

"QUESTIONS FOR DR. PAUL TOMPKINS"

by

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June 29, 1970

[Over the past several months we have been voluntarily assisting Dr. Tompkins in the Review of the Federal Radiation Council Guidelines. Now we find that it would help us in our further efforts to be helpful if Dr. Tompkins would answer a few questions for us. And since the questions may interest many who are concerned with this problem, this document serves to make these questions generally available. We trust Dr. Tompkins may make the replies equally available.]

QUESTIONS FOR DR. TOMPKINS

1. Dr. Tompkins, is it not true that ICRP and FRC both refuse to assume any safe threshold dose of radiation?

2. If, then, FRC does not assume any safe threshold dose of radiation, we must operate in the real world consistent with that position.
 - (a) If you in FRC assume no safe threshold of radiation, do you or do you not adhere to your assumptions in practice?
 - (b) We understand that AEC follows FRC guidance in such matters as setting standards. This must mean AEC assumes no safe threshold of radiation, doesn't it?
 - (c) Don't you at FRC have difficulty understanding how the AEC can make the following statements in support of a safe threshold?
 1. In "Environmental Effects of Electric Power" JCAE Hearings AEC Staff Comments, p. 692:

"There is evidence for an effective or practical threshold, yet no allowance has been made (by Gofman and Tamplin) for levels of radiation below which cancer cannot be causally related".
 2. Dr. Glenn Seaborg, being interviewed by Mr. Joseph Benti on CBS Morning News, said, "I believe there is a threshold".

3. In view of the fact that such responsible bodies as ICRP and FRC refuse to assume any safe radiation threshold, is it not reasonable to eliminate discussion of any such threshold for purposes of evaluating risks or hazards of radiation?

4. ICRP and FRC regard the linear relationship between cancer and leukemia production and radiation as the conservative assumption that should be used in setting standards, do they not?
5. If we say we are going to be conservative and use the linear extrapolation, would you feel it is reasonable to practice what we say we are practicing?
6. Why, then, do so many AEC spokesmen immediately jump on hazard calculations because (in part only) they are derived from linear extrapolation from high doses to low doses? Would you say this represents saying one thing, but doing another for opportunistic reasons?
7. The ICRP recommends that one should consider, for risk evaluation, that all radiation doses should be considered as cumulative. Therefore, one cannot consider any protection due to dose-rate for cancer production. Would you agree with ICRP on this, or do you not believe in being conservative with respect to protection of the public health?
8. If you agree with this position of ICRP on not counting on any protection from dose-rate, can you understand the AEC (p. 692, Hearings above) bringing up the dose-rate issue in criticizing the Gofman-Tamplin estimates of cancer risk from radiation?

Dr. Tompkins, we are at a loss when a governmental agency says it adheres to one set of principles, and then denies hazard estimates made using those very assumptions. Can you help us out?

9. Dr. Tompkins, all responsible bodies:

- (a) Refuse to assume any safe threshold,
- (b) Consider linear extrapolation as a conservative assumption to use,
- (c) Consider all doses cumulative, no matter what the dose rate.

Further, the relationship of leukemia incidence to radiation dose is well known from the British Studies and the Japanese Studies, as well as others.

Further, from the British data of Court-Brown and Doll, we have the ratio of occurrence of several other forms of cancer in irradiated tissues to that for leukemia. Now, if one accepts the responsible views of the ICRP as a basis for estimating hazard, all the points just listed do provide us, unequivocally, with ample data to calculate the hazard of cancer plus leukemia for exposure of people to FRC Guideline radiation doses.

- (a) Have you made such calculations yourself?
- (b) If yes, how do your calculations compare with those of Gofman and Tamplin?
- (c) Can you explain the following?

On March 4, 1970 at Hearings before the City Council of New York Councilman Weiss asked for this calculation of Dr. William Burr of the Division of Biology and Medicine, U. S. Atomic Energy Commission. Dr. Burr's response was "We prefer not to play the numbers game".

