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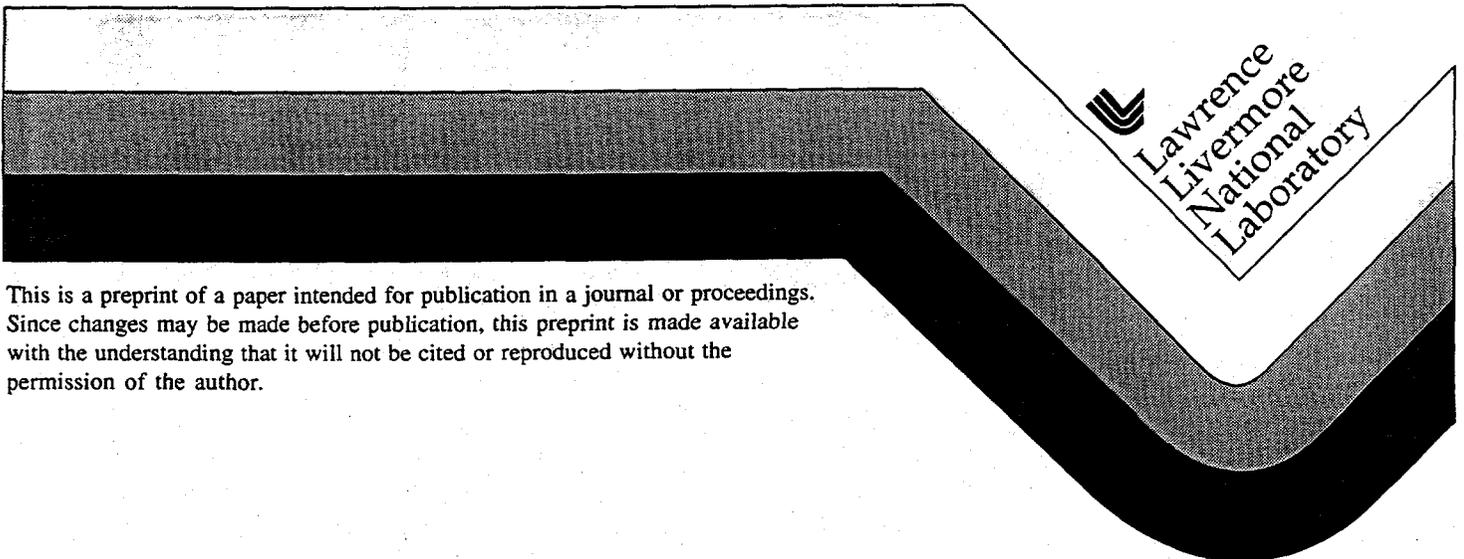
What is Desirable and Feasible in Dose Reconstruction for Application in Epidemiological Studies?

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WHAT IS DESIRABLE AND FEASIBLE IN DOSE RECONSTRUCTION FOR APPLICATION IN EPIDEMIOLOGICAL STUDIES?

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Abstract. Formal epidemiologic studies are intended to increase scientific knowledge about the quantitative risk that is associated with radiation exposure. Dosimetric data are needed for such studies.

What dosimetric data are desirable? Doses are needed for a large number of people with a large gradation of radiation exposures in order to ensure a sufficient power for the epidemiological study. The characteristics of the desirable doses are, in some respects, different from those calculated for radiation protection purposes. The desirable data are: (1) absorbed doses to the individual organs or tissues of interest, instead of effective doses; (2) absorbed doses delivered over limited time periods, instead of committed doses; (3) doses specific to the individuals that are subjects in the epidemiological studies, instead of average doses over population groups; and (4) very accurate and precise doses.

What dosimetric data are feasible? Most of the characteristics of the desirable dosimetric data are usually achievable. However, uncertainties can be fairly large and estimated with a large degree of subjectivity. Also, for practical reasons, it may not be feasible to estimate individual doses for all subjects.

1. Introduction.

Epidemiological studies of populations are of two general forms, monitoring or formal, and serve several possible purposes. Monitoring studies inform members of potentially affected population groups of the nature and magnitude of the risks that might have been imposed on them. Formal epidemiological studies can increase scientific knowledge about the quantitative risk that attends



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exposure. Risks of human health due to radiation exposure are most appropriately estimated by means of formal epidemiological studies.

