utilized to the fullest extent in bringing his influence to bear upon the younger men to stimulate them to undertake experimental work, and upon the older men to impress them with the value and necessity of such work. As far as I can ascertain his distinguished services did not bring him any academic calls. Whether or not he would have made a successful professor is perhaps open to question. Most likely his qualities were not such as would have made a good instructor for beginners, although for the few really interested individuals he would no doubt have been a constant strong source of inspiration. His work as an investigator did, however, bring him a call of a most complimentary kind from the Rockefeller Institute of Medical Research.

He was asked in 1904 to take charge of a department of experimental physiology and pharmacology. This invitation presented a serious dilemma. On the one hand, it offered the opportunities that he craved of abundant facilities for research, but, on the other, it meant the suspension of his work as a practitioner. He did not hesitate in making his decision. At a very considerable financial sacrifice he accepted the post, and the long series of important investigations which he published from this laboratory is abundant proof that the selection was a wise one. He retained this position for 15 years, resigning in May, 1919. Shortly before his withdrawal, in 1917, the institute had his portrait painted by Adolphe Borie to commemorate his services. During his latter years at the institute and for the remainder of his life he was in poor health. He had long been a sufferer from diabetes. His own careful supervision of his diet enabled him to control this condition successfully for many years, but during the last 15 years he was restricted to an almost entirely carbohydrate-free dietary. During the last year or two of his life he was a very sick-looking man, wan and feeble, but he did not surrender to his condition. He continued his reading and experimenting and attended faithfully his scientific meetings. Death came to him finally while at work in his study at night. It was his custom apparently when he could not sleep to go into his study to read, and it was on an occasion of this kind that the end came, let us hope suddenly and painlessly. He had long realized that his life was precarious, but his only expressed regret was that he might not have time to do some of the important work that he had planned.

The latter years of his life were saddened, not only by ill health and the consequent limitation of his power to work, but also to a considerable extent by the conditions created by the Great War. Meltzer's education had been obtained in Germany and he had always a feeling of gratitude and appreciation for the opportunities opened to him at that period of his life. He had besides a sincere admiration for the great contributions made to medicine by German physicians and professors, with many of whom he was personally acquainted. When the war started and the tide of anti-German sentiment began to rise rapidly in this country it was directed not only against the policies of the German Government, but oftentimes in an unreasoning way against German science and German scientists. This feeling was augmented

no doubt by the brutally frank expressions of policy contained in the so-called manifesto of the intellectuals and signed by many eminent German professors. Feeling was intense and intolerance was exhibited in academic as well as nonacademic circles to an extent that is scarcely comprehensible now, although only a few years have elapsed. Meltzer, with his philosophic training, his warm affection for the Germany that he knew and admired, his loyal love for his adopted country, and his great belief in the cosmopolitanism of science was greatly distressed for fear that the bitterness engendered by the War might injure permanently the spirit of cooperation and fraternity among scientific workers of different nationalities. Indeed there was much reason at that time to fear that such a result might occur.

On the occasion of the fourth annual dinner of the Biochemical Association of Columbia University he delivered a fine address on "The deplorable contrast between intranational and international ethics and the mission of medical science and medical men." This address was published subsequently in the *Biochemical Bulletin* (Vol. IV, 1915) and in *Science* (Vol. XII, p. 515, 1915). In it he drew a vivid picture of the inhumanity created by war, and emphasized the contrast in this respect of the generous medical service rendered by physicians to friend and foe alike. On this basis he suggested the formation of a "medical brotherhood for the purpose of upholding and accelerating the progress of international morality." This idea grew in his mind; he talked it over with all of his friends and finally organized definitely an association which he designated as a "Fraternitas Medicorum." He secured the cooperation of 150 of the leading medical men of the country and issued an appeal for membership in a statement printed in the *Journal of the American Medical Association*, July 31, 1915. The appeal was successful, some 16,000 names were secured in this country alone, and interest in the project was shown by leading physicians in other countries. Whatever progress might have been made if conditions had remained as they were when the brotherhood was organized, with this country as a neutral power, its actual operations were brought to a close temporarily by the fact that we entered the war. Under such conditions it was probable that any activity that might be initiated would be interpreted as unpatriotic, and in a letter to the editor of the *Journal of the American Medical Association* Meltzer announced that the sending out of literature would be suspended. After the war was over he made an attempt to revive the organization, hoping especially to induce some other leader in medicine whose German affiliations were less evident than his to undertake the direction of its work. As it turned out interest in the project lapsed somewhat after the cessation of the war, and it would seem as though the whole movement had come to naught. But it was a noble plan that did credit to Meltzer's heart and mind. It is in line with that evolution of the moral sense among mankind which to Huxley's mind constitutes the essential basis and hope of a progressive civilization, and we may assume that sooner or later the seed planted by Meltzer will bear fruit. There will be a world-wide organization such as he dreamed of which will aim to raise international ethics to that standard which now prevails within the confines of every civilized nation.

After Doctor Meltzer's death memorial exercises were held by several of the societies with whose activities he had been especially identified. At the Christmas meeting of the Federation of American Societies for Experimental Biology, held at Chicago, December 28, 1920, Prof. W. H. Howell read a paper commemorative of his life and work in relation to American physiology which was published in *Science*, February 4, 1921. At a meeting of the Society of Clinical Investigation a similar paper was read by Dr. W. T. Longcope, and at a special memorial meeting of the Society for Experimental Biology and Medicine, held in New York on January 6, 1921, addresses were made as follows: Memorial remarks by the president of the society, Prof. Gary N. Calkins; "A tribute to Doctor Meltzer's life and service," by Prof. George B. Wallace; "Doctor Meltzer's message to the present generation," by Dr. Phoebus A. Levene; "Personal Reminiscences of Doctor Meltzer," by Prof. Graham Lusk; "Doctor Meltzer's influence on American physiology," by Prof. W. H. Howell; "Doctor Meltzer's place in American medicine," by Prof. W. H. Welch. These addresses were subsequently published in full by the society in a memorial number of the proceedings of the society, 1921.

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