SCIENTIFIC PUBLISHING CENTENNIAL

1916-2016

AACR American Association for Cancer Research

1916 AACR Launches the First English-Language Cancer Journal, *The Journal of Cancer Research*

RICHARD WEIL, MD, EDITOR, 1916-1917

Early in his short career, Dr. Weil became an expert on hemolysis and on anaphylaxis, setting the stage for his interest in cancer immunology. He earned his MD from Columbia University College of Physicians and Surgeons in 1900 and did postdoctoral studies in Europe. He was chair of the Department of Experimental Medicine at Cornell University Medical College and president of the American Association of Immunologists. Commissioned into the Army Medical Corps in 1917, Dr. Weil was appointed chief of the medical staff at Camp Wheeler in Georgia, where he contracted pneumonia and died in 1917 at age 41. Given today's emphasis on immune therapy, it is fitting that 100 years ago the first AACR editor was an immunologist.

THE JOURNAL OF CANCER RESEARCH

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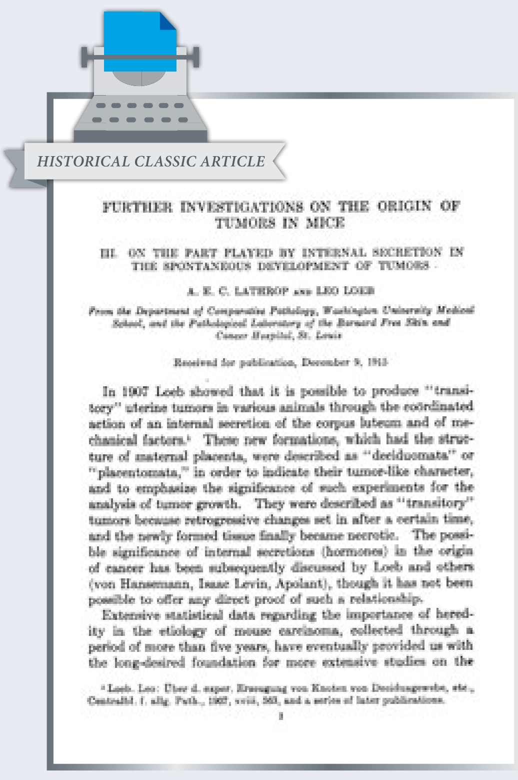
Pioneering Report Links Hormones to Cancer



HISTORICAL CLASSIC ARTICLE

FURTHER INVESTIGATIONS ON THE ORIGIN OF TUMORS IN MICE

III. ON THE PART PLAYED BY INTERNAL SECRETION IN THE SPONTANEOUS DEVELOPMENT OF TUMORS

A. E. C. LATHROP AND LEO LOEB

From the Department of Comparative Pathology, Washington University Medical School, and the Pathological Laboratory of the Barnard Free Skin and Cancer Hospital, St. Louis

Received for publication, December 9, 1915

In 1907 Loeb showed that it is possible to produce "transitory" uterine tumors in various animals through the coördinated action of an internal secretion of the corpus luteum and of mechanical factors.[1] These new formations, which had the structure of maternal placenta, were described as "deciduomata" or "placentomata," in order to indicate their tumor-like character, and to emphasize the significance of such experiments for the analysis of tumor growth. They were described as "transitory" tumors because retrogressive changes set in after a certain time, and the newly formed tissue finally became necrotic. The possible significance of internal secretions (hormones) in the origin of cancer has been subsequently discussed by Loeb and others (von Hansemann, Isaac Levin, Apolant), though it has not been possible to offer any direct proof of such a relationship.

Extensive statistical data regarding the importance of heredity in the etiology of mouse carcinoma, collected through a period of more than five years, have eventually provided us with the long-desired foundation for more extensive studies on the

[1] Loeb, Leo: Über d. exper. Erzeugung von Knoten von Deciduagewebe, etc., Centralbl. f. allg. Path., 1907, xviii, 563, and a series of later publications.

