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**PANEL DISCUSSION ON
HEALTH EFFECTS OF LOW-DOSE IONIZING RADIATION :
SCIENTIFIC FINDINGS AND NON-THRESHOLD HYPOTHESIS
— FROM AN IAEA INTERREGIONAL TRAINING COURSE ON HEALTH
EFFECTS OF LOW-DOSE IONIZING RADIATION HELD IN THE
NUCLEAR EDUCATION CENTER, JAERI, TOKYO
February 28 to March 18, 1994 —**

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Nuclear Education Center

**日本原子力研究所
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Panel Discussion on
Health Effects of Low-dose Ionizing Radiation:
Scientific Findings and Non-threshold Hypothesis

— From an IAEA Interregional Training Course on Health
Effects of Low-dose Ionizing Radiation Held in the
Nuclear Education Center, JAERI, Tokyo
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Japan Atomic Energy Research Institute
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This is a record of a panel discussion in the IAEA Interregional Training Course. In current radiation work, protection measures are taken on the assumption that any amount of radiation, however small, entails a risk of deleterious effects. This so-called non-threshold assumption of radiation effects, on the one hand, creates public distrust of radiation use. However, because the health effects of low-dose ionizing radiation are difficult to verify, wide views ranging from the non-threshold hypothesis to one which sees small amounts of radiation as rather useful and necessary are presented. In this panel discussion, how the health effects of low-dose ionizing radiation should be considered from the standpoint of radiation protection was discussed. Panelists included such eminent scientists as Dr. Sugahara and Dr. Okada, who are deeply interested in this field and are playing leading parts in radiobiology research in Japan, and Dr. Stather, deputy Director of NRPB, UK, who, in UNSCEAR and ICRP, is actively participating in the international review of radiation effects and the preparation of reports on radiation protection recommendations. They agreed with each other that although it is reasonable, under the current scientific understanding, to follow the recommendation of ICRP, research in this area should be strongly promoted

hereafter, for basing radiation protection on firm scientific grounds. Many participants actively asked about and discussed problems in their own field.

Keywords: Low-dose, Health Effects, Non-threshold Hypothesis, Radiation Protection, ICRP

低線量放射線の健康影響：科学的知見と非しきい値仮説
に関するパネルディスカッション

— 低線量放射線の健康影響に関する IAEA 全地域トレーニングコース
原子力総合研修センター、日本原子力研究所、東京
1994年2月28日－3月18日、から —

日本原子力研究所
原子力総合研修センター

(1995年4月24日受理)

IAEA 全地域トレーニングコースにおけるパネルディスカッションの記録である。現行の放射線業務においては、いかなる少線量の放射線被曝といえども、それに伴うリスクがあるものとする、いわゆる“非しきい値仮説”に基づいて、諸々の防護方策が講じられている。そして、このことが、一方において、一般大衆の放射線利用への不信感をも生み出している。しかし、低線量放射線の健康影響については、実証が困難なために、しきい値がないとするものから、あるとするもの、さらにある程度の被曝はむしろ有益、必要であるとするものまで、幅広い見解が提出されている。本パネルディスカッションでは、低線量放射線の健康影響問題に強い関心をもち、わが国の放射線生物学研究において指導的立場にある菅原、岡田両博士、また、UNSCEARおよびICRPにおいて、国際的に、放射線影響のレビューまた放射線防護勧告書の作成に活躍中のスタザー博士（英国 NRPB 副所長）らをパネリストに迎え、低線量放射線の健康影響を、放射線防護上、どう考えるべきかが議論された。科学的理解がまだ完全ではない現段階においては、ICRP 勧告の考え方に従うのが妥当であるが、放射線防護をしっかりと科学的根拠に基づいたものとするために、この分野に対する研究は今後積極的に推進する必要があるとする点でパネリストらの意見は一致した。研修生は、それぞれ、自分の分野の問題について活発に質問し、議論に参加した。

**Panel Discussion on Health Effects of Low-Dose Ionizing Radiation:
Scientific Findings and Non-threshold Hypothesis**

— From an IAEA Interregional Training Course on Health Effects of Low-Dose Ionizing Radiation held in the Nuclear Education Center, JAERI, Tokyo, February 28 to March 18, 1994 —

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- Panelists: S.Kobayashi (*NIRS, Chiba*)
R.Mukherjee (*IAEA, Austria, Course Coordinator*)
S.Okada (*Nuclear System Association, Tokyo*)
J.W.Stather (*NRPB, UK*)
- Participants: Y.L.Aksu (*Turkey*)
B.Chen (*China*)
T.Galichanskaya (*Ukraine*)
O.Garcia (*Cuba*)
I.Gyuleva-Angelova (*Bulgaria*)
T.Hirayama (*Brazil*)
G.Kozak (*Syria*)
Y.Lusiyanti (*Indonesia*)
N.B.Nasazzi (*Argentina*)
B.Nasri (*Morocco*)
G.Nesterenko (*Belarus*)
H.J.Oh (*Korea*)
E.K.Osei (*Ghana*)
C.Panlaque-Aguilar (*Philippines*)
I.M.Petcu (*Romania*)
- Course Coordinator: K.Takada (*JAERI, Tokyo*)

