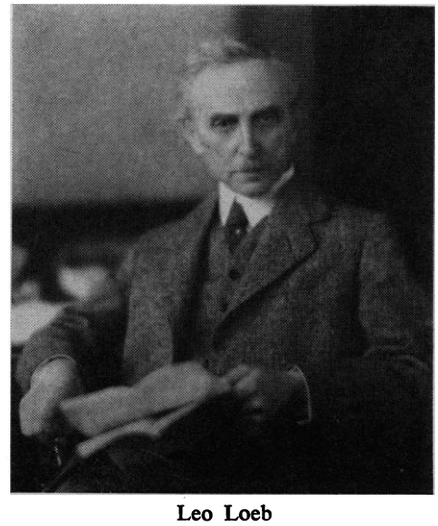
Leo Loeb, Experimental Pathologist and Humanitarian

The year 1959 was celebrated by pathologists the world over as the centennial of the founding of cellular pathology by Rudolf Virchow. The end of the past year (28 December) also witnessed the passing of Leo Loeb, whose scientific accomplishments played a large role in establishing experimental pathology as an important segment of the total discipline of pathology. In its earliest period pathology, along with certain other medical sciences, was largely descriptive and served to correlate the gross and microscopic characteristics of disease with clinical symptoms and to offer a rational basis for therapy. It soon became evident, however, that only by the experimental approach would it be possible to establish with certainty that the conclusions drawn from the descriptive pathological anatomy were valid. Such reasoning provided the motivating force which led to the establishment of experimental pathology shortly before the turn of the century, when Leo Loeb began his scientific career.

The accomplishments of a man are inevitably compared not only with those of his contemporaries but also with those of his predecessors. In this instance, Loeb lived and worked not only during the "Golden Age" of the medical renaissance but also well into the present period, which has seen massive structures erected on the foundations established during the earlier era. His work, as recorded in well over 400 articles, monographs, and volumes, establishes him as a giant of both periods. His name belongs in the "Hall of Fame" of pathology besides the names of Virchow, Rokitansky, Aschoff, Cohnheim, Ribbert, Wells, Welch, MacCallum, Hektoen, and Flexner of the first period, and along with those of Wohlbach, Opie, Goodpasture, Oliver, Ewing, Councilman, Karsner, Bell, and Winternitz of more modern times and the present day.

Loeb was born on 21 September 1869, in Mayen, Germany, when Virchow was 48 years of age. He studied natural sciences and medicine at the universities of Heidelberg, Berlin, Freiburg, Edinburgh, London, and Zurich, in accordance with the custom of the period of studying at various universities in order to work under various prominent men. He received the M.D. degree from the University of Zurich, and for his medical thesis, which was required before he could practice medicine, he chose to carry out experiments in the pathological institute of Hugo Ribbert. Here he carried out his first studies on transplantation, observing the movement of chromatophores and pigmented epithelium that followed the transplantation of black skin into defects in white skin, and vice versa, in the guinea pig.

Shortly after completion of this thesis he came to the United States, in 1897, because he did not approve of the prevailing nationalism and militarism in Germany. He went to Chicago, where his brother, Jacques Loeb, had recently been appointed professor of physiology at the University of Chicago, and set up practice near the university. During this period he continued his research, in a rented room behind a drugstore. His first academic position was as adjunct professor of pathology at the medical school which later became the medical school of the University of Illinois. Later he spent several months in the department of pathology of the Johns Hopkins School of Medicine, at a time when Welch and Flexner were active. He subsequently spent a year as a research fellow at McGill University and then went to the University of Pennsylvania as assistant professor of experimental pathology. He remained at Pennsylvania from 1903 to 1910, when he accepted a position as director of research at the Barnard Skin and Cancer Hospital in St. Louis. In 1915 he became professor of comparative pathology at Washington University School of Medicine, and in 1924, at the age of 55, he succeeded Eugene Opie as professor and chairman of the department of pathology. He remained active in this position until 1937, when he became emeritus professor of pathology, and he continued active in research until 1941. From then on until his death he continued to work at home, gathering material for two books, one on cancer and the other, a philosophical work, on some general problems of human life.



Leo Loeb

In 1922 he married Georgiana Sand, who had studied medicine at Johns Hopkins and had served as an interne under Osler. Their more than 37 years of married life were happy ones. Mrs. Loeb was very much interested in the scientific activities of her husband, advising him in his work and assisting in the editing of his publications. They spent their summers at Woods Hole, Massachusetts, where Loeb was able to combine work and pleasant relaxation, away from the heat of St. Louis.