1

Abbie E.C. Lathrop

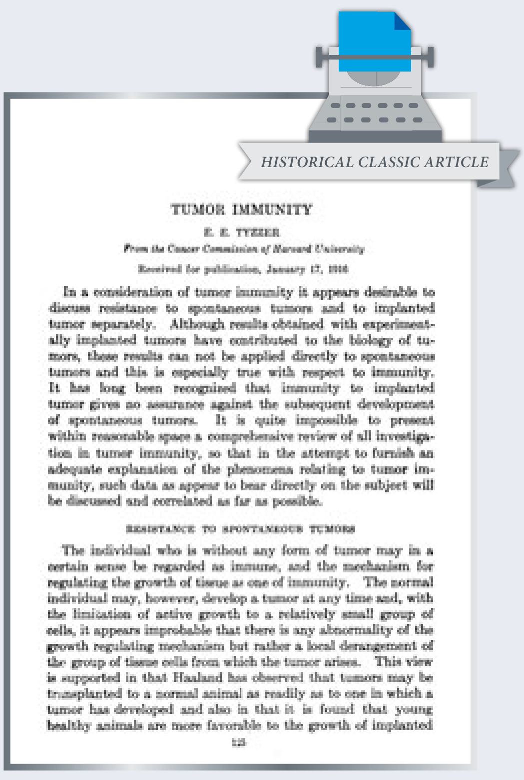
Leo Loeb

One of the first published animal studies suggesting that hormones (secretions from the corpus luteum) play a role in tumorigenesis. The study showed that tumor development can be delayed or eliminated by removing the ovaries of young female mice. The hormone was identified as estrogen 8 years later by Edgar Allen and Edward Doisy. The article also represents one of the first studies in prevention (oophorectomy).

First Use of the Term "Somatic Mutation" in Discussing Cancer Proliferation

Ernest E. Tyzzer

In a ground-breaking early report on the role of genetics in the propagation of cancer, AACR past president Ernest E. Tyzzer discussed the concepts of immune reaction, inflammation, and the tumor microenvironment. He is the first to propose the use of the term somatic mutation.



HISTORICAL CLASSIC ARTICLE

TUMOR IMMUNITY

E. E. TYZZER

From the Cancer Commission of Harvard University

Received for publication, January 17, 1916

In a consideration of tumor immunity it appears desirable to discuss resistance to spontaneous tumors and to implanted tumor separately. Although results obtained with experimentally implanted tumors have contributed to the biology of tumors, these results can not be applied directly to spontaneous tumors and this is especially true with respect to immunity. It has long been recognized that immunity to implanted tumor gives no assurance against the subsequent development of spontaneous tumors. It is quite impossible to present within reasonable space a comprehensive review of all investigation in tumor immunity, so that in the attempt to furnish an adequate explanation of the phenomena relating to tumor immunity, such data as appear to bear directly on the subject will be discussed and correlated as far as possible.

RESISTANCE TO SPONTANEOUS TUMORS

The individual who is without any form of tumor may in a certain sense be regarded as immune, and the mechanism for regulating the growth of tissue as one of immunity. The normal individual may, however, develop a tumor at any time and, with the limitation of active growth to a relatively small group of cells, it appears improbable that there is any abnormality of the growth regulating mechanism but rather a local derangement of the group of tissue cells from which the tumor arises. This view is supported in that Haaland has observed that tumors may be transplanted to a normal animal as readily as to one in which a tumor has developed and also in that it is found that young healthy animals are more favorable to the growth of implanted

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Annual Meeting Proceedings Published (1915 Annual Meeting)

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AACR American Association for Cancer Research

1917

AACR Secretary-Treasurer Selected as New Editor

WILLIAM H. WOGLOM, MD, EDITOR, 1917-1923

A pioneer in the study of tumor transplantation, Dr. Woglom was known for his many thoughtful, scholarly treatises such as the 1913 review, "The Study of Experimental Tumors." Dr. Woglom received his MD from the College of Physicians and Surgeons of Columbia University in 1901 and worked in pathology and bacteriology in several New York hospitals before he joined Columbia's cancer research institute, which became the George Crocker Special Research Fund. The Crocker Fund provided financial aid to two early AACR journals. Dr. Woglom was AACR Secretary-Treasurer from 1917 to 1935 and President in 1936. His sustaining vision throughout his career was that "effectual interference with incessantly proliferating cells will become a reality."