目 次 な し

Chair (Dr. T. Sugahara): Good afternoon, ladies and gentlemen. We shall start our panel discussion. I think you know all the members of the panel except myself. I am sorry to have to introduce myself. I am Dr. Sugahara from Kyoto University, but I retired more than 10 years ago. I am a radiobiologist interested in the low-dose effect and also cancer treatment through radiation. And so I am very happy to chair this panel discussion as a radiobiologist, on the topic of the health effects of low-dose ionizing radiation. I am told that the participants have different disciplines. Some of you are radiobiologists working in the research field, and some of you are engineers or health physicists of radiation protection, and some are medical doctors. So, if possible, before starting our panel discussion, I would briefly like to know what is our aim, and what did you expect from this training course? Then after the panel discussion, I would like to make a summary of our responses to your requests. So, are there any radiobiologists here? Would you express your opinion about what was your purpose, and what do you expect? Not a conclusion, conclusions we will have at the end of our meeting. So is there anyone in the field of radiobiology?

Mr. O. Garcia (Cuba): I'm in cytogenetics. It's my principal field. But I've really been interested in hormesis since the first time that I heard about it. Of course I expected more information about this phenomenon during this course. But for me it became possible to think that hormesis exists.

Dr. T. Sugahara: Thank you. Are there any health physicists or radiation protection majors? Many! (laughter) Is there anyone who would like to state their ideas? What do you expect concerning the low-dose effect?

Mr. Y.L. Aksu (Turkey): I am working in radiation protection. I expect more knowledge about the low level radiation effect. Our department wants to implement our regulation due to ICRP 60. And then we want to learn what is the mechanism of the low level radiation effect, and what is the philosophy of decreasing the limits, population and worker's limits.

Dr. T. Sugahara: Thank you. I am told there are some clinical medical doctors. What did you expect here?

Ms. G. Nesterenko (Belarus): I am a medical doctor. My main duties are the organization and providing of medical assistance to the affected population and analysis of the health effects of ionizing radiation due to the Chernobyl Nuclear Plant disaster. Therefore, I've expected to receive knowledge about new achievements in the field of health effects from low-dose ionizing radiation. It's very important, especially given our present condition. The long-term influence of radiation factors simultaneously combined with a number of other harmful factors may result in unexpected effects. So, this training course is of great value for me. Thank you.

Dr. T. Sugahara: Thank you. So based upon these participant interests, we would like to start our panel discussion. And as a panel discussion, we'd like to have two rounds; the first round to ask our panelists to offer our discussion materials and what they would like to emphasize about low-dose effects from their own viewpoint. In the second round, first we will have some questions after the panelists' presentation, and second, we will have a general discussion. If possible, I will present some broad topics one by one, and have a discussion about each. And after the second round, we'll have some concluding remarks. So first I would like to ask Dr. Okada to give his presentation.

Dr. S. Okada: I gave a keynote speech for this course, so what I'm planning to do is give a brief summary of the problems we are going to discuss today.

What are the low dose and the low dose rate? I suggest that when we discuss the low dose we are mainly concerned with 1-10 rem or 10-100 mSv. Are you in agreement with this? Would anyone like to expand more? The low dose rate I put at 1 mSv per year. This is natural background radiation. Radiation workers receive maybe several tens to several hundred mSv per year. Over 1 mSv per year could be the minimum dose rate. So we could study with a higher dose rate. Do you have any argument with this? Will it be acceptable? Now, second, I would like to give you three new — well, Dr. Sugahara said new — findings, and they are findings that are interesting to us at the low dose level. The first one is adaptive response, and this you have heard from many people, which is probably the biological defense mechanism at the cellular level. You give a priming dose of 1-10 rads, and by giving this low dose, the activation of genes takes place. Then the proteins, new proteins are synthesized, including maybe repair enzymes. So when new proteins are synthesized, and if you give a large challenging dose, that will result in the reduction of DNA damage by these repair enzymes, and lead to the decrease of chromosome aberration, micronuclide production, mutation and cell killing. One thing we hoped this would also decrease is in vitro carcinogenesis or transformation, but Dr. Sasaki of Kyoto found that this will increase. So, it looks like in vitro carcinogenesis is a little bit of a different story. However, there are many questions to be answered. One of you asked me when I gave my lecture if a priming dose, and initial dose, is given at a low dose rate, what happens? And I think that is a very good question, especially from the aspect of radiation protection, the priming dose at a low dose rate is the one that should be studied carefully. And then the second big question I thought was how adaptive response will affect the human risk at a low dose. Human risk means carcinogenesis, mutagenesis, teratogenesis, and so on. We have no data at all on this.