Dosimetric data are essential for any epidemiological study, but the detail and accuracy needed depend on the purposes to be served. If the need is for a monitoring study, then general information about doses will suffice. However, a formal study that is expected to contribute to scientific information about quantitative radiation risk requires careful individual dose estimation.

This paper is devoted to the discussion of dosimetric data needed for formal epidemiological studies of populations exposed as a result of nuclear power operations. The recommendations made by the National Research Council [1] have largely been followed. The examples used in this paper are relevant to the Chernobyl accident, which caused a large number of people to be exposed at relatively high doses and provided an opportunity for formal epidemiological studies to be initiated. The studies that are singled out are those of thyroid cancer among children who resided in Belarus and in Ukraine at the time of the accident, and those of leukemia among workers involved in the mitigation of the accident and in clean-up operations.

2. What dosimetric data are desirable?

The characteristics of the desirable dosimetric data are presented and discussed.

2.1. Magnitude of the dose and dose distribution

First of all, formal epidemiological studies require a large number of people to be studied, with a large gradation of doses among those people. The potential informativeness of a formal study often is measured in terms of statistical power, which can roughly be defined as the probability of rejecting the hypothesis of no effect (null hypothesis), when in fact it is false and the alternative hypothesis is correct. An example would be that one would conclude that there is no increase rate of disease in the exposed population when, in fact, the radiation exposure does have an effect of the expected magnitude. For the studies considered here, there are two aims that are of primary interest. The first pertains to the probability of detecting a dose-related effect if an effect is present, given the expected size of that effect as derived from the risk estimates that form the basis of radiation protection standards [2-6]. Second, even when a study does not detect an effect, it can yield valuable information if it establishes an upper bound on risk that will increase confidence in the standard radiation risk estimates.

The sample sizes required to achieve adequate statistical power increase greatly as the magnitude of the dose decreases. Under the assumption of linearity between dose and effect, the sample size required to be likely to detect the effect varies roughly as the inverse of the square of the average dose. For example, if it is assumed that each member of a population with an age and sex distribution typical of the United States as a whole was exposed to a specific whole-body dose and followed over a lifetime, the size of the exposed



population needed to have an 80% chance of seeing an excess of total cancer mortality against general population rates is estimated to be 20,000 for a whole-body dose of 100 mGy, 220,000 for a dose of 30 mGy, and 2,000,000 for a dose of 10 mGy [1]. Extrapolating these results to higher doses would result in a population size of 2,200 for 30 mGy and of 200 for 1 Gy. However, several caveats should be made regarding these sample size calculations. Normally, one would have a range of doses in the population rather than a uniform dose. Performing a dose-response analysis would create some gain in statistical power (and a corresponding reduction in the required sample size) relative to the simple comparison of the total exposed group to the general population used above; it can be shown that having a modest fraction of more highly exposed persons in the population considered increases the statistical power appreciably and that the greater the spread in dose the greater the increase in statistical power that can be achieved if a dose-response analysis is used [7,8]. Also, the number of persons required is smaller for types of cancer such as leukemia, thyroid and breast cancer if the population considered consists only of children, who are more susceptible to the effects of ionizing radiation than adults for those types of cancer and who have lower baseline rates of disease [7]. On the other hand, several factors would tend to diminish statistical power. First, the uncertainty in estimating individual doses tends to diminish statistical power and increase the required sample size [9,10]. Second, the calculations above assume a full lifetime follow-up, whereas most studies have a much shorter average follow-up. Third, it is generally agreed that beta or gamma irradiation delivered at low doses and low dose rates is less effective, when normalized to unit dose, than the high, acute doses that were used to derive the population sizes given above. Considering all these factors together, the sample sizes given above probably err on the side of underestimating the required sample sizes.

2.2 Type of dose

In contrast to radiation protection purposes, for which the committed effective dose averaged over a population group is often the preferred dose quantity because it provides a measure of the total radiation impact resulting from a given exposure to the population group considered, the type of dose that is desirable for application in formal epidemiological studies is specific of the disease considered, specific of each individual considered in the study, and includes as much information as possible on the physical and temporal characteristics of the dose.