1918

Landmark Report of Coal Tar Inducing Carcinoma (findings first published in Japanese in 1915)

HISTORICAL CLASSIC ARTICLE

EXPERIMENTAL STUDY OF THE PATHOGENESIS OF CARCINOMA[1]

KATSUSABURO YAMAGIWA AND KOICHI ICHIKAWA

From the Pathological Institute of the Medical College of the Imperial University, Tokyo, Japan

Received for publication, May 24, 1917

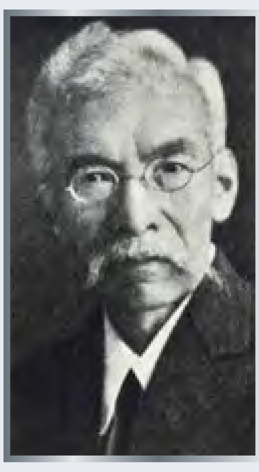
The problem of the etiology of tumors, and in particular of carcinoma, has been investigated for a great many years, but has not yet been solved. Many suggestions have been offered, among which Virchow's and Cohnheim's are especially prominent; both of these, however, were the result of clinical experience rather than of experimental study; hence, the adherents of these hypotheses have tried subsequently to establish them by means of experiments, the object of which has been artificially to produce carcinoma. But all attempts have proved negative, until Fibiger (1), of Copenhagen, finally succeeded in producing papilloma and carcinoma in the stomach and the esophagus of rats by infecting them with spiroptera; the origin of these new growths he referred to irritation of the mucous membrane of the stomach and the esophagus by the parasite. Thus the soundness of Virchow's irritation hypothesis has been demonstrated experimentally for the first time.

To this problem we also have devoted ourselves for four years (12, 13, 14, 15, 16, 17, 18, 19, 20), pursuing experiments in accordance with Yamagiwa's view (2), which he has expressed as follows: The repetition or continuation of chronic irritation may cause a precancerous alteration in epithelium previously normal. If the irritant continue its action, carcinoma may be the outcome, even though no specific agent has been interpolated.

[1] The authors have not read the proof of this article.

1

The authors used an irritant in the form of coal tar to induce carcinoma on the ears of rabbits, with continual application. Lymph node metastases were subsequently discovered in two animals. These studies ushered in the field of experimental chemical carcinogenesis and were also important in studies of occupational exposure to carcinogens.



Katsusaburo Yamagiwa

Koichi Ichikawa

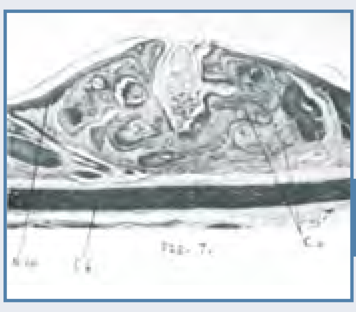


FIGURE 7. Fourth case of carcinoma in its earliest stage, 118th day. Hematoxylin-eosin. Zeiss microplanar 35 mm.

1924

Director of Columbia's Crocker Institute Named Editor

FRANCES C. WOOD, MD, EDITOR, 1924-1940

Renowned as an expert in pathology and the use of radiation in cancer, Dr. Wood founded both the Crocker Institute at Columbia and the pathology laboratory at St. Luke's Hospital in New York. He raised funds to buy Marie Curie radium and made important discoveries about voltage and duration in radiotherapy. Dr. Wood received his MD degree in 1884 from Columbia College of Physicians and Surgeons and later studied in Europe. He served two terms as AACR President (1917 and 1931). He was a prolific writer of articles and books, and during his term as Editor many claims for cancer cures were made. Dr. Wood remained a sceptic of such claims, noting "There are many cures for cancer; the problem is to keep the patient alive."

First Presidential Address Published (Willy Meyer, President in 1922)

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1925

Extensive Family Study Establishes the Inheritability of Some Cancers


HISTORICAL CLASSIC ARTICLE

THE FURTHER STUDY OF A CANCER FAMILY

ALDRED SCOTT WARTHIN

An extensive study of a high degree of inheritability of cancer in a family, known as Family G (the finding was initially called cancer family syndrome, later Lynch syndrome). These studies led to establishing that colorectal cancer and endometrial cancer occurred in relatives. Family G continued to be studied for decades.

