Preliminary Communication

MALIGNANT DISEASE IN CHILDHOOD AND DIAGNOSTIC IRRADIATION IN UTERO

Public-Health departments all over the country are engaged in an environmental survey which will eventually cover some 1500 children who died of leukæmia or malignant disease before the age of 10 in the years 1953-55. As yet only approximately a third of the casematerial has been gathered, but preliminary analysis has yielded a result which should, we feel, be reported without further delay.

The survey covers the whole of England and takes the following form.

The addresses of all children certified as dying from leukemia or malignant disease during the three years 1953-55 have been collected and the attendant doctors asked for permission to approach the parents. Where the request has been approved, the mother is invited to cooperate by allowing a doctor from the local-authority health department to call and interview her. An interview by the same doctor is also arranged with the mother of a control child of the same age and sex, chosen at random from a list of births in the town or rural district in which the affected child's parents were living when the death occurred.

Of necessity a large number of doctors are conducting these interviews, but they are all following the same conventions and using standard schedules. Provided the parents of the dead child have not moved out of the area, only one doctor interviews each case-control pair. questionnaires for the children who have died are designed to elicit information about the child's health before the onset of the fatal illness, and the mother's health before and during the relevant pregnancy. All investigations and treatments are recorded, and wherever possible X-ray data are checked with hospital notes. A note is also made of any cases of leukæmia and malignant disease in the family, any degree of consanguinity between parents and grandparents, and certain features of the child's diet and home background. The schedules for the controls ensure that the same facts are obtained up to the age when the corresponding case first showed signs of the fatal illness.

PAST HISTORIES* OF X-RAY EXAMINATIONS AND ANTIBIOTICS IN 547 CHILDREN WITH MALIGNANT DISEASE AND 547 CONTROLS MATCHED FOR AGE, SEX, AND LOCALITY

No. of mothers and children X-rayed		Leukæmia		Other malignant diseases		All malignant diseases	
Period	Type of exposure	269 cases	269 con- trols	278 cases	278 con- trols	547 cases	547 con- trols
Antenatal	Diagnostic— Abdomen Other	12 25	24 23	43 33	21 32	85 58	45 55
Before conception of survey child	Therapeutic Diagnostic— Abdomen Other	17 103	24 88	28 108	30 119	45 211	5 ± 207
Postnatal (children only)	Therapeutic Diagnostic Shoe-fittings	1 45 55	49 52	1 46 40	50 46	2 91 95	99 98
†Total no. of mothers Total no. of children Either mother or child X-rayed		140 89 179	130 91 172	160 75	154 84 198	300 164 373	284 175 370
	medication (chil		1		100	313	1
Sulphonam Antibiotics		51 68	45 52	42 50	42 58	93 118	87 110

One reason for attempting a nation-wide survey was the possibility that the peak of leukamia mortality in early life noted by Hewitt 1 might be explained if weak irradiation could initiate malignant changes in a feetus or very young child. Hence this preliminary analysis of the completed schedules is focused mainly on the X-ray histories. The accompanying table shows the numbers of cases and controls with a history of irradiation of the mother or child. It also gives the numbers of children who received antibiotics or sulphonamides before the onset of the fatal illness or the equivalent date.

It will be seen that although they are alike in other respects, there is one important difference between the children who died and their controls: the number of mothers who had an X ray of their abdomen during the relevant pregnancy was 85 for the cases and only 45 for the controls. In the group labelled Other Malignant Diseases the corresponding figures for growths in different parts of the body were:

	C'ases	Controls
Brain and appendages	 11	9
Kidneys	 10	2
Suprarenals	 9	4
Lymph-nodes	 4	2
All other sites	 9	4

So large a total difference between the cases and controls can hardly be fortuitous. Nor, in view of the other resemblances, is it likely to be due to faulty choice of controls or to bias in recording. It could, however, be explained if children who are X-rayed before they are born are more prone to develop leukæmia and other malignant diseases than children who have not been X-rayed in utero.

DISCUSSION

The following facts have been known for some time. First, excessive exposure to radioactive materials may cause not only immediate radiation sickness and death but also the subsequent development of leukæmia and cancer. Secondly, the immediate ill-effects of radiation are disproportionately great when the whole body is exposed. Thirdly, therapeutic irradiation of pregnant women is liable to cause microcephaly and other congenital defects in the fœtus.2

In the last twelve months two other disturbing facts about X rays have come to light. In the first place it is now known that radiotherapy can cause leukæmia in adults 3 and cancer in children. 4 Secondly, the dose of irradiation received by the feetal gonads during diagnostic pelvimetry frequently exceeds 2.5r.5 The present investigation suggests that, besides causing genetic damage, this apparently harmless examination may occasionally cause leukæmia or cancer in the unborn child.

We acknowledge with gratitude all the help we have received from the health departments of counties and county boroughs, from the mothers of the survey children and from the General Register Office. We also thank the Lady Tata Memorial Trust for contributing generously towards the cost of the survey.

One of us (J. W.) receives a grant from the Medical Research Council.

> ALICE STEWART M.D. Camb., F.R.C.P. JOSEFINE WEBB M.B. Lond. DAWN GILES B.A. Oxfd. DAVID HEWITT M.A. Oxfd.

Department of Social Medicine, University of Oxford

- Hewitt, D. Brit. J. prev. soc. Med., 1955, 9, 81.
 Murphy, D. P. Congenital Malformations. Philadelphia, 1947.
 Court Brown, W. M., Doll, R. Medical Research Council Report. Cmd. 9780. H.M. Stationery Office, 1956; p. 87.
 Simpson, C. L., Hempelmann, L. H., Fuller, L. M. Radiology, 1955, 64, 840.
- 5. Osbern, S. B., Smith, E. E. Lancet, 1956, i, 949.

<sup>i.e., before the onset of the fatal illness in the affected child or equivalent period in the control child.
† Since a mother or child may appear in more than one X-ray category, the totals in this category are less than the sum of totals in the three preceding ones.</sup>