The second finding I would like to go into is — one of you asked is radiation hormesis, and probably we should pay attention to radiation hormesis here. And the adaptive response is a biological defense mechanism at several levels, but here radiation hormesis by Luckey is the one biological defense mechanism at whole body levels. In his scheme, if a low dose of 10-100 mSv is given, the immune mechanisms of the whole body will be activated, stimulated, and this results in prolongation of the life span or suppression of growth of implanted tumors. And some of these experiments are indeed reproducible. Some of them, I think, are still questionable, so we have to be very careful about this. And also the big question we have is, does hormesis contribute to reduction of human risk? There we have almost no data at all.

This is an overhead slide I already showed you (Fig. 1), showing various dose rates, and at a low dose rate, there's a prolongation of the life span, at a higher dose rate, there's a shortening of the life span. This type of experiment has been conducted by several groups.

Now, if you plot them according to Luckey, the life span study I showed you is, the low dose, resulting in life prolongation, and the higher dose, resulting in life shortening. However, if you — the ordinate of this one is upside down, making a beneficial effect here, and an injury here, this curve will become this curve. And this is natural background radiation. According to Luckey he proposed that cancer mortality, growth, life span, reproduction, all of these, if one puts them together, we'll get this type of curve (Fig. 2). And he extends — this is natural background radiation — extends this to below the natural background radiation level. And so you have to decide for yourself whether you believe this or not. It's up to you. A very irresponsible statement, I guess.

This is Shimizu's work on A-bomb survivors (Fig. 3); for leukemia, you could draw a curve like this. But none of these are significant. This is a solid tumor, except for leukemia,

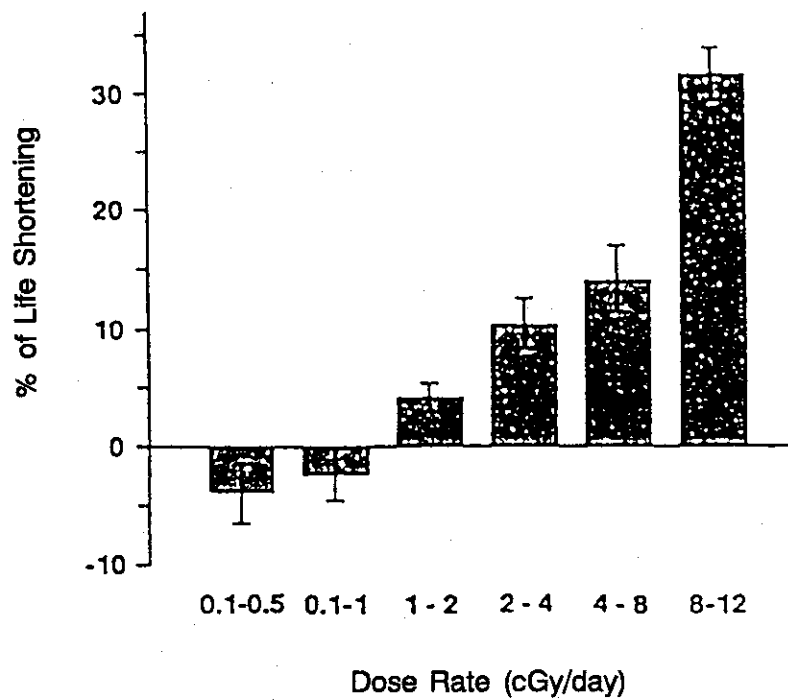


Fig. 1. Relationship between dose rate and life shortening (Lorenz et al., 1954).

