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BROOKHAVEN NATIONAL LABORATORY

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MEMORANDUM

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DATE: 23 May 1973

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BOX No. 1
FOLDER COHN-Whole Body Studies

TO: E. P. Cronkite, M.D.

FROM: S. H. Cohn, Ph.D. SHC

SUBJECT: EXTRAPOLATION FROM ANIMAL DATA

You emphasized the danger of extrapolating from animal data to man in discussing radiosensitity following Fleidner's seminar Monday.

You may not have seen this recent article by A. Stewart which bears on the subject. It seems to me that in the neutron-irradiation vs mammary tumor problem , we may be, once again, extrapolating from a highly radiosensitive species to a far less radiosensitive species (man) for this biological end point.

SHC:mas

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symmetry of table 5 has been quoted by Dr. Miller as a reason for not regarding the Oxford Survey as a reliable source of information about the carcinogenic effects of low-level radiation. If, however, childhood cancers are really fetal cancers, we should not expect the cases caused by obstetric radiography to bear the same relationship to other (fetal) cancers as the cases caused by the A-bomb to other (adult) cancers.

RADIOSENSITIVITY AND CANCER SENSITIVITY

We need only consult official statistics of mortality to discover that the risk of a child dying from leukaemia is three times as great as the risk of dying from a cerebral tumor and five times as great as the risk of dying from a kidney tumor; and need only consult the Oxford Survey to discover that the obstetric radiography hazard is greater for leukaemia than for cerebral tumors or kidney tumors. There is, in fact, such close correspondence between the radiosensitivity of fetal tissues (as judged by the Oxford Survey) and their natural cancer sensitivity, and such lack of correspondence between the radiosensitivity of adult tissues (as judged by the ICRP) and their natural cancer sensitivity (table 10) that we are forced to the conclusion that there are very few causes of childhood cancers (and very many causes of adult cancers) which do not fall into the category of random

TABLE 10. *Cancer and radiosensitivity ratings for adults and children.*

Cancer sites	Cancer ratings[a]		Radiosensitivity ratings	
	Adults	Children	Adults (ICRP)	Children (Oxford Survey)
Digestive	1	6	5	6
Respiratory	2	8	4	8
Genito-urinary	3	3	7	3
Breast	4	9	6	9
Skin	5	7	9	7
Lymphoma	6	4	3	4
Leukaemia	7	1	1	1
Neurological	8	2	10	2
Skeletal	9	5	8	5
Thyroid	10	10	2	10

[a]Cancer Notifications England and Wales (1962-65). Registrar General's Statistical Review; Supplement on Cancers.

From, Alice Steward - An epidemiologist takes a look at radiation risks, DHEW - 73-8024 - JAN 1973

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mutations, or the nuclear accidents which are an inevitable consequence of whole-body exposure to radiation and a possible cause of a mutant cell species.

For mutant cells to produce a tumor they must have a high growth potential and be in a position to express this characteristic, which implies survival of the cell species as well as survival of the host. So when theorizing about the causes of cancers, two possibilities must be considered; either tumor formation demands an initiator followed by a promotor, in which case the longer the interval between the two events the greater the chance of grafting malignant properties on to a "premalignant" tissue (Multi-hit theory), or the process demands an initiator followed by an inhibitor, in which case there might be only a brief period before it became difficult for even a powerful inhibitor to destroy all the mutant cells (Single-hit theory).

The first theory is clearly impossible to reconcile with constant intervals between the initiating event and the tumor detection (see tables 7 and 8) and we have been told that no single-hit theory can account for the steep age-dependence of cancer mortality (22) (fig. 12). If, however, tumor formation is a pathological process which is easily nipped in the bud by a healthy tissue, and is only a recognizable process after it has become irreversible, there would be no substance in the second objection.

The fact that malignant cells can be present in increasing numbers without causing symptoms is only mildly surprising when one considers the natural history of tuberculosis and syphilis: how often the primary and secondary stages of these diseases are missed; how long are the intervals between the primary and tertiary stages; and how ubiquitous are the pathogens by the time they declare themselves. And the age dependence of cancer mortality should occasion no surprise, since it is only an expression of a natural law illustrated in fig. 12 and made memorable by Shakespeare:

"Nativity, once in the main of light,
Crawls to maturity, wherewith being crowned,
Crooked eclipses 'gainst his glory fight,
And Time that gave doth now his gift confound.
Time doth transfix the flourish set on youth,
And delves the parallels in beauty's brow;
Feeds on the rarities of nature's truth,
And nothing stands but for his scythe to mow."

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