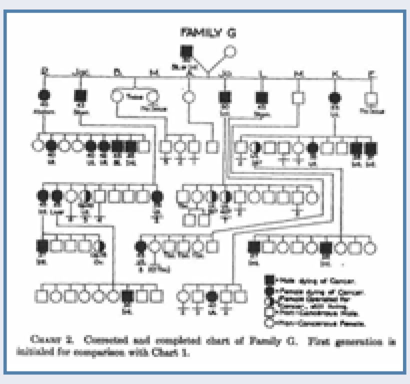
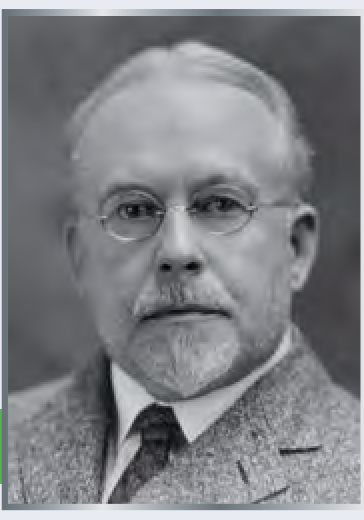


CHART 2. Corrected and completed chart of Family G. First generation is initialed for comparison with Chart 1.


Aldred Scott Warthin

1928

Ovarian Secretions Linked to Breast Cancer

A key study that demonstrated the protective effect of ovariectomy in the development of mammary tumors in mice as well as the protective effect of not breeding. The study also showed that if carefully inbred mouse strains are used, mammary carcinomas could be produced in castrated male mice implanted with ovaries.


William S. Murray


HISTORICAL CLASSIC ARTICLE

OVARIAN SECRETION AND TUMOR INCIDENCE

WILLIAM S. MURRAY

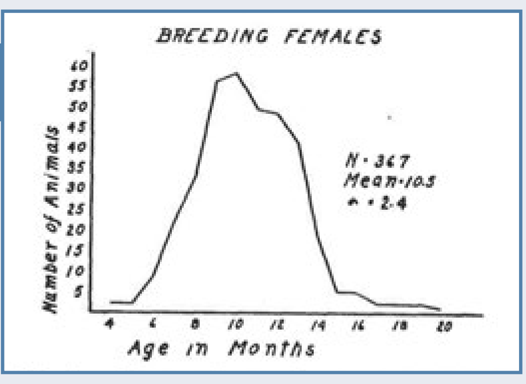


FIGURE 1. This curve shows the relative frequencies with which the neoplasms occur during successive thirty-day periods.

1931

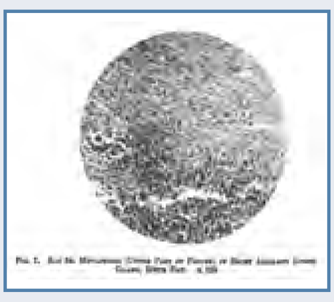
The American Journal of Cancer Replaces *The Journal of Cancer Research*

1932

Early Evidence Links Cancer to Smoking; Cited in 1964 Surgeon General's Report


HISTORICAL CLASSIC ARTICLE

THE EXPERIMENTAL PRODUCTION OF TUMOURS OF CONNECTIVE TISSUE



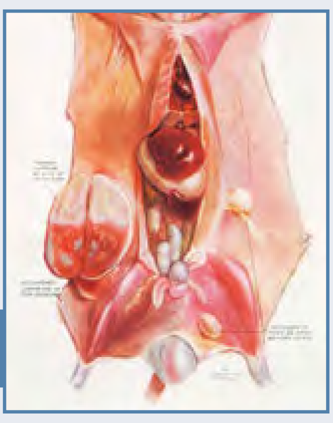


FIGURE 12. Rat 14: Primary tumour, 176th day; secondary growths in peritoneum, and autographs.

The isolation of chemical compounds from coal tar elicited numerous studies to find chemical structure analogues for carcinogenic activity. Such studies were largely reported piecemeal in the chemistry literature. The report by Kennaway and colleagues was the first in the cancer literature to report the use of hydrocarbons of the benzanthracene group to produce connective tissue tumors in mice. Two reports later in 1932 further implicated tar in smoking-related cancer (McNally WD. The tar in cigarette smoke and its possible effects. Am J Cancer 1932;16:1502-14. Bogen E, Loomis RN. Tobacco tar: experimental investigation of its alleged carcinogenic action. Am J Cancer 1932;16:1515-21).