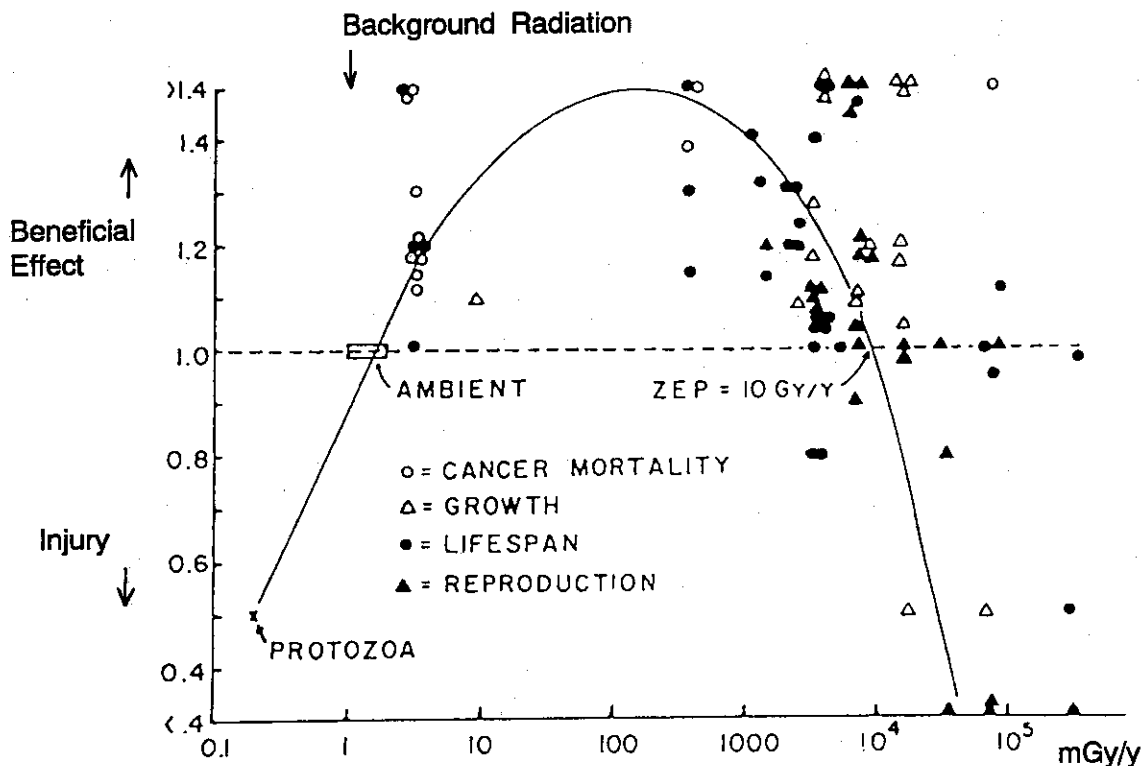


Fig. 2. Radiation hormesis. Chronic whole-body exposure of humans (data on the left side) and experimental mice and rats (data on the right side) to low LET radiation. The ordinate indicates the ratio of exposed/control performance for the different parameters indicated (Luckey, 1991).

Number of subjects and cancer deaths by each organ dose[†]

	DS86 Radiation Dose (Sv)							
	Total	0	0.010- 0.019	0.020- 0.049	0.050- 0.099	0.100- 0.199	0.200- 0.499	≥0.500
Number of subjects	86520	45148	7430	9235	6439	5316	6271	6681
Number of cancer deaths								
Leukemia	211	81	11	14	8	11	21	75
All cancers except leukemia	6501	3246	498	717	516	400	533	573

[†]For all cancers except leukemia, doses for large intestine is used.

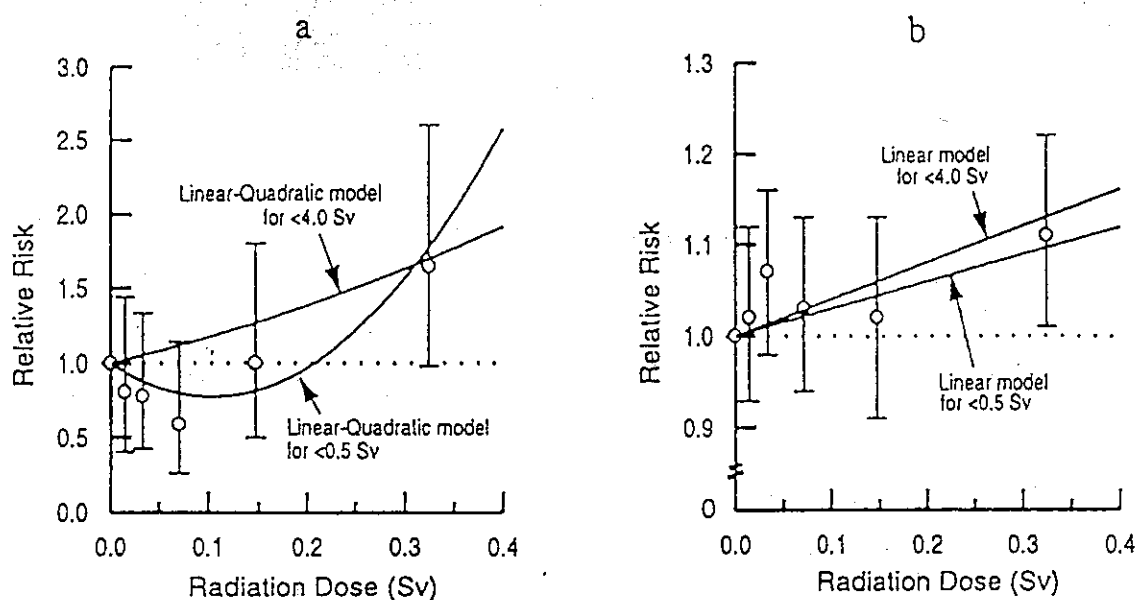


Fig. 3. Relative risk by dose group of : a) mortality from leukemia; and b) mortality from all cancers other than leukemia, 1966-85, for those who were less than 40 years old at the time of bombing (95% confidence interval) (Shimizu, 1992).

and might be a straight line. But the only points which are statistically significant are over about 0.33 Sievert. These are not significant at all. So, well, we'll come to this one again.