Taking as an example an epidemiologic study of thyroid disease among children exposed as a consequence of the Chernobyl accident, it is only the thyroid dose that is of interest. That thyroid dose should be estimated for all children included in the study. In addition, it is important to separate the contributions to the thyroid dose of external irradiation, of internal irradiation due to short-lived radioiodines (mainly I-132 and I-133) and of internal irradiation due to I-131 because those three components of the thyroid dose may not have the same effectiveness to cause thyroid cancer. Also, even though



most of the thyroid dose is expected to have been delivered within a few weeks after the accident, it is helpful to provide information on the protracted dose, due to the long-lived radiocesiums, which have been and will continue to be delivered at low rate, both from external and from internal irradiation.

If leukemia is the disease that is considered, then the bone-marrow dose should be estimated. For members of the public exposed as a result of the Chernobyl accident, it is desirable to estimate separately the contributions to the bone-marrow dose arising from external irradiation and from internal irradiation as those two components are of similar magnitude but with different temporal distributions. The contribution from external irradiation resulted from short-lived radionuclides soon after the accident, whereas it is currently due essentially to the radiocesiums that were deposited on ground surfaces; the contribution from internal irradiation is mainly due to the consumption of foods contaminated with radiocesiums and radiostrontiums. So far, the internal doses from the radiocesiums have been greater, on average, than those from the radiostrontiums, but that trend is expected to be reversed in the future. For workers, however, only the dose from external irradiation would need to be carefully estimated for most individuals, as occupational bone-marrow doses arise for the most part from external irradiation; however, a rough assessment of the bone-marrow dose from internal irradiation would be needed to make sure that it can be neglected.

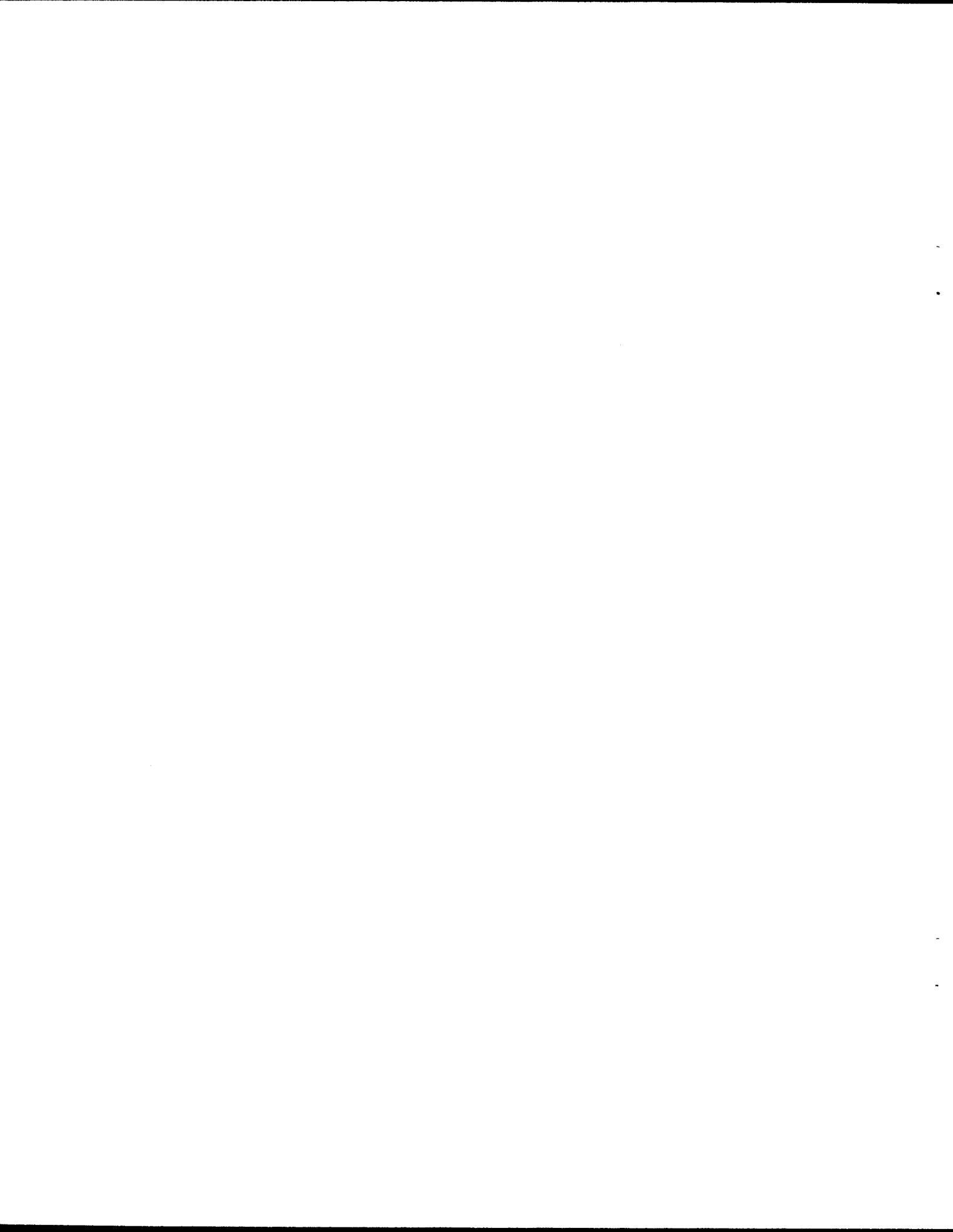
It is usually sufficient to estimate for all individuals the integrated dose from the beginning of the radiation exposure considered until the time when the disease is diagnosed. However, information on the time dependence of the protracted doses is also desirable.