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1933

The American Journal of Cancer Begins Monthly Publication

1934

Carcinomas in Frogs Linked to a Virus

HISTORICAL CLASSIC ARTICLE

A NEOPLASTIC DISEASE OF THE KIDNEY OF THE FROG, RANA PIPIENS

BALDUIN LUCKÉ

Extensively documented cases showed virally induced renal tumors in frogs, with the author also doing a broad review of the literature. Support for the author's conclusion of a viral origin came several years later. Such veterinary studies advanced the field of human tumor virology substantially.

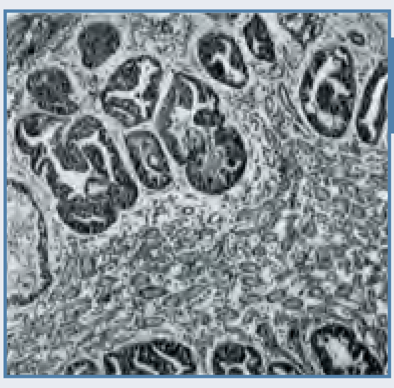


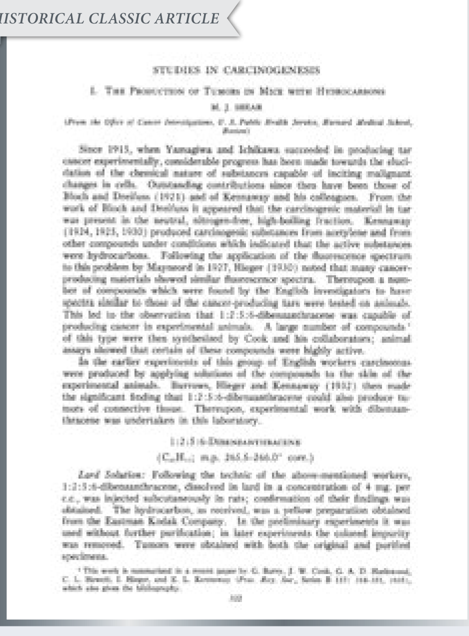
FIGURE 9. Margin of a tumor, showing many gland-like projections of the principal growth extending into the adjacent kidney tissue.

FIGURE 16. Camera lucida drawing of the nuclei to illustrate variation in size and shape of nuclei and of their inclusions.

1936

Studies of Chemical Carcinogenesis Trigger Chemotherapy Investigations

HISTORICAL CLASSIC ARTICLE

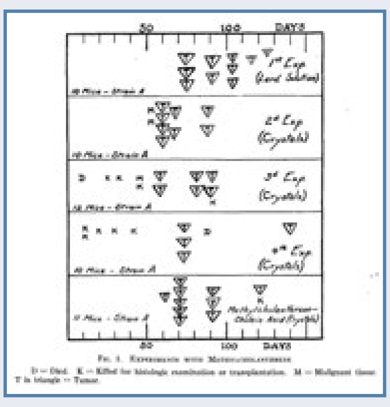


STUDIES IN CARCINOGENESIS

I. The Production of Tumors in Mice with Hydrocarbons

M. J. SHEAR

The first article of an extended series in AACR journals reported studies on chemical carcinogenesis. These seminal investigations reinforced the notion that if chemicals could produce cancer they might also eliminate it; subsequently Shear and other investigators began the study of chemotherapy at the National Cancer Institute.

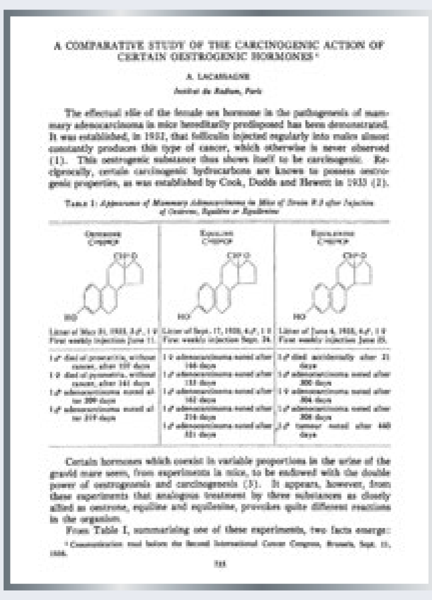


Murray J. Shear

Estrogen Plays a Key Role in Breast Cancer

HISTORICAL CLASSIC ARTICLE

THE AMERICAN JOURNAL OF CANCER



A COMPARATIVE STUDY OF THE CARCINOGENIC ACTION OF CERTAIN OESTROGENIC HORMONES

A. LACASSAGNE

In the first English-language reports of estrogen inducing mammary tumors in mice, Lacassagne hypothesized that an antagonist was needed to stop the action of estrogen in women with a hereditary disposition to breast cancer. His work caused a sensation when presented at the 1936 AACR Annual Meeting.