The third point I would like to mention is spontaneous and radiation-induced DNA damage (an OHP slide was cut). And I told you we are exposed to oxygen while, somehow, we believe or thought the DNA in the cells is stable. However, according to Lindahl and several other people, DNA in the cells is not stable; it is unstable; it is always subject to oxidation. This is the oxidation attacking the bases, or deaminating or hydrolyzing base and sugar bonds, releasing base, methylation and all oxidation, hydrolysis, methylation going on. Natural cells spontaneously. And according to him, we are getting 100 to 500 damages or decays of DNA per hour per cell. And if I look at these types of damages, and compare them with radiation-induced damages, they are very similar. An exception to this is that radiation might induce double-strand breaks, and spontaneously induced DNA damage does not have double-strand breaks, or very few have double-strand breaks.

The reason why is that heavy high energy radiation has dense ionization and excitation, or as the particle goes through, dense ionization and excitation take place, and will probably cause multiple damage, including double-strand breaks. Low LET radiation induces ionization and excitation like that, but they also have delta rays, or slow, low-energy electrons emitted. And this will induce excitation and dense ionization. So this high LET fraction of low LET radiation could also induce multiple damage on DNA and maybe double-strand breaks.

I showed you this cartoon (an OHP slide was cut), and we are exposed to many kinds of things, including smoking, various types of food and ultraviolet radiation from the sun; we also respire oxygen, and oxygen, I'm sure you know, produces active oxygen and can damage DNA.

This is the Doll and Peto data (Table 1). I'm showing that about 30% of cancers are due to cigarette smoking; and food, about 35%; as for radiation, including medical exposure, it is less than a few percent. So spontaneously we are making lots of damage, not only to DNA, but we can see these carcinogenesis.

Last time I showed you 12 items on how to prevent cancers. But at that time I had only 11; I missed 12 somehow. Number 12 is keep your body clean.

Well, I am spending too much time. According to Ames and Gold, quite recently, they say that 75% of cancers are preventable; the other 25% are non-preventable (an OHP slide was cut). And about two-thirds of preventable cancers are due to smoking and diet, and about 25% are due to hormones, and so on. Radiation is maybe very little. I don't know whether they are putting here or not, but it is insignificant compared to that. So his advice is, if you receive a low dose of radiation, better give up smoking and eat more fruits and vegetables, and less fat. That will cut down your low-dose effects. I guess that's all.

Table 1. Proportions of cancer deaths attributed to various different factors (Doll and Peto, 1981).

Factor or class of factors	Percent of all cancer deaths	
	Best estimate	Range of acceptable estimates
Tobacco	30	25-40
Alcohol	3	2-4
Diet	35	10-70
Food additives	<1	-5 -2
Reproductive and sexual behaviour	7	1-13
Occupation	4	2-8
Pollution	2	<1-5
Industrial products	<1	<1-2
Medicines and medical procedures	1	0.5-3
Geophysical factors	3	2-4
Infection	10 ?	1-?
Unknown	?	?

Dr. T. Sugahara: Thank you. Next Dr. Stather, please.

Dr. J.W. Stather: I wasn't proposing to repeat the lecture that I have already given you on the effects of radiation at low doses. I would like though to remind you of one or two points that I made. I will mainly refer to the new ICRP Recommendations, the biological basis for the new dose limits and how they might change in the future, with better information. In putting together Publication 60, ICRP explained in Annex B how it quantifies radiation risks, both of genetic disease and of cancer. We now believe, and I think not just ICRP, but most international organizations believe, that it is the risk of cancer that is more important in setting dose limits than the risk of hereditary disease. The main uncertainty then relates to the assessment of the risk of cancer. I explained to you why estimates of this risk have changed in recent years. We now fit a multiplicative model to the Life Span Study for solid cancers and we have to project the risks observed to-date over the life span of the population. There are clearly uncertainties in this. In the A-bomb survivors to-date, we have only seen something like 260 radiation-induced solid cancers and 80 radiation-induced leukaemias out of a total of about 6,000 cancer deaths. So we actually haven't seen very many radiation-induced cancers in that population at all. When they are separated into different ages at exposure, different tissue types and different times after exposure, then there aren't very many in any one particular group. The multiplicative model that we fit to calculate lifetime cancer risks is really an empirical fit to the present data. There isn't a real modelling basis or fundamental understanding behind that model. So there clearly must be uncertainties about the lifetime estimates of risk.

There are other uncertainties, low doses we might come back to, but how the risk is transferred from one population to another is clearly another uncertainty that we discussed. ICRP have used two different models to make that transfer but there may be even better ones that will be developed in the future. In practice, whichever model is used, the overall risks don't vary very much. We obviously have to work out what the risks are at low doses because we are basing our risk estimates almost exclusively on groups exposed to fairly high doses at high dose-rates. The data come predominantly from the Life Span Study of the A-bomb survivors and I have explained how we make allowance for the dose-rate. We put in a reduction factor (a DDREF) to allow for the fact that for radiation protection purposes we are concerned about low doses and low dose-rates. As you have heard defined by Dr Okada, there must be some uncertainty here. One point that has certainly struck me is that in the animal studies where quantitative information is available on dose-rate effects, then if the dose rate is reduced by a factor of up to a few thousand, the risk of cancer per unit dose may be reduced by a factor of only 2-5. So, whilst there clearly are repair processes going on, they are really not all that effective. I should also remind you that the low dose-rate studies in animals were being carried out at something like 100 mGy d^{-1} , which is still very much higher than the few mGy y^{-1} that we would all be exposed to from natural background radiation. However, we should obviously be careful about how we set protection standards and perhaps there is a degree of caution here. The mechanistic studies which were reviewed in the 1993 UNSCEAR Report would suggest that if radiation-induced cancer is due to single genes being damaged as a result of effects of DNA in single cells, if there is repair of DNA and if that repair isn't completely effective, then there is probably no argument for the suggestion that there will be some threshold dose beneath which there will be no effect. The argument must be that any radiation dose could give some risk of cancer, even though it might be very low.