2.3 Uncertainties attached to the dose estimates

Uncertainties have to be estimated for all individual doses. It is desirable to reduce the uncertainties to the lowest possible level, to separate the random uncertainties and the biases, and to calculate these uncertainties in an objective manner that does not leave any room for subjective judgments. Also, the extent to which these uncertainties are correlated across subjects must be understood. Although complex, statistical methods to account for uncertainties in dose estimates in the analysis of epidemiologic studies have been developed [11-13].

3. What dosimetric data are feasible?

What is feasible in dose reconstruction studies is often much less than what is desirable. At best, individual doses can be estimated with subjective, usually large, uncertainties. Sometimes, it is necessary to resort to group doses because resources are not sufficient to estimate individual doses for all subjects or because the database available does not allow for the identification of individual-specific parameter values.



3.1 Individual doses

In the estimation of individual doses, every effort should be made to use data that are specific of the persons that are considered.

In the case of internal irradiation, the best data are those that are related to the measurement of the contents of radioactive materials in the body. For example, following the Chernobyl accident, several hundreds of thousands of measurements of exposure rates against the neck of individuals were made for the purpose of estimating the I-131 content of the thyroid [14-17]; also, a very large number of whole-body burden measurements have been made in order to evaluate the internal doses due to intake of radiocesiums [18]. Even though the measurements of exposure rates against the neck (usually called "thyroid measurements") were not made in all cases under highly standardized conditions and with the same, uniformly calibrated equipment [12], they provide the best basis from which the thyroid doses can be estimated.

It is important to note that those measurements of radiation originating from the body provide only information on the dose rates received at the time of measurement. Unless the individuals considered were measured many times during the time period when the dose was delivered, the variation of the dose rate as a function of time must be estimated using other sources of information. For example, the additional information needed to reconstruct the thyroid dose resulting from the intake, by inhalation or by ingestion, of I-131 is: (1) the history of I-131 intake by the measured individual both before and after the thyroid measurement, and (2) the metabolic data to permit the conversion from I-131 intake to thyroid dose. Because of the knowledge of the thyroid dose rate at the time of the thyroid measurement, only relative intakes of I-131 from inhalation and from ingestion are needed.

