

# This Week's Citation Classic

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Stewart A, Webb J & Hewitt D. A survey of childhood malignancies.

*Brit. Med. J.* 1:1495-508,1958. [Department of Social Medicine, Oxford University, England]

**An association between fetal irradiation and cancers exists which is difficult to detect because childhood cancers may have near-conception origins and early (precancer) effects which increase the risk of dying at an early stage of development. The principal effect of preleukemia is loss of immunological incompetence, but there may also be intolerance of the anoxic conditions of parturition. [The *SCJ*<sup>®</sup> indicates that this paper has been cited over 315 times since 1961.]**

Alice M. Stewart  
Regional Cancer Registry  
Queen Elizabeth Medical Center  
Birmingham B15 2TH England

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"The fetal irradiation story is a triumph for a small group of epidemiologists who used a retrospective survey to detect the cancer association and the same approach to show why so many prospective surveys had negative findings. We were anxious to discover why the post-war increase in leukemia had produced an early peak of leukemia mortality consisting only of lymphatic cases, but we had difficulty in coming to grips with the problem because, even with the increase, leukemia remained a rare cause of childhood deaths. We drew up a plan which entailed asking a nationwide network of medical officers of health to interview mothers of cases and controls under standardized conditions, but this was rejected by the MRC. However, we had enough money to pay for the necessary train

fares, so we went it alone with the results shown in the 1958 paper.

"In this paper there are no answers to our original problem, but it paved the way for a study of any cancer effects of fetal irradiation which eventually showed that 40% of our X-rayed cases (leukemia and solid tumors) were radiation-induced. These cases proved to be a fraction older than a much larger number of idiopathic cases, so we incidentally discovered that all childhood cancers have fetal origins. The paper mentions an association between pneumonia and leukemia which told us that cancers of the immune system might be influencing reactions to other diseases before they were clinically recognizable. With this thought in mind we eventually uncovered a number of facts which led to two conclusions: (1) Infections and injuries are important causes of *pre-cancer* deaths; and (2) These deaths may take the form of abortions, stillbirths, or cot deaths. According to one of our estimates, based on our own data and official statistics, children who develop pneumonia when in an advanced stage of preleukemia are 300 times as likely to have a fatal attack as a normal child!

"For several years, negative findings of prospective surveys were threatening the very existence of our survey. However, obstetric X-rays and difficult deliveries go hand in hand, and none of the rival surveys had controlled either for this effect or for any later environmental influences.

"Finally, antibiotics can prevent infection deaths but not stillbirths or cot deaths, and myeloid leukemias have exceptionally short latent periods. Therefore, the answer to our original problem could be 'selective action of antibiotics on myeloid and lymphatic leukemias with fetal origins.' "