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SYMPOSIUM: HIGHLIGHTS OF THE ISOLS/MSTS 2009 MEETING

Biographical Sketch

Otto Heinrich Warburg, PhD, MD

Richard A. Brand MD

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Abstract This biographical sketch of Otto Heinrich Warburg corresponds to the historic text, The Classic: The Chemical Constitution of Respiration Ferment (1928), available at DOI 10.1007/s11999-010-1534-y.

Otto Heinrich Warburg was born in 1883 in Freiburg, Germany, of a prominent family: his forebears included philosophers, scientists, artists, financiers, and philanthropists [1]. He studied chemistry under Emil Fischer in Berlin, and received a doctorate in chemistry in 1906. He subsequently studied medicine at Heidelberg, where he was awarded his doctorate of medicine in 1911. From 1908–1914 he was associated with the Stazione Zoologica in Naples, where he began research into oxygen consumption in sea urchin eggs and discovered after fertilization the respiration rates increased as much as 6 fold.

Warburg, a lifelong equestrian, served in an elite cavalry unit during WW I, and was awarded the Iron Cross. Toward the end of the war, Albert Einstein (a friend of Otto's father, Emil, a famous physicist) encouraged him to return to academia, and he assumed a position as Professor in the Kaiser Wilhelm Institute for Biology (subsequently renamed the Max Planck Society in 1948, and a source of 34 Nobel Laureates).

In a paper published in 1928 which we reproduce here as a Classic, "The Chemical Constitution of Respiration Ferment" [4], Warburg described the essential "ferments" involved in cell respiration. Warburg defined ferments as "substances which effected chemical reaction in living matter" and which occurred in such small concentrations they were hitherto unmeasurable: attempts to identify the substances usually destroyed them. (While ferments by definition converted one substance to another they included but were neither limited to enzymes nor to living systems.) He found, "…the respiratory ferment has three characteristics: It reacts reversibly with CO and O_2; it is distributed between CO and O_2 according to the definite equation of distribution; in combination with CO it is sensitive to light."

In 1931 Warburg became director of the Kaiser Wilhelm Institute for Cell Physiology. It was in that same year he was awarded the Nobel Prize in Physiology Or Medicine for his work on the aerobic and anaerobic metabolic process in cells:

> "At Heidelberg he worked on the process of oxidation. His special interest in the investigation of vital processes by physical and chemical methods led to attempts to relate these processes to phenomena of the inorganic world. His methods involved detailed studies on the assimilation of carbon dioxide in plants, the metabolism of tumors, and the chemical constituent of the oxygen transferring respiratory ferment. Warburg was never a teacher, and he has always been grateful for his opportunities to devote his whole time to scientific research. His later researches at the Kaiser Wilhelm Institute have led to the discovery that the flavins and the nicotinamide were the active groups of the hydrogen-transferring enzymes. This, together with the iron-oxygenase discovered earlier, has given a complete account of the oxidations and reductions in the living world.

R. A. Brand (✉)
Clinical Orthopaedics and Related Research, 1600 Spruce Street, Philadelphia, PA 19103, USA
e-mail: dick.brand@clinorthop.org

> For his discovery of the nature and mode of action of the respiratory enzyme, the Nobel Prize has been awarded to him in 1931. This discovery has opened up new ways in the fields of cellular metabolism and cellular respiration. He has shown, among other things, that cancerous cells can live and develop, even in the absence of oxygen" [3].

Warburg was nominated for a second Nobel Prize in 1944 for his work on fermentation, and according to some sources was awarded the second prize, but was unable to accept it owing to a 1937 decree by Hitler preventing Germans from accepting the award [1]. Among many other honors and awards, he was a member of the Royal Society of London, and holder of the French l'Ordre pour le Mérite, and in 1965 received an honorary doctorate from Oxford.

In a later paper, "The Metabolism of Tumors in the Body" [6] Warburg raised the question, "of whether tumor cells in living animals can be killed off through lack of energy, and the related question of how the tumors are supplied with oxygen and glucose in the body." He began with the premise that: "…tumor cells obtain the energy required for their existence in two ways: by respiration and by fermentation. In respiration they burn organic materials to carbon dioxide and water; in fermentation they split glucose to lactic acid." (Respiration is an aerobic process requiring oxygen, while fermentation is an anaerobic process.) He noted that all tumors studied at the time behaved the same. Since tumor cells could exist by respiration independent of fermentation, they did not need glucose, and therefore starving tumor cells of glucose would not kill them. On the other hand, "In order to kill tumor cells…through want of energy it is necessary…to stop respiration as well as fermentation." He kept animals with tumors for 40 hours in an atmosphere of 5 volume-per-cent oxygen with ammonia to prevent acidosis and found most tumor cells had died.

In a 1966 lecture to the meeting of Nobel Laureates at Lindau on Lake Constance, Warburg commented,

> "Cancer, above all other diseases, has countless secondary causes. But, even for cancer, there is only one prime cause. Summarized in a few words, the prime cause of cancer is the replacement of the respiration of oxygen in normal body cells by a fermentation of sugar. All normal body cells meet their energy needs by respiration of oxygen, whereas cancer cells meet their energy needs in great part by fermentation. All normal body cells are thus obligate aerobes, whereas all cancer cells are partial anaerobes. From the standpoint of the physics and chemistry of life this difference between normal and cancer cells is so great that one can scarcely picture a greater difference. Oxygen gas, the donor of energy in plants and animals is dethroned in the cancer cells and replaced by an energy yielding reaction of the lowest living forms, namely, a fermentation of glucose" [5].

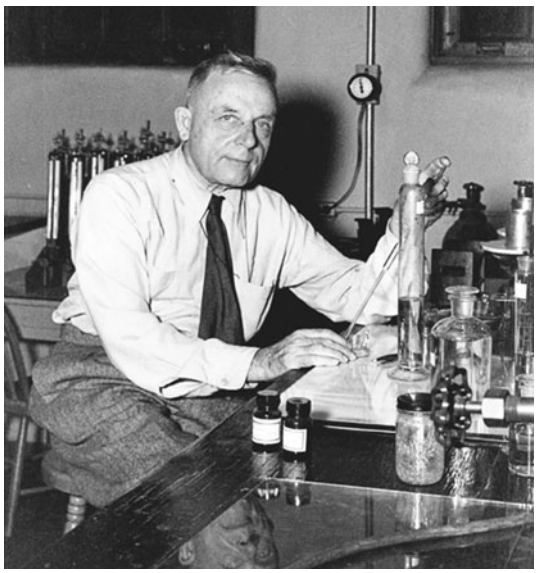

Fig. 1 Otto Heinrich Warburg, PhD, MD is shown. Archiv der Max-Planck-Gesellschaft, Berlin-Dahlem.

While Warburg's basic discoveries have not resulted in treatments for cancer, he always believed they had the potential to do so and research continues today in this potentially fruitful area. Warburg never married and showed little interest in social activities. Rather, he preferred working long hours and maintained his life-long interest in equestrian activities [2]. In his later life, he apparently became somewhat eccentric regarding his eating habits, insisting on organic foods long before the current trend, even taking his own produce to restaurants. He maintained his post as director of the Max Planck Institute until his death in 1970.

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