The main difficulty though for assessing risks at low doses is that, whether we go to animal studies or human epidemiology, we really don't see any significant excess at acute

doses of less than about 200 mGy. You have already seen Shimizu's data on the Life Span Study and the lowest dose at which it is possible to detect significant excesses of cancer is in the group exposed between 200 and 500 mGy. Although there are some increases in risk at lower doses they are not statistically significant. If we go to Roy Schull's data on thyroid cancer following thymus irradiation, there we can see an increased risk of thyroid cancer at doses around 160 mGy. I would also remind you that the Oxford Survey of Childhood Cancer examined the effects of prenatal obstetric radiography. It showed that doses as low as about 10 mGy give an increased risk of cancer in childhood, particularly leukaemia. So that is the one epidemiological study I can point to which suggests that, even at really quite low doses, it is possible to detect a risk of cancer in people, which is manifest in this case in the first 10-15 years of life. It may be argued that the risks will be much greater in the fetus than in the young child or in an older person, but I don't believe there could be a completely different mechanism operating. So I suggest, even at low doses, we can actually detect in human populations a risk of cancer. Of course, the reason we can detect the risk is that the cancer rate in children is very low. When we are looking for excess risks of cancer in adult populations exposed to radiation, then the basic difficulty is that there is likely to be a high background incidence; roughly a quarter of the population will die of cancer. At very low doses the increase in the risk is very small and cannot be detected. Very large populations need to be followed if an effect at very low doses is to be detected.

Well, that is where I think we stand in protection terms. It may be somewhat conservative, but I think the only reasonable approach, on the basis of the information we have at present, is to assume that any radiation dose might give some risk of cancer and therefore a dose limit cannot be set below which there will be no risk. UNSCEAR and the American BEIR V Committee have also adopted basically the same approach.

Dr. T. Sugahara: Okay. Then we are going to Dr. Kobayashi.

Dr. S. Kobayashi: I am in a rather advantageous position since I talked to you this morning, and so you remember what was already mentioned. But for the sake of the other panelists, I will briefly show what I already mentioned. One of the most important cancers which is now growing not only in Japan but all over the world is lung cancer. The causes for this lung cancer are notably the smoking of tobacco, and also as you might have already heard from the other speakers, radon at home. As regards the health risks of radon, I have made a summary here that there was epidemiological research done on miners who were subjected to a high dose, or to a medium dose, and the answer is, yes. And based on this research, ICRP has developed recommendations. Now, as to the public, there were many, many reports. Some of them were affirmative and some of them were negative, but this morning I showed you one study in Sweden which is rather convincing. It argued rather convincingly through radiobiological experimental study using rats and dogs, and we certainly can see the causation of lung cancer by radon. Recently in molecular biology we notice that by radon exposure there is a change in P53, which is a notable tumor inhibitor and suppressor which has undergone mutation so that lung cancer developed. So this is the present status of the health risk from radon. As to the relative significance of radiation in the overall estimation of the risk to which we are always exposed to, I presented this table (Fig. 4). Here are several classes of disease. They cluster around the range 10^{-3} to 10^{-5} on this risk scale, and then we have the radiation risk calculated here according to the age distribution of the Japanese population. And this is like this. And then we have the occupational exposure as such. And we notice that the actual or estimated risk due to radiation exposure is rather low at present, almost to an

Diseases		Social activities		Occupation		Radiation
Death or incidence /yr.	Accidental death /yr.			Death or casualties /yr.	Death by cancer /yr. (mean risk per 1 year of life expectancy)	
● Hereditary disease (new-born)		10^{-1}	1/10	● Mining, Forestry		
		10^{-2}	1/100	● Building	10 Sv	
● All cancers (all ages)		10^{-3}	1/1,000	● Manufacturing		
● Congenital anomalies (new-born)				● Transportation		
● Heart disease (all ages)				● All occupations	1 Sv	
● Cerebrovascular disease (all ages)	● Accidental death (less than 10)	10^{-4}	1/10,000	● Electricity, gas and water supply		
● Stomach cancer (male)	● Accident while walking (above 70)			● Construction		
● Lung cancer (male)	● Motorcycle (teen-age)			● Transportation (all occupations)	0.1 Sv	
● Stomach cancer (female)	● Hang-gliding					
● Lung cancer (female)	● Fishing			● Manufacturing		
● Breast cancer (female)	● Diving			● Agriculture		
● Hereditary metabolic abnormality (new-born)	● Mountain climbing			● Electricity, gas and water supply		
● Diabetes mellitus	● Swimming				10 mSv	
● Leukemia	● Fire				1 Medical exposure (Japan)	
	● Hunting				1 Natural background (international average)	
	● Accident on the highway				1 mSv	
	● Train accident				Occupational exposure (Japan, 1987)	
	● All sports				0.1 mSv	
	● Murder without a cause					
	● Thunderbolt				0.01 mSv	