This response of Dr. Burr of AEC puzzles us, for surely the AEC representatives to FRC must have participated in such calculations in the weighing of benefits of radiation exposure against risks. Or does the AEC have some mystical methods of estimating risks that do not require numbers?

10. Dr. Tompkins, are you aware of the number of cancer + leukemia deaths which are to be expected annually through the use of the ICRP Publication 14? (We calculate a minimum of 11,000 to 18,000 deaths from cancer + leukemia from FRC Guideline Radiation). This estimate doesn't require the doubling dose concept or any "theories". It comes right out of the British Ankylosing Spondylitis data -- and has nothing to do with Gofman and Tamplin.

- (a) If you do admit these numbers, will you explain to us precisely how the FRC calculated that the benefits of atomic energy justify this number of deaths from cancer plus leukemia? Surely, you much have calculated out how many lives are going to be saved, lengthened, or improved in order to balance the benefits versus risk.
- (b) Dr. Tompkins, wouldn't you agree that anything less than such a balanced calculation is shocking as a basis for going ahead with any peaceful application of atomic energy? How can we go ahead saying we balance benefits versus risks if, in fact, that task hasn't even been started?
- (c) Dr. Tompkins, if you do not admit to knowing what the number of cancers + leukemias from guideline radiation will be, how is it conceivably possible to balance benefits versus risks?
- (d) If we don't know the benefits, and we don't know the risks, how is it possible to even consider balancing these two unknowns?
- (e) Wouldn't you have to agree that setting any guideline for population radiation in the absence of a valid benefit vs risk calculation represents the height of public irresponsibility?

11. Dr. Tompkins, you have stated that "operational requirements" can be as important as health considerations in setting guidelines for population exposure to ionizing radiation. Since we are talking about peaceful aspects of atomic energy development, we can eliminate any considerations of national security.

Now, if "operational needs" means that which is consistent with optimum progress in atomic energy development we must necessarily conclude that the FRC has made some decision that optimum development of atomic energy is worth killing some number of humans.

- (a) Could you tell us what price in lives "optimum atomic energy development" requires?
- (b) Could you tell us how many dollars in Gross National Product stimulation via atomic energy you of FRC equate with one case of cancer or leukemia?
- (c) If you have not equated how many dollars in atomic energy development is worth one human life, how can FRC be sure the dollar benefits are worth the misery of cancer or leukemia deaths?
- (d) Do you think the public should know how FRC relates dollars saved to humans killed?

12. (a) You have been quoted as saying that the FRC Guidelines are based upon genetic risks more than upon cancer or leukemia risks. Is this true?
- (b) If genetic risks were dominant in setting the FRC Guidelines, how is it conceivable that the FRC failed to act upon the new data concerning somatic risks (1965) from Court-Brown and Doll, which indicated a steep increase in cancer risk from radiation?

12. (c) Don't you keep reviewing new evidence and reset guidelines accordingly?

(d) Don't you think the Court-Brown and Doll data which leads to an estimate of a minimum of 11,000-18,000 deaths per year at FRC guidelines for the USA should have led to a revision immediately of the guidelines, or at least an announcement of this extreme hazard? Or don't you consider cancer a serious disease?

13. (a) Let us consider the genetic problem in a little detail, Dr. Tompkins, since you and others may have indicated the genetic hazard to be a major basis for FRC Guidelines. Further, you have recently indicated that "new evidence" would have allowed a higher FRC Guideline than was set in 1960. Could you tell us if this new evidence comes from the mouse genetics studies of the Russells at Oak Ridge?

(b) We presume, therefore, you are quite impressed that mouse results can be directly translated to man. Is this correct? (We shall later return to further mouse to man results - both on life expectancy and cancer). Let us stay with the genetics data for the moment.

We understand that the mutation rate for the seven visible genetic traits in the Russells' mice differ by a factor of thirty from the easiest to the hardest to mutate.

