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SATURDAY, AUGUST 12, 1939

METABOLIC CHARACTERISTICS OF CANCEROUS TISSUE

The first significant advance in the study of the metabolism of tumors was made by Warburg,¹ who developed evidence of an altered carbohydrate metabolism of tumors. Thus was shown the ability of tumors to ferment aerobically from 90 to 95 per cent of available dextrose with the formation of lactic acid instead of oxidizing the carbohydrate to carbon dioxide and water as in normal tissue metabolism. This abnormal type of metabolism is not limited to malignant tissue, however. It has been found to be characteristic of all fast growing tissues. Kögl and Erxleben² have recently reported that several amino acids in malignant tissues occur as the unnatural stereo-isomers. While the significance of this remarkable fact cannot now be adequately evaluated, it is the first definite evidence of a qualitative difference in the metabolism of normal and malignant tissues.

An analysis of the protein hydrolysates of four malignant tumors indicated that as much as 42 per cent of the glutamic acid was present in the unnatural dextro-rotatory form. Lysine and leucine were also found as their unnatural stereo-isomers in smaller quantities. Similar hydrolysis of normal tissue yielded only the natural levorotatory forms of these amino acids. Since the enzyme system involved in the synthesis and degradation of each of the optically active isomers is highly specific, the presence of the unnatural forms would indicate that the particular tumor enzymes needed to metabolize these amino acids are less specific or are present in forms not native to normal tissue. The synthesis of protein, which is represented in the tumor by its rapid growth, is a result of the coordinating action of these different proteolytic enzymes; such a marked qualitative difference in behavior might greatly alter the rate of growth or regression (lysis) of the tumor.

1. Warburg, Otto: Ueber den Stoffwechsel der Tumoren, Berlin, Julius Springer, 1926.

2. Kögl, Fritz, and Erxleben, Hanni: Ztschr. f. physiol. Chem. **258**: 57 (Nos. 2 and 3) 1939.

In view of the important role which recent progress in biochemistry has given to glutamic acid in linking intermediary carbohydrate metabolism with protein metabolism, the results reported by Kögl and Erxleben are of special importance. Euler and his co-workers³ have separated from normal liver tissue a specific enzyme which, when supplemented with the oxidized form of coenzyme (dehydrocozymase), dehydrogenated glutamic acid, while, in the presence of the reduced form of the coenzyme, the enzyme synthesized glutamic acid from ammonia and α -ketoglutaric acid, which is a product of carbohydrate metabolism. Only the normal levorotatory form of glutamic acid is dehydrogenated by this enzyme from normal liver.

Braunstein and Kritzmann⁴ have further shown the importance of glutamic acid as a key substance in tissue metabolism by experiments in which the enzyme system of tissues was able to transfer the amino group from certain amino acids to α -ketoglutaric acid with the formation of glutamic acid, or reverse this transfer. While these authors found this transaminating enzyme system in all tissues except tumor tissue or nucleated red blood cells, Euler reports that it is present in tumor tissue but in smaller amounts than in muscle tissue.

The intensive investigations of tissue metabolism are constantly yielding new knowledge concerning the enzymic activities of normal and malignant tissues. If the observations of Kögl and Erxleben can be confirmed by other workers and it is found that all types of malignant tissues contain the unnatural forms of amino acids, a new and fertile field for study into the nature of cancer will be opened.

LISTERINE AND ALKA-SELTZER—THE FEDERAL TRADE COMMISSION TAKES ACTION

Some of the most interesting folklore in the development of American advertising—legends long accepted by many popular periodicals and by many people—is about to pass into the limbo of forgotten things. The Wheeler-Lea legislation seems to be functioning.

On August 3 the Federal Trade Commission entered into a stipulation with the Lambert Pharmacal Company of St. Louis, manufacturer of "Listerine Antiseptic," to cease and desist from "representing, by direct statement or by inference, that all dandruff is due to an infection with Pityrosporon ovale or any other organism; that dandruff necessarily is a germ disease; that the dandruff germ has been isolated or identified; that the presence of Pityrosporon ovale necessarily means dandruff or that with its destruction dandruff disappears; that dandruff is necessarily infectious, contagious or 'catching' or is in all instances passed from one person to another, or that any of the foregoing

3. von Euler, Hans; Adler, Erich; Günther, Gunnar, and Das, Nalin Bandhu: Ztschr. f. physiol. Chem. **254**: 61 (No. 2) 1938.

4. Braunstein, A. E., and Kritzmann, M. G.: Nature **140**: 503, 1937. Enzymologia **2**: 129, 1937.

assertions have been proven by findings of scientists or otherwise, or is a 'scientific fact' or a 'fact definitely established by scientists.'"