Fig. 4. The risk scale (Kobayashi, 1993).

acceptable level, such as 10^{-6} to 10^{-8} , something in this range. As professor Okada and Dr. Stather mentioned already, the low dose effect, if it really exists, is covered, the expression of such an effect is covered by the effect of some other environmental agents. And also it may be modified by environmental factors, the factors that are involved in our lifestyle or our living environment. Professor Okada has already shown some tables, which are repeated here again in a different way, and they are an estimation of the potential for cancer prevention here in Japan (an OHP slide was cut). There are several kinds. One is primary prevention, like controlling the amount you smoke, by which about 8% could be controlled or reduced, by optimistic estimates. And through dietary improvement, like eating fresh vegetables, green, yellow vegetables, we can control about 12%. By prevention of virus infections, improvement of the work environment and improvement of air pollution, etc., we can achieve the reduction of about one-third of all cancers, as Professor Okada mentioned. And then as a secondary prevention we'll have this so-called screening campaign, and in Japan we have campaigns for stomach cancer, cancer of the cervix, breast cancer, lung cancer, and colorectal cancer. We have these for the mass screening process. By achieving these we can obtain about a 13% reduction in the risk of cancer. As a final approach, that of treatment, application of current state-of-the-art treatment, the most advanced cancer therapies like the ones you have seen in our institute — heavy ion accelerator etc., through these we can achieve about 10%. So the cheapest way to control cancer induction is of course here, by dietary improvement, eating a lot of green and yellow vegetables and fruit. And by these methods, any effect of cancer incidence due to low-dose radiation would be covered, and would not manifest itself. This is my first statement, Mr. Chairman. Thank you very much for your attention.

Dr. T. Sugahara: Thank you. Dr. Mukherjee please.

Dr. R. Mukherjee: Well, Chairman, panelists, participants, I have been asked to comment on this subject as to what is IAEA's role in this area. Well, as you see, low-dose radiation affects understanding and dissemination. We are holding this course, so obviously this brings us into that subject field. So as you see it is these IAEA activities in the low dose area that I will highlight, and in so doing, I would like to first mention that, because it states that IAEA policy, and as you know IAEA is an international organization, an intergovernmental organization of the UN family, it's statutory objectives are what decides where we are primarily concerned. And it seeks to accelerate and enlarge the contribution of atomic energy to peace, health, and prosperity throughout the world. So it promotes the beneficial applications of ionizing radiation for peaceful purposes. IAEA statutes are particularly...in the particular areas of health and safety, it endeavors to establish or adopt standards of safety for the protection of health and for minimization of danger to life and property, and in that way it sets the standards relating to the workplace even.

IAEA safety standards are to be applied to IAEA's own operations as well as to those making use of materials, services, equipment, facilities and information supplied through the agency, if other bodies provide to another country through IAEA mediation. Where appropriate, IAEA is required to consult or collaborate with other specialized agencies in developing or adopting these safety standards. This sets the framework for the agency's activities and policies.

Now, coming to this question of low dose radiation and human health safety. In the International Atomic Energy Agency, this one specialized department, which is vested with the task of nuclear technology safety — and under this there are the division of nuclear safety, radiological protection services to member states, radiological safety, development and

implementation, and also extended to nuclear energy vis a vis other energy sources to assess comparative risks and to develop criteria and guidelines about how we can implement these approaches — and to say that right from the inception, nuclear technology has taken a strong, stringent approach of quantitative, quantified safety development. It's one of the energy sectors which is most safety oriented, and it has a scientific knowhow base guideline to proceed with that. The other conventional energies have not gone through this — up until the time when we are acting behind the clock — and environmental pollution and all other things are putting public pressure on them to come back to that safety culture, and nuclear safety development expertise and experiences have much to contribute towards that development. So they are providing guidance.

Well, with this introduction, I would summarize that in the nuclear safety field, the nuclear safety department, development strategies and development of safety strategies — a basic safety series — under all radiation application circumstances, safety series are developed through expert advice and guidance, and is actually transmitted to the member states in their development of national nuclear programs so that the safe handling of radiation sources and radiation facilities and establishments can be adhered to. And of course in all these basic safety series, the information conforms to what international regulatory organizations like UNSCEAR and ICRP, or very well-advanced national regulatory guidelines, recommend — these are taken into consideration. And they, from time to time, as our knowledge and information advances, are subjected to updates and revisions, and from the outcome of these reviews, recommendation are made.