(c) Would you tell us how the mutation rate for mouse traits compares with the mutation rate for the important genetic traits in humans?

13. (d) Could you tell us the 5 most important genetic traits in humans that FRC used in assessing the genetic hazard of radiation?
- (e) Dr. Tompkins, we understand the radiation-induced mutation rate for the 7 visible traits in mouse varies from trait to trait by a factor of 30-fold. Can you tell us the difference in radiation-inducible mutation rate among the 5 most important human genetic traits?
- (f) If this is not known, Dr. Tompkins, tell us how you figure out that new data would allow even higher guidelines by a factor of 3? One-third of some very high unknown mutation rate for an important genetic trait in humans could be a very large number. Tell us how your committee of experts took this into account? Which human genetic trait was chosen to make this calculation? Or was it just done on mouse?
- (g) We are sure you are aware that the highest numerical cause of death in the human population in the USA is coronary heart disease. Since coronary heart disease is the largest single cause of death in the United States, it would appear extremely important to know something of the genetic aspects of this disease; would you not agree? And of radiation sensitivity of the genes involved?
- (h) Dr. Tompkins, we are unable to find any reference as to how the well-known genetic aspects of coronary heart disease were taken into account by your expert advisors. Can you give us the precise references to (1) the spontaneous mutation rates for the genetic traits in coronary heart disease considered by the expert advisors to FRC, and (2) the radiation-induced mutation rate for the important genetic traits involved in coronary heart disease? We wouldn't expect you necessarily

to know the answers but surely you can give us the precise references to these answers for the most important cause of death in the USA, can't you? We have been unable to find the specific consideration of this extremely grave problem in any FRC documents. Since it is one of the most vital issues to consider in Guidelines, we request your help on this, please.

(i) Diabetes mellitus is well known to have an extremely important genetic component. And several million Americans suffer from this extremely important disease.

(1) Can you give us the reference on how the spontaneous mutation rate for genetic traits in human diabetes mellitus compares with those for the 7 visible traits in Russells' mice?

(2) Can you give us the reference for this comparison for radiation-induced mutations in the human genetic traits for diabetes mellitus versus the 7 visible traits of mice?

14. Dr. Tompkins, since you quote the mouse data as suggesting evidence that is translatable to man, let us consider life shortening by radiation. For the rodent, it appears that life shortening by 100 rads of radiation is in the neighborhood of 1-5%. For the Beagle Dog it is approximately 10% life shortening for 100 rads.

(a) If we use normal life span of the species as a guide, the appropriate human value for 100 rads might be 15, 20, or 25%, might it not?

(b) Or would you regard the fragmentary data on radiologists versus other physicians, with almost unknown dose estimates, as very reliable to estimate life shortening per 100 rads in man.

15. Several AEC officials have suggested that Gofman and Tamplin should have considered experimental animal data more extensively in making their estimates. Let us consider this important issue for a moment. If one looks at all the recent evidence from Bond and co-workers on breast cancer in rats, Dr. Upton on myeloid leukemia and ovarian cancer in mice, and Dr. Finkel on bone sarcoma in mice, all these studies indicate a direct linear relationship between dose and cancer incidence, down to very low doses. Therefore, the doubling dose concept is directly applicable. Furthermore, the data indicate the doubling doses for such experimental animal cancers are below 20 rads. Now (1), if we feel the experimental animal data should be used in evaluating human risk of cancer, this would suggest we should use 20 rads as a conservative doubling dose for human cancers, in the absence of direct evidence on humans.

(2), If Gofman and Tamplin arrive at 32,000 extra cancers + leukemias from FRC Guideline exposure using a 50 rad doubling dose, the use of the 20 rad doubling dose would suggest 80,000 extra cancers plus leukemias per year in the U.S. population for FRC Guideline exposure.

In view of this, has the FRC considered the implications of the experimental animal data, now so extensive and beautiful, in making its benefit versus risk calculations? (To the extent that any such calculations have ever been made).