The intake rates of I-131 from inhalation depend on the I-131 concentrations in the air that was breathed and on the breathing rates of the individuals considered. There is very little information on the air concentrations of I-131, which varied both in time and in space. The assumption that has been made so far is that of a single intake during the first day after the accident. Large uncertainties are associated with the estimation of the uncertainties attached to the inhalation doses. However, for the populations of Belarus, Ukraine, and Russia who were affected by the Chernobyl accident, the I-131 intake by inhalation was, in general, much smaller than that from ingestion. Notable exceptions are the early evacuees who inhaled contaminated air before and during evacuation, did not consume contaminated foodstuffs before or during evacuation, and were provided with uncontaminated foodstuffs after evacuation.

Intake of I-131 from ingestion arose from the consumption of contaminated milk and, to a lesser extent, of other contaminated foodstuffs, such as leafy vegetables. Unfortunately, the database on I-131 concentrations on foodstuffs is very limited and has to be complemented by means of environmental transfer models that take into account, among other factors, the influence of the official milk ban in some of the contaminated areas.



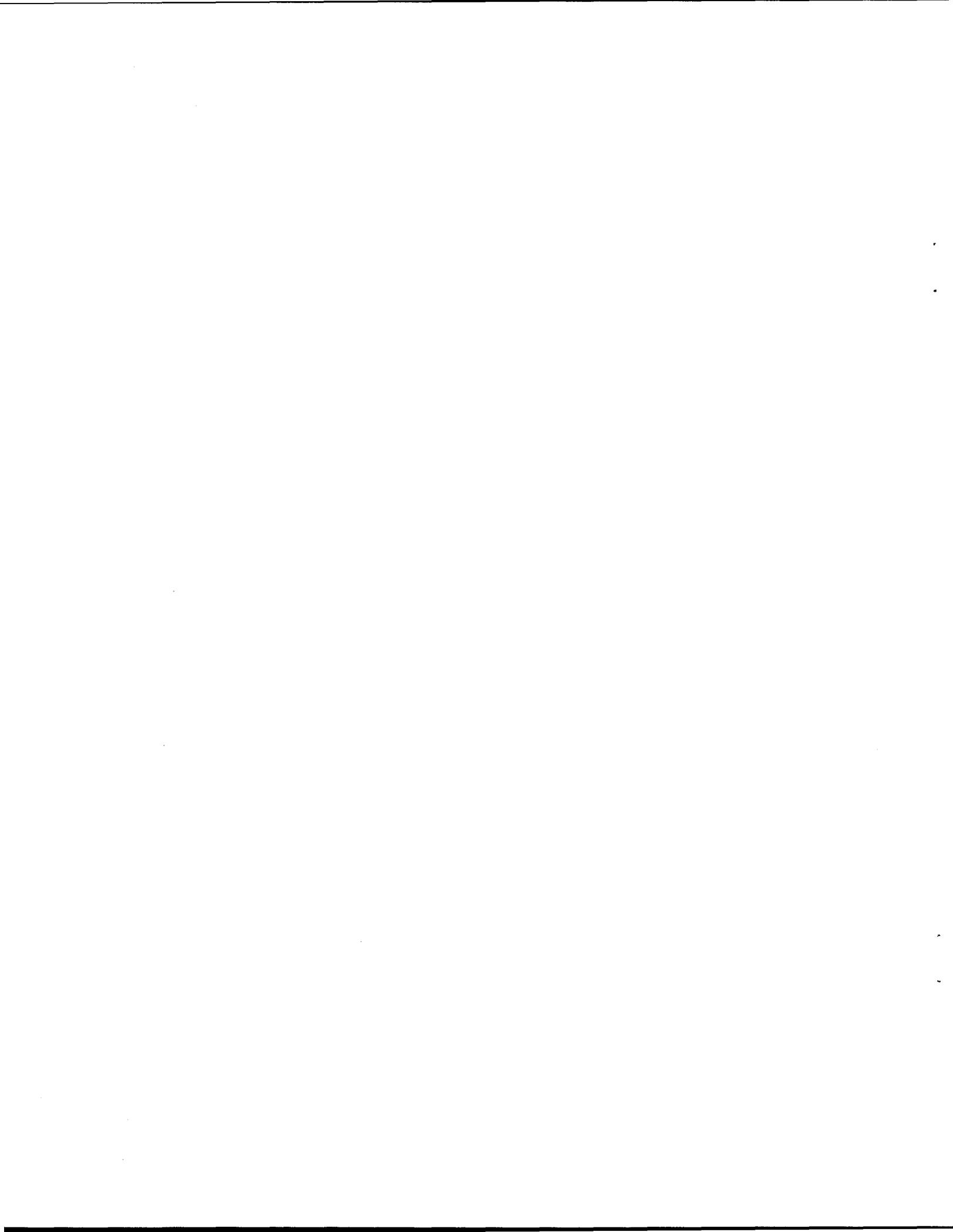
Information on (1) the consumption rates of the contaminated foodstuffs, (2) the origin of those foodstuffs, and (3) the possible intake of iodine pills or solutions in order to block the thyroid uptake can be obtained by means of personal interviews. It is acknowledged that the data obtained in these interviews are highly uncertain and possibly biased.