Many interesting anecdotes of Loeb's life are told in his autobiographical notes, published in *Perspectives in Biology and Medicine* in 1958 and written at the request of the editors. With characteristic shyness, modesty, and humility, his own evaluation of his scientific accomplishments in this article hardly does justice to their significance. His earliest studies on wound healing and the movement of epithelial cells through the blood clot covering the wound led to work on the cultivation of tissues in clots in test tubes. Thus he became one of the pioneer investi-

gators in the field of tissue culture. These early studies also stimulated studies on blood coagulation and the demonstration of tissue factors involved in this phenomenon, including tissue fibrinolysins; concomitant investigations were carried out on the movement and migration of cells and on the coagulation of protoplasm in various invertebrates and vertebrates. Loeb ventured into an unrelated field and became interested in the effects of the venom of *Heloderma*; the results of this work were published in a separate volume by the Carnegie Institution in Washington, in 1913. His work on edema was published in a separate monograph in 1923 and was the forerunner of present-day work on inflammation.

A large part of Loeb's scientific life was spent in studying growth and transplantation—work which probably also stemmed from his initial interest in wound healing and tissue culture. In successfully transplanting tumors he became the originator of a technique which has served investigators in the field of oncological research to the present day and has led to much of our knowledge about cancer. His studies on the fate of a tumor transplanted into hosts bearing spontaneous tumors or an initial tumor transplant constituted one of the earliest demonstrations of immune processes against tumor cells. For a time he also worked in the field of cancer chemotherapy, testing the effects of colloidal copper, hirudin, and other substances on cancer cells.

He was intensely interested in the influence of hormones on growth processes. In this connection he worked out the cyclic changes in the ovaries and mammary glands and their regulation by the anterior hypophysis. He investigated the responses of the endometrium to ovarian hormones, including the development of placentomata by a combination of corpus luteum hormone and local mechanical stimulus. He also demonstrated factors which regulate the life of the corpus luteum. A by-product of these studies on the ovary was the discovery of the phenomenon of parthenogenesis in the guinea-pig ovary. The recognition of the regulatory role of the anterior hypophysis led to the demonstration of the relation between the thyroid and pituitary, in which Loeb was able to demonstrate the role of thyroid-stimulating hormone in the development of hyperthyroidism and exophthalmos. The phenomenon of compensatory hypertrophy of endocrine glands and the influence of nutritional factors on endocrine activity also occupied his interest for a time. Much of this work was instrumental in establishing the nature of homeostatic mechanisms operative in the endocrine system. His work on experimental myocarditis and cardiac hypertrophy produced by adrenalin was a forerunner of present-day studies on alarm and stress phenomena.

Probably Loeb's most important contribution in the field of cancer was that dealing with the interrelation of hereditary and hormonal factors in the development of mammary cancer. His studies describing the progressive growth changes in the mammary gland leading to cancer have led to the present-day concept of malignancy with hormone dependency preceding the development of tumor autonomy, a concept which establishes the rationale for the present-day practice of performing a gonadectomy or hypophysectomy, or both, in the treatment of certain malignancies.

There is presently much activity in the field of transplantation, and for this, Loeb is largely responsible. He first worked out the role of genetic constitution in the determination of the fate of a transplant. He also studied the influence of an initial graft on the fate of a second graft in the same host. The first type of experimentation led to his basic concept of the "individuality differential," and the second, to a demonstration of the role of immune processes in the transplantation reaction. A by-product of these studies was the demonstration of the potential immortality of mammalian tissues, by successive homografts of the same transplant through a number of generations of hosts. The work on transplantation was published in a volume titled *The Biological Basis of Individuality*, published in 1941, and this should be required reading for all investigators working in this field.

These monumental contributions did not go without recognition during Loeb's life. In 1935 he was awarded the Phillips memorial prize for the work on thyroid-pituitary relations. In the same year a lectureship was established in his honor at Washington University. In recognition of his work on hormones and aging processes he was invited to deliver a Harvey lecture in 1941. A special number of the *A.M.A. Archives of Pathology* was dedicated to him in 1950, and a few years ago he received a medal from the City of Hope for his work on cancer research. He was elected president of the Association for Cancer Research in 1911, and of the American Association of Pathologists and Bacteriologists in 1914.

While Loeb's scientific accomplishments are well known, few people are familiar with his thoughts on "psychical factors in human life." The latter appeared in print in brief form only, in his autobiographical notes. In the sphere of human psychical activity he described "hypnosuggestion," a process part hypnotic and part suggestive, which is more or less automatic and dominates such things as learning, tradition, conversation, and fashion. He considered hypnosuggestion to be responsible for imitation, conventionality, and even cruelty. At a higher level of mental activity he placed "reasoning thought," which motivates our competitive struggle for material and psychical goods, and at a still higher level, philosophic and scientific thought, through which human beings identify their own interests with those of their fellow men. It is evident from his briefly published notes that his interest in psychical factors was motivated by a desire to understand the deficiencies in human life and the compensatory reactions which are at the root of "man's inhumanity to man," since it is only through the universal understanding of the basis of such deficiencies that man's lot on this earth can be improved. Here we find the exemplification of Leo Loeb the philosopher and humanitarian, and gain insight into those values which motivated his life and which he has left as a legacy to be passed on to future generations.

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