16. (a) Dr. Tompkins, do you know the name Dr. Karl Z. Morgan?
- (b) Is Dr. Morgan a member of the highly respected International Commission on Radiological Protection?

16. (c) Do you know of the magnitude of the hazards (approx. 20,000-88,000 deaths/year) associated with FRC Guideline radiation calculated by Dr. Karl Z. Morgan, the very highly esteemed Health Physicist?
- (d) Are you aware that this estimate was made before the new data from the ankylosing spondylitics was taken into account, and that this will materially increase the 20,000-88,000 extra deaths per year?
- (e) Dr. Tompkins, can you tell us the specific benefits the FRC weighed against a number like 20,000-88,000 deaths in arriving at the so-called "tolerable" or "permissible" Guideline exposures?
17. (a) We continue to be positively appalled by an irrelevancy constantly introduced into such considerations by AEC and by the nuclear electricity industry. Whenever confronted by the stark reality of the extremely high casualties to be expected from U.S. population exposure to Guideline radiation, the irrelevant answer is always given that actual, current exposures are far below the Guidelines. It is rather obvious that a cyanide gas chamber is no hazard if there is no gas turned on, but that hardly justifies a disastrous "permissible" guideline for cyanide exposure? How would the radiation situation differ?
- (b) If, indeed, Dr. Tompkins the disastrous results expected at FRC Guideline exposure are to be avoided, wouldn't common sense dictate setting grossly lower guideline values?
- (c) And wouldn't it be appropriate for the FRC to have accomplished what it talks about so freely; namely, a benefit-risk calculation with real numbers, before setting any "permissible" guideline dosages?

17. (d) In the May 20, 1970 Wall Street Journal was an article which is quoted directly, "An AEC spokesman declines to predict when the 170 millirad limit might be reached, noting the uncertainty of the Plowshare Program among other things".

Dr. Tompkins, wouldn't you agree that this statement leads to grave doubt about the frequent AEC statements that exposure of the U.S. population to 170 millirads is never going to happen?

- (e) Some AEC officials say that even though they will keep the exposures low, on the average, they need higher guidelines of allowable exposure to allow for operational incidents. Now, since the guidelines already average over a year period, this surely takes care of operational incidents, doesn't it?

- (f) Or would you suggest that we might need 10 or 20 years to average out an overexposure in one particular year if we reduced the guidelines to a sensible value?

18. (a) May we quote from the United Nations Scientific Committee on the Effects of Atomic Radiation?

"It should be emphasized that the limit (5 rems per generation for the genetic dose to the whole population) may not in fact represent a proper balance between possible harm and probable benefit, because of the uncertainty in assessing the risks and the benefits that would justify the exposure."

For an eminent body such as UNSCEAR to make this statement means that the FRC Guideline, insofar as genetic hazard is concerned, represents a kind of Russian Roulette being played upon the population of the USA, wouldn't you agree? We'll try it and see what happens to the species?

18. (b) Since you have recently said we could justify raising the guidelines three-fold based upon recent evidence, are we to presume the large area of our ignorance of human genetic effects has suddenly been reduced? Tell us about these new advances in human genetics that permit such a raising of guidelines.
- (c) Dr. Tompkins, would you say that where we have a large area of ignorance concerning human genetics, that some mouse experiments now give us 1/3 that amount of ignorance, and we should set standards upon 1/3 of a great amount of ignorance?
- (d) Genetic effects can be either due to point mutations or to chromosomal effects, such as deletions. Are you aware that practically all of our knowledge of chromosomal alterations and their impact on humans was obtained after the setting of the 5 rem per generation guideline for genetic effects on humans?
- (e) Or, Dr. Tompkins, would you say we should just disregard massive new information?
- (f) Most genetics and chromosome experts indicate that polygenic factors in inheritance (effects due to many genes) may be major factors determining health or the susceptibility to disease broadly.