Personal metabolic data are also largely unknown in the absence of individual measurements of retention of iodine in the thyroid. However, the use of literature data does not lead to large uncertainties for individuals because of the low range of variability of the effective half-time of retention of I-131 in the thyroid.

In addition to the doses resulting from the intake of I-131, doses arising from the presence of short-lived radioiodines (mainly I-132 and I-133) in the thyroid, from internal irradiation of the thyroid due to the presence of radiocesiums in the body, and from external irradiation originating from the deposition of radioactive materials on the ground and on the clothes, skin, and hair need to be estimated. It is not feasible to estimate the magnitude of these dose contributions for all individuals, as most of the relevant information is not available. These dose components can only be obtained by means of models developed using information from a very small database. Fortunately, the contribution of those dose components to the total thyroid dose is relatively small for most individuals.

In summary, it is clear that, even for individuals with thyroid measurements, the estimation of the thyroid dose over the time period of interest is fraught with large uncertainties, which are very difficult, if not impossible, to quantify in an objective manner.

In the case of external irradiation, individual doses can be recorded by means of personal dosimeters when the radiation exposure occurs, or be derived from biological dosimetry, if the doses are high enough, after the exposure. For example, in the case of the clean-up workers (also called "liquidators") involved in the mitigation of the Chernobyl accident, a measure of the dose from external irradiation is provided from the processing of the badges that they were required to wear. Unfortunately, not all liquidators wore badges during the first few weeks after the accident and the badges worn by highly exposed people during the night of the accident were overexposed. Concern has also been expressed about the validity of some of the recorded doses. There are at least two ways to verify the validity of the recorded doses. One is to perform biological dosimetry, using for example the fluorescent in situ hybridization (FISH) technique to measure the frequency of certain stable chromosome aberrations in blood samples [19] or the Electron Paramagnetic Resonance (EPR) technique to measure the radiation dose accumulated in tooth enamel. These techniques, however, are still in the experimental stage and are not helpful for doses below 0.1-0.2 Gy. The other method that can be used to verify the validity of the recorded doses is to perform detailed time and motion studies, in which the liquidator reconstructs as best as possible where and when he was during the time period he was exposed and the knowledge of the radiation field in various reactor locations allows an estimate of the radiation



dose received by the liquidator to be made. Both methods present large uncertainties and may have to be used in conjunction in order to improve the accuracy of the dose estimates.

3.2 Group doses

Although the estimation of individual doses is highly recommended in formal epidemiological studies, it is sometimes necessary to resort to group doses because resources are not sufficient to estimate individual doses for all subjects or because the database available does not allow for the identification of individual-specific parameter values. Group doses are estimates of average doses for population groups presenting similar characteristics. For example, for thyroid studies related to the Chernobyl accident, the same dose could be assigned to children of the same village and the same age group presenting similar dietary and lifestyle habits. Also, liquidators without badges could be assigned the same dose if they were members of a team that carried out a given operation. Uncertainties attached to group doses are, as a rule, larger than those associated with individual doses when they are assigned to individuals in that group.

4. Discussion

Although much could be learned from the Chernobyl accident, it must be emphasized that deriving new scientific knowledge will be difficult. As is the case in most studies of exposed populations around nuclear facilities, the radiation doses received by the individuals exposed cannot be quantified precisely. The dosimetric data that are currently feasible do not present all of the desirable characteristics requested by the epidemiologists. In particular, a substantial effort will have to be made by the dosimetrists in order to provide dose estimates with reasonably low uncertainties.

