Leukemia in Infants and Young Children
A New Etiological Concept

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• Dr. McCormick is an active physician of 81 years. He has written numerous papers on nutrition and the hazards of tobacco. He has long been interested in vitamin C deficiency and its relation to the degenerative diseases.

In recent years, mostly within the last decade, there has been an alarming increase in the incidence of leukemia in infants and young children, the cause of which has led to much investigative research and conjecture. In the United States more children, 5 to 14 years of age, are victims of this disease than of any other, and it is invariably fatal[1]. In a recently published report from the Sainte Justine Children's Hospital in Montreal the admissions for leukemia in infants and young children for the five-year period ending with 1958 was approximately twice the total of the previous ten years.[2]

Regarding the cause of this disease, Pierce[3], of the university of Chicago, states that the pathogenesis of congenital leukemia is as obscure as it is in the childhood form, but that existence of the disease in utero suggests that maternal and genetic factors are etiologically significant in both forms. Forty-five cases in the literature are reviewed. Most of these with signs of leukemia at birth had severe systemic involvement and died within a few years. Hemorrhagic manifestations occurred in all cases, ranging from scattered petechiae to confluent ecchymoses and bleeding from the umbilical stump, the gastrointestinal and genitourinary tracts.

Cramblett et al[4] make the first recorded report of the concurrent incidence of leukemia in a mother and her infant. Near the end of the seventh month of pregnancy petechiae and ecchymoses developed spontaneously on the abdomen and lower extremities. Three weeks before delivery gingival bleeding also developed. Eight days after spontaneous labor and birth of an apparently healthy boy the mother developed symptoms of acute leukemia with white-blood-cell count of 25,000 and died about two months later. Her son, at nine months of age, also developed the same disease with white-blood-cell count of 40,000 and the usual hemorrhagic manifestations,--easy bruising, bleeding from the gums, petechiae, ecchymoses and purpuric areas were scattered over the trunk, extremities and

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skull. (The correlated incidence of these two cases is strongly suggestive of the likelihood of unsuspected and unrecognized maternal transmission of this disease in many such cases.—W. J. McC.)

The most generally accepted culpable etiological factor in these infantile leukemic cases has been the exposure of the pregnant mother to diagnostic or therapeutic X rays, thus exposing the unborn child to unintentional irradiation. However, from a careful analysis of this factor Swartz and Upton[5] conclude that prenatal irradiation can account for only a small part of the increasing incidence in infantile subjects.

There is, we think, another major factor in the possible solution of this problem which has been apparently overlooked or ignored, and that is the tobacco smoking of mothers during pregnancy. Tobacco smoking by our female population began on this continent about 40 years ago, following the first Great War, and it must be admitted that the female addiction in this respect is rapidly overtaking that of the male. It must also be recognized that by this time a greatly increasing number of our female population have become heavily addicted (30 to 50 or more cigarettes daily), while at the same time qualifying as contributors to our exploding population.

About 26 years ago a scientific study of the effect of cigarette smoking by prospective mothers on the heart function of their unborn babies was conducted at Antioch College, Yellow Springs, Ohio, by Doctors Sontag and Wallace[6] as part of a study on the effect of prenatal environment. They made over eighty tests on several prospective mothers who were habitual smokers. To begin with, during the interval between smoking, their babies' heart beats averaged 144 per minute, which was 14 beats faster than the normal average, 130, as reported by obstetricians at the turn of the century, before women began smoking. Then when they resumed smoking for the tests their babies' heart beats, within ten minutes, were speeded up to an average of 149 to the minute thus making a total increase of 19 beats per minute above the normal average. It should be pointed out that when these tests were made, very little was known about the cancerogenic tars and other toxic elements in tobacco smoke, and when one considers that many millions of our unborn progeny are continually receiving these and other toxic food preservatives through the medium of their prospective mother's blood, it is little wonder that at the present rate of increase it has been estimated that one-third of our present population may expect to die of cancer. Incidentally, lung cancer and blood cancer (leukemia) are the two most rapidly increasing forms of this disease today.

In confirmation of our hypothesis we cite the observations of Lawrence and Donlan[7] as follows,—"It seems clear that several types of embryonic tissue have a high degree of sensitivity to cancerogenic agents. The acute leukemias are an example of disease that may have such an origin. Leukemia seems to be increasing in recent years, especially in young children under five years, suggestively due to carcinogenic stimulation in prenatal life."