Further, chromosome experts tell us we are in nearly total ignorance concerning such polygenic factors in determining human health although we know major human diseases have a multi-gene basis. And certainly the effects of radiation upon chromosomes carrying such factors is only now beginning to be approached. Yet you claim we know enough to raise the guidelines, insofar as genetic effects are concerned.

How do you at FRC achieve such confidence, in the absence of any knowledge concerning such effects - an absence quickly admitted by experts in the field?

19. (a) Dr. Tompkins, are you familiar with the work of Dr. Alice Stewart and Dr. Brian MacMahon?

(b) Can we read you a quote, 1969, from Professor MacMahon, a highly respected Epidemiologist at Harvard?

(Quote) "While a great deal more is known now than was known 20 years ago, it must be admitted that we still don't have most of the data that would be required for an informed judgment on the maximum limits of exposure advisable for individuals or populations".

Are we to presume, in the light of this statement that the FRC set guidelines without having the "informed judgment" referred to by Professor MacMahon?

(c) Or, is the FRC in possession of a body of information that has somehow escaped Dr. MacMahon's and most other biologists' attention?

(d) Both Dr. Stewart and Dr. MacMahon, with by far the largest body of data available on the subject, agree that the very small amount of x-ray exposure associated with diagnostic pelvimetry during pregnancy results in a 50% increase in childhood cancer + leukemia.

Are you aware that the highly respected publication ICRP 14 accepts these estimates of hazard?

(e) Dr. Tompkins, have you read the paper by Draper and Stewart in the December 20, 1969 Lancet, where it is shown that the increase in risk of childhood cancer + leukemia rises in proportion to the number of x-ray pictures taken?

19. (f) Let me give you some data from Dr. Stewart and Dr. Kneale, from their study entitled "Radiation Dose Effects in Relation to Obstetric X-Rays and Childhood Cancers", Lancet June 6, 1970 pp 1185-1188.

<u>No. of X-Ray films taken</u>	<u>% Increase in Cancer Risk</u>
0	0
1	20%
2	~ 28%
3	70%
4	100%
5	110%

This represents the classical dose-response curve required by so many people in establishing cause-effect relationships. In view of this evidence, do you think perhaps the AEC might properly stop talking about all the evidence on human cancer coming from 50 to 100 rads, when in truth the Stewart-Kneale data are for ~ $\frac{1}{2}$ rad to $2\frac{1}{2}$ rads?

- (g) Or, Dr. Tompkins, do you not consider human babies as particularly relevant members of the human species?
- (h) The Stewart-Kneale-MacMahon data indicate that babies in utero are 10 times as sensitive to cancer and leukemia production as adults. The Hempelmann and other data on thyroid cancer production in children indicate, similarly, that children are much more sensitive to cancer production than adults.
- (i) Does this not give you any pause concerning the validity of the FRC Guidelines, which totally neglect this difference in sensitivity?
- (j) Of course, we understand you have stated already that the FRC essentially neglected the whole cancer + leukemia risk in its focus on genetic effects? Since FRC neglected a tremendous part of the overall hazard, it is understandable, is it not, that FRC failed to take into account the greatly increased hazard of its Guidelines for children?

19. (k) The Stewart-Kneale data indicate further that first trimester radiation is many fold more serious than radiation in later pregnancy. Does this not prove especially worrisome to FRC?
- (l) Dr. Tompkins, in FRC's focus on genetic hazards, and its neglect of somatic effects upon this generation, are we to presume FRC considers the health of this generation unimportant? Has the public widely been informed of this total neglect of the hazard to this generation?
20. (a) Dr. Tompkins, do you think man depends upon his ecosystems for survival and health?
- (b) Are all ecosystems in varying regions of the country identical?
- (c) Are you aware that major changes in man's ecosystems can take 10-20-30 years to become manifest?
- (d) Nuclear plants with releases of radioactivity upon man's ecosystems are being built all over this country. Can you tell us of the studies, in depth, that have been performed in each such region, over a period of 10-30 years, that assure us we will not disastrously modify man's ecosystems by such releases, to say nothing of thermal pollution?
- (e) Dr. Tompkins, as a responsible official involved in setting standards for the public health and welfare, is it your philosophy that, "In ignorance, go full speed ahead"?
- (f) Would you say that Russian Roulette is a good game to play with our ecosystems, in view of our abysmal ignorance of effects upon them?