5. Acknowledgments

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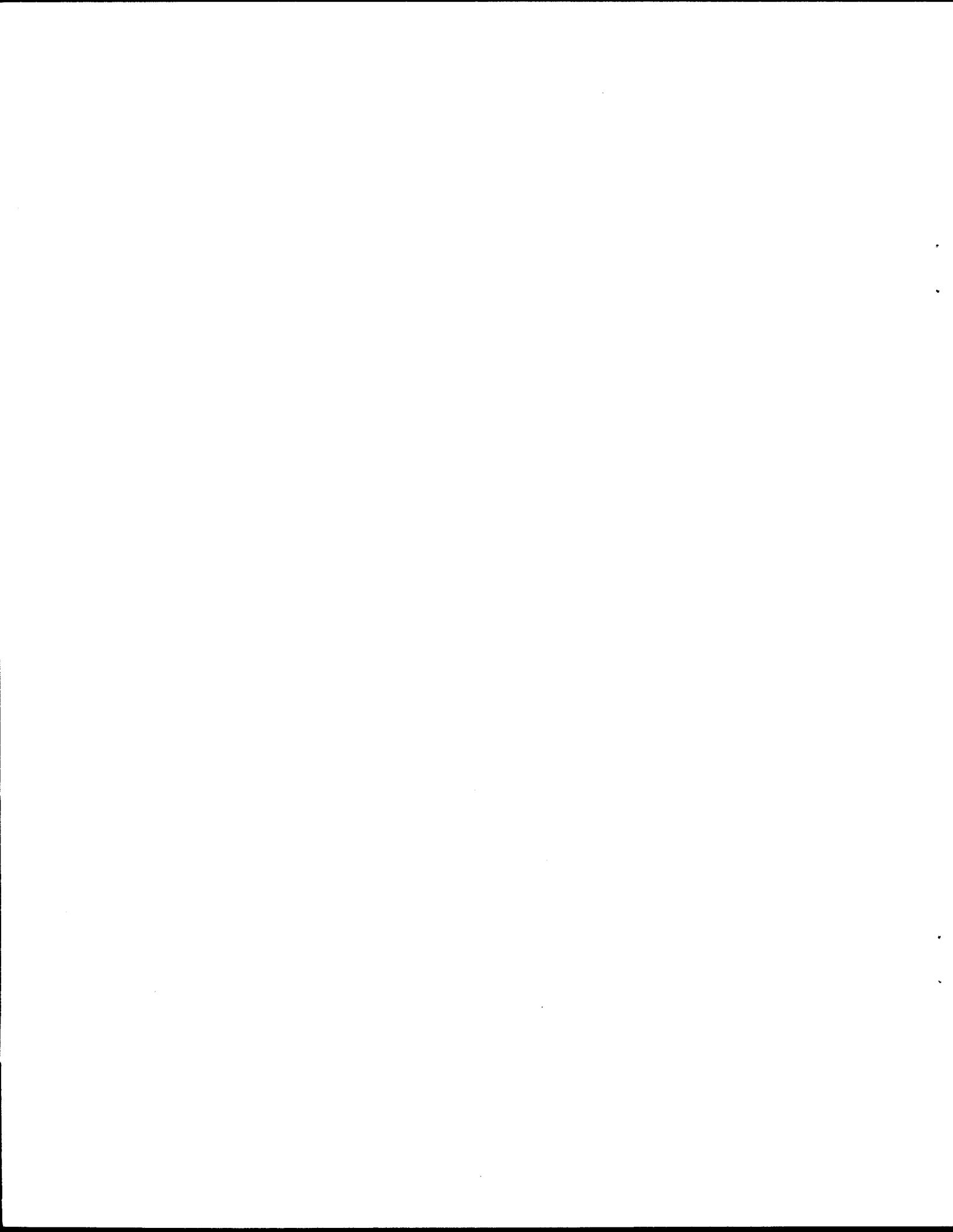
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