In further support of our hypothesis we cite the work of Ehrhart, Stich and Benoit[8] in which they gave varying doses of a toxic chemical ("indole") to a strain of mice with a normally low incidence of leukemia. To one group they gave 50 mg. of this chemical in divided doses, resulting in an incidence of leukemia in 55% of the animals. To another group of the same strain of mice they gave a smaller dose of the chemical,—30 mg. in divided doses,—which led to an incidence of only 16% of leukemia. These observations give definite support to our concept that tobacco carcinogens, transmitted maternally in prenatal life, may be the culpable agent in the recent upsurge in incidence of infantile leukemia.

A striking feature in all the leukemic cases referred to in this treatise is the uniformity in the incidence of hemorrhagic manifestations, — easy bruising, petechiae, ecchymoses, gingival bleeding, bleeding from the mucous membranes of the gastrointestinal and genitourinary tracts, etc., all of which are very suggestive of a scorbutic background. It is also quite possible that many of the scurvy victims of centuries ago had leukemic complications which were not recognized in the absence of microscopic hematology. As a matter of fact, the great plague,—"the Black Death," which ravaged Europe and Asia in the fourteenth century, got its name from the prevalence of dark "black and blue" patches on the skin, the result of subcutaneous bleeding,—in reality a manifestation of scurvy. It is also worthy of note that an ulcerative and hemorrhagic prelude is usually associated with cancer, which Martini[9] thus relates to scurvy and the "Plague", all of which is indicative of an unrecognized etiological situation warranting investigation,—suggestively vitamin-C deficiency? The recent increase in the incidence of infantile scurvy in our children's hospitals lends support to this concept. However, infants and young children are not unique in this respect. By chemical test we find that fully 90% of our adult population are definitely deficient in vitamin-C status. The increasing use of tea, coffee, tobacco and alcohol are the major contributing factors to this debacle. We regard tobacco as the major offender in this respect, since the toxic fumes are known to have a neutralizing effect on vitamin C[10], and this may, we think, be a preconditioning factor in pathogenesis of cancer[11], including leukemia.

SUMMARY

The author reports a marked increase in the incidence of leukemia in infants and young children, which he attributes to prenatal transmission of cancerogens from tobacco smoking mothers. Several citations are made in support of this concept, and correlation of vitamin-C deficiency (subclinical scurvy) is postulated as the basic etiological factor in the development of the hemorrhagic manifestations.

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ADDENDA

Since publication of this treatise the author has found additional citations from Nothnagel's Encyclopedia of Practical Medicine, American Edition (W. B. Saunders & Co., Philadelphia, 1905) which add support to our concept of Etiology.

In the volume on diseases of the blood, sub-section "Acute Lymphatic Leukemia", we find the following: (under symptoms — pages 552-/74) — "The most striking clinical symptoms of this disease are the hemorrhages and their sequelae. We refer especially to hemorrhages into the skin, the visible mucous membranes and the posterior eye ground; and further, the hemorrhages in the interior of the body — those that are recognizable during life by their clinical results, as of the intestine, the bladder, the brain, and the labyrinth of the ear. Sometime large and deep necroses of the skin arise, which spread rapidly and show not the slightest tendency to heal. The teeth sit loosely imbedded in the spongey remains of the mucous membrane. Every touch produces hemorrhage, making a condition completely identical with that of scorbutus (Scurvy). Especially interesting in this regard is the case of acute leukemia in a seventeen-year-old girl who never, or at most only rarely, ate fresh vegetables, a deficiency always named among the primary causes of scorbutus."

This close linkage with scurvy seems to have been completely overlooked by modern writers on leukemia, the major stress being given to genetic changes in chromosomes, irrespective of possible adverse maternal contributing factors. Ingalls (1956) has this to say: "Congenital defects are not all determined at the moment of conception: many are acquired during the ensuing fetal development. The latter are usually fetal manifestations of critical stress on the mother during pregnancy. Just as the genetically determined defects have been studied in the fruit fly by breeding experiments so the acquired defects have been studied in the gravid mouse by using hypoxia (lack of oxygen) as a standard stress applied to the mother. A large class of congenital defects is therefore preventable".

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