21. Dr. Tompkins, since ICRP 14 and our own data suggest other cancers to dwarf leukemia as an effect of ionizing radiation, does this not suggest whole body allowable dose for occupational exposure needs to be reduced 10 or 20 times to be consistent with your prior estimates of "acceptable" occupational risk?
22. Dr. Tompkins, we realize that you agree with us that perhaps the most important radiosensitive human system involved in heredity is represented by the chromosomes. And that you realize we are just beginning to learn the meaning of a variety of chromosome anomalies, including deletions and translocations for numerous aspects of human health and disease, to say nothing of the truly astounding frequency of chromosome aberrations in spontaneous abortions in humans.
- (a) Does it make you at all uneasy that this spectacular field of human cytogenetics is now in its infancy, after all the decisions had been made which led to the setting of Federal Radiation Council Guidelines for radiation exposure of populations?
- (b) We wonder how it is that a radiosensitive system, perhaps the most radiosensitive human hereditary system, somatically and genetically, has become known after standards were set and you are still quoted as saying, "I think the standards are damned low"? Do you have some privileged information that allows you to dismiss the radiosensitive chromosome system as unimportant, in view of the spectacular medical disorders demonstrated to be related to it? Can you, perhaps, give us some references to such information?

22. (c) Among the seven visible genetic traits studied in the mouse by the Russells, we know there is apparently a thirty-fold difference in radiation-induced mutation rate. While it cannot be proven to be the case, it appears that the most reasonable explanation for these phenomena is that chromosome breaks, with deletions, must represent the major mechanism operative.

Dr. Tompkins, can you tell us whether the observed differences found for radiation-induced mutation rate is due to position of the gene along the chromosome, or is there some difference in ease of chromosome breakage along the chromosome length? Spontaneously? Radiation-induced?

- (d) Dr. Tompkins, we have just been referring to ease of chromosome breakage in the mouse. However, what we would really like some help on is the ease of breakage along each of the 22 autosomal chromosomes and the X and Y chromosomes of the human complement.
- (e) Since all of the information relating to every aspect of human health and disease must reside in these autosomes, plus sex chromosomes, would it not seem urgent, for setting radiation standards, with radiation being a most potent agent capable of breaking such chromosomes, to know something about the radiation-sensitivity along the length of all the 22 human autosomes and the X and Y chromosomes? But could you help us, say, just for the 22 autosomes?

22. (f) Incidentally, Dr. Tompkins, to our knowledge almost nothing is known concerning the chromosomal location of human trait information. Doesn't this make it a bit difficult to know the meaning of, say, a particular chromosome deletion, and radiosensitivity in production thereof, when we don't have the vaguest information concerning the health implications of such deletions?
- (g) The significance of radiation-inducible deletions along the various human chromosomes is of special interest. Are you aware of the implications for human health and disease (including all the major human diseases) of, say, 5% deletions, 10% deletions, 15% deletions along the various of the 22 autosomal chromosomes and the X chromosome? From our survey of the literature of quantitative cytogenetics, we find almost nothing is known concerning the distribution of such deletions for any of the 22 autosomal chromosomes in the population of the USA. While this represents a fabulously exciting area of the medicine of the future, the requisite measurements will be laborious and difficult. Do you have access to some measurements of the frequencies of all such deletions in the population?, any such deletions? the meaning for health or disease of all, or any, such deletions?
- (h) It would be amazing to have a set of "safe" radiation standards already in existence in the absence of such knowledge concerning chromosome deletions in the human, don't you think, Dr. Tompkins?
- (i) Some cytogeneticists and geneticists suggest that it would be the height of human arrogance to say what the implications of radiation exposure may be in the absence of such knowledge concerning chromosome injuries and their meanings. Wouldn't you be inclined to agree, Dr. Tompkins?