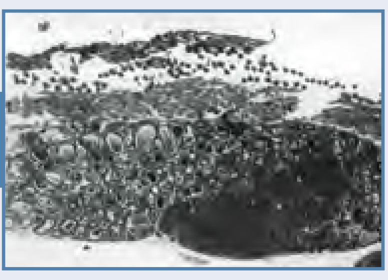


FIGURE 6. Breast of male mouse 179 days after beginning of oestrone injections, showing adenocarcinoma.

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AACR American Association for Cancer Research

1936

Radiation Produces Genetic Changes Leading to Cancer in Mice

HISTORICAL CLASSIC ARTICLE

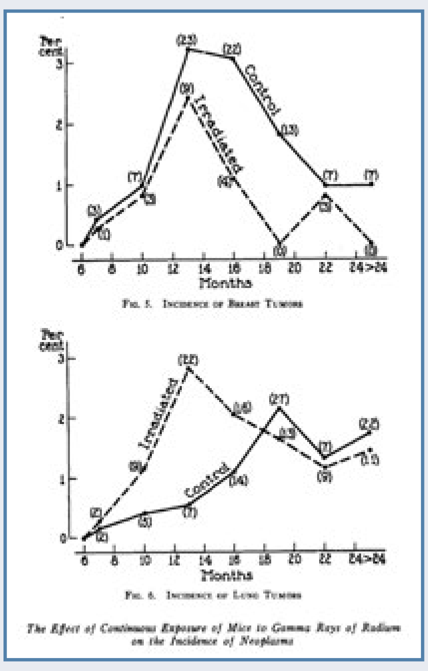

Fig. 5. Incidence of Breast Tumors

Fig. 6. Incidence of Lung Tumors

The Effect of Continuous Exposure of Mice to Gamma Rays of Radium on the Incidence of Neoplasms

Ionizing radiation caused the induction of leukemia and other cancers in strains of inbred mice. Although this was not the first report of radiation-induced cancer, previously the cancer was thought to be the result of the burns, not the x-rays causing a genetic change and a "malignant transformation."

1937

Transplanting Even One Malignant Cell Can Produce Leukemia in Mice

A landmark study evoked the principles of cancer stem cells by showing that a single leukemic cell could transmit and maintain systemic disease when transplanted into a mouse.

Jacob Furth

HISTORICAL CLASSIC ARTICLE

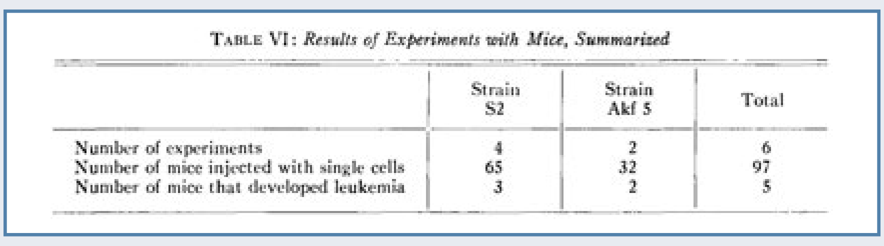

Table VI: *Results of Experiments with Mice, Summarized*

	Strain S2	Strain Akf 5	Total
Number of experiments	4	2	6
Number of mice injected with single cells	65	32	97
Number of mice that developed leukemia	3	2	5

1940

Caloric Intake Affects Tumor Growth

HISTORICAL CLASSIC ARTICLE

Pioneering studies lead to the first report linking caloric intake to the initiation and growth of tumors in mice. Caloric restriction of one third of an unrestricted diet led to a reduction in growth of spontaneous and induced tumors.

FIGURE 2. Representative animals of Experiment III: Five on the left underfed; those on the right full fed.

The American Journal of Cancer Ceases Publication; Launch of *Cancer Research* is Announced

THE AMERICAN JOURNAL OF CANCER

A Continuation of The Journal of Cancer Research

Volume XL — December, 1940 — Number 4

Editorial

HISTORICAL CLASSIC ARTICLE

SCIENTIFIC PUBLISHING CENTENNIAL

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