The Federal Trade Commission said, moreover, "that it is also stipulated that the respondent desist from representing that the product either cures or permanently relieves dandruff; that the product 'kills the dandruff germ,' 'attacks the cause of dandruff,' 'or gets at the cause' or 'at the root of the trouble' or penetrates infected hair follicles or 'annihilates' the dandruff germ; that the product frees the scalp and hair follicles of the parasite that saps their vitality or 'spreads a germ-killing film over the scalp'; that the product has 'marked curative properties due to certain ingredients in a unique combination shared by no other antiseptic'; that ordinary remedies 'aren't even antiseptic,' are 'smelly,' affect only surface symptoms, or merely remove surface symptoms temporarily, or that competitive products are obviously inferior to 'Listerine Antiseptic' as a remedy for dandruff—when such are not the facts."

The so-called research on which the claims of the manufacturer for this alleged virtue of listerine were based had never been accepted by competent dermatologists as authoritative; certainly there was not the slightest controlled evidence to indicate that listerine or any similar combination could have such virtue in controlling dandruff. Thus this product, which is essentially a formula like the liquor antisepticus of the National Formulary, will return to its original claims in relation to overcoming halitosis.

The history of the advertising of listerine as a preventive of halitosis has been told on many occasions. It laid the basis for many a vast advertising campaign associated with diseases discovered by advertising geniuses who thumbed the medical dictionaries. Out of the announcements of halitosis came such emphasis as has been placed on acidosis, athlete's foot, dyskinesia and similar conditions. The halitosis campaign reached its apotheosis with the advertisement which announced that "She Built Her Bridge Table Two Feet Wider." Obviously her breath could be detected two feet away but not four feet from her. Then she tried listerine and didn't have to stretch any more for the cards in the dummy.

The second decision of the Federal Trade Commission, dated August 6, involved a stipulation of the Miles Laboratories, Inc., Elkhart, Ind., with the Federal Trade Commission to discontinue misleading representation in the sale and distribution of Alka-Seltzer. This product is essentially a mixture of sodium acetylsalicylic acid with baking soda, and citric acid. Every one is familiar with the claims that have been made for the product over the radio and in other advertising.

Now the respondent company agrees "to cease the use of advertising matter implying that colds, neuralgia, distress after meals, and 'common everyday ailments' result from excess acidity of the blood, an acid condition of the blood, or deficient alkaline reserve of the blood,

and that alkalinizing effect of 'Alka-Seltzer,' by correcting such acid condition or restoring the alkaline reserve, will be a proper treatment for the ailments mentioned."

The respondent further agreed "to discontinue representations implying that headaches, upset stomach, and aches and pains result from, or are associated with, excess acidity of the blood, an acid condition of the blood, or a deficiency in the alkaline reserve of the blood, except when the ailments mentioned may be shown by competent scientific evidence to be directly associated with such conditions of the blood, and subject to this exception, to cease making representations implying that the taking of 'Alka-Seltzer,' by correcting the acid condition of the blood or restoring its alkaline reserve, will be a proper treatment for such ailments."

The respondent also stipulated "that it would cease representing that other therapeutic effects of 'Alka-Seltzer' exceed the recognized benefits to be derived from neutralization of hyperacidity of the gastric contents or the analgesic and other effects of sodium acetylsalicylate together with the action of buffer salts."

According to an examination of the product in 1932, persons who follow the directions to dissolve two tablets of alka-seltzer in a glass of water get nearly 9 grains of aspirin and nearly 1 grain of salicylic acid with their mixture of citric acid and baking soda. Those who do as suggested and take sixteen such tablets a day get over 70 grains of aspirin and 6 grains of salicylic acid in twenty-four hours. Whether or not the formula has been changed since that time is not known.

It will be interesting to see what the Miles Laboratories, Inc., find to talk about now that the government has told them what they cannot say. Perhaps they will decide to tell the people that what they are offering is essentially an effervescent tablet of aspirin.

THE NATIONAL HEALTH PROGRAM

The Seventy-Sixth Congress adjourned sine die August 5 without acting on the Wagner Health Bill, S. 1620. The Senate Committee on Education and Labor, however, submitted a preliminary report¹ August 4 and announced its intention to submit a definite report soon after the next session of Congress convenes. The subcommittee which has the bill under its immediate consideration plans to report an amended bill. The committee expresses the opinion that federal legislation along the general lines of the Wagner Health Bill is necessary to strengthen the health services of the nation and to make provision for progressive and effective improvement of health conditions in all parts of the country and among all groups of people. The committee was not convinced that the enactment of the bill would bring about revolutionary or dangerous changes in the established methods of medical service.

Congress passed in the last hours of the session just ended an act to amend the Social Security Act, and for other purposes, H. R. 6635, which covers primarily

1. Senate Report No. 1139, 76th Congress, 1st Session.