23. The problem of chromosome deletions, even up to 20% of chromosome length, intrigues us a great deal. Tens or hundreds of genes can be involved in such a deletion, and the genetic implications, therefore, of such a deletion could be tremendous. Also, as we all know, production of such simple deletions appear to be linearly related to dose of ionizing radiation.

- (a) Do you know where the mythology has arisen that we need not be concerned about such autosomal deletions since they will all be lethal? References in the human?
- (b) Do you think such deletions, so difficult to measure, and to our knowledge never yet measured, might account for a significant part of the 75% of spontaneous abortions that are not caused by gross chromosomal aberrations? We presume it is even possible that most of the 75% of unexplained spontaneous abortions could be due to such deletions, don't you think?
- (c) Also, it would be most interesting to know what proportion of fetal and neo-natal deaths might be due to such deletions in chromosomes, wouldn't it? It is especially intriguing, since we have essentially no measurements that are relevant, to consider the possibility that radiation-inducible deletions might account for a large share of such a major medical problem. Certainly those who set standards for radiation exposure must share our suspense concerning the outcome of new scientific developments concerning a major medical problem they haven't even considered in their deliberations concerning radiation safety, don't you think? Or should we not consider the human tragedy of fetal and neo-natal deaths important, especially in view of the population explosion?

24. We should like to return to the questions (See question 13) concerning the truly major diseases of our time, such as ischemic (coronary) heart disease, our largest killer by far, diabetes mellitus with its tragic complications, schizophrenia, and rheumatoid arthritis. As you probably know, the evidence is by now overwhelming that all these major diseases, and others of great societal importance, have a major genetic component. Since the data do not fit the classical single-gene inheritance patterns, it is by now clear that multiple genes, interacting in an unknown fashion with environmental factors, are at the basis of these diseases. This multi-gene basis is well described by Dr. C. O. Carter (Hospital Practice 5, 45-59, May 1970). Certainly the genetic factors for these major killing and socially maiming diseases must be at the very center of our attention with respect to all mutagenic influences, such as ionizing radiation.

It is entirely possible that the crucial genes disturbed, say, in leading to ischemic heart disease (e.g. determinative of lipid metabolism or possibly determinative of arterial wall structure) might be grouped in a particular region of one of the autosomes.

- (a) If such a reasonable possibility exists for ischemic heart disease, wouldn't it be rather crucial to know the radiation-effect in producing deletions of such a chromosomal region?
- (b) Wouldn't it be something of a disaster to overlook the possibility that chromosome deletions related to the major killing disease of our time, coronary heart disease, were just overlooked in considering radiation standards? Or does the assurance that this could not be so exist somewhere that has escaped our notice? References, please?

24. (c) Some scientists would consider that overlooking the possible role of radiation-inducible chromosome deletions important for these multi-gene diseases, such as schizophrenia, rheumatoid arthritis, or coronary heart disease might be an unparalleled disaster of judgment - almost a kind of Russian Roulette with the health of the people of the USA. Wouldn't you, Dr. Tompkins, be inclined to agree?

(d) Suppose our evolving knowledge shows that chromosome deletions are the major underlying factors in the heritable part of such major diseases as coronary heart disease or schizophrenia. Let us consider further the possibility that such chromosomal deletions interfere only slightly with reproductive fitness. Reproductive fitness of heterozygotes is commonly considered to determine the rate of removal of mutations introduced into the population. If these chromosome deletions do interfere minimally with reproductive fitness, would it not be possible through induction of such deletions to increase steadily toward high values ischemic heart disease, schizophrenia, rheumatoid arthritis, and other serious diseases in our population? Couldn't this lead to a progressive deterioration in the human species, in the quality of life, and in longevity itself? We wonder if there are some data which rule all these possibilities out as a consequence of exposure to FRC Guideline radiation?