So, to cite a specific example, when this reactor accident took place, these two member states, at their request, received accident management help, and mitigation steps were taken. The International Chernobyl Committee was constructed through the Agency's mediation, and all other experts from the member states pooled their expertise together, and the Agency was the executing organization. If accidental overexposure takes place, there is round-the-clock service there even if it is at an odd hour of the night or something. Requests come from any part of the world. There is a body which is already identified, and they will take off immediately and provide services. Fortunately, we haven't had to resort to these services very often, but it did happen several times. In development and updating of these strategies, research support and workshops and advisory missions are taken, and also training courses to train the safety teams in national member states' governments are held, and these are directed for public information, because for public alleviation of radiophobia and radiation — what is radiation, what is it all about — this type of information is actually very important. Why the public has undue apprehension about radiation is because of the fact that in the course of the development of radiation techniques and technology, there was not so much communication between the elite group, who were developing this information, and the members of the general public. And as a result, they have much opportunity for misinformation and misconceptions.

This last one is in my division because, as we see, the safety from radiation exposure, involves both physical parameters of radiation and radiation dose measurement and dose reduction, and characterization, that's there. But it is very important that radiobiological studies, the biological effects of radiation — that information has to be developed in parallel. And as a result, my division, which is the division of human health, is closely involved with the division of nuclear safety, and there are joint research programs, activities on elucidation of low level radiation effects. As I mentioned the other day about this hot particle radiation — both radiological elucidation and radiobiological elucidation of such sources in terms of the risk of lung cancer and skin cancer. Then there is the mechanism of adaptive response. This also

supported, and expert research is generated. There is such information, and it is coordinated. We have manpower training by holding training courses, and awarding fellowships, and we hold meetings and publish the proceedings which become a source of information for member states. So with this information, I would just like to say that the International Atomic Energy Agency conforms to the safety guidelines that prevail internationally and nationally, and it disseminates all this information to all member states. Of course, with regard to their standard setting and implementation in the national context of radiological safety, the national authorities make use of this information to make policy and accept judgement. Thank you.

Dr. T. Sugahara: Thank you Dr. Mukherjee. At the end of the first round of discussion, I will give you some thoughts, not as the chairman, but as one of the panelists. As I told you, I am a radiobiologist interested in this field, and I would like to propose one new aspect, or remind you of a very important point. Initially, when considering biological events and radiation effects, usually people concentrate on the DNA damage, and then mutation. And so cancer is originated based on the genetic change induced by ionizing radiation. But as you learned in this training course, there is some adaptive response. This is one of the examples of epigenetic nature, because it starts from the damage to DNA, but the response is not a mutation, not a change of DNA itself, but just a gene expression. So this is a really epigenetic nature. And so there are many — recently, radiobiologists are finding many such kind of responses, epigenetic responses. Here is a table (Table 2) presented by Dr. Adams at the Kyoto meeting in 1992 we organized : an international conference on low-dose effect and defense mechanisms. At that time he presented various kinds of biological responses to several stresses, and almost all of them are epigenetic in nature. Some are an increase in metastatic properties or growth, or mitogenic stimulation, drug resistance, and so on. And some are oncogene expressions, protooncogene expressions, also induced by ionizing radiation. And recently we added one, apoptosis. Apoptosis is also induced by ionizing radiation, and it is well known. But probably this may be a kind of epigenetic nature. It was a switched-on, programmed cell death. You can see this in thymocytes, or stem cells in intestinal crypts. So we can see apoptosis, which is induced by epigenetic nature. And I will show you some examples of this in Fig. 5. For example, this one is still under speculation. This signal transduction model of the G1-S checkpoint via P53. And gamma-rays or UV-rays or chemicals induce some DNA damage. I'm not sure what kind of damage this is originally. So we have a question here. And this damage induced AT gene product. And it increased P53 protein, and then this induces a G1 arrest. Usually if this is all okay, we have G1 arrest and we can expect DNA repair. But when the AT gene is mutated, in AT, ataxia telangiectasia patients, this activity is not present, so there is no G1 arrest, and mutation accumulation, and cell death and/or cancer will be originated. And a completely different point is that this is still of the epigenetic nature. Figure 6 is the case of induction of metastasis. The left panel is an in vitro experiment, and the right one is an in vivo experiment. This is a B16 cell adhesion to fibronectin in vitro. The abscissa is zero, 0.25, 0.5, 1.5, 2.5 Gy in both figures. So this is a centi-Gray order. At 50 cGy we have the highest response. And in vivo, you can see the same thing happened. This is in vivo, so cancer cells were given intravenously to C57 black mice to obtain experimental metastasis. And here you can see, after irradiation of 50 cGy, we have the highest incidence of the metastasis. And a very important point is that if we check the integrin receptor expression by using the monoclonal antibody, we can see the increase of this receptor expression as a result, an important point, in all irradiated cells. Radiation effects are usually random. But in this case, all irradiated cells responded rapidly, and again it's very rapidly, within five minutes. And this is reversible, so it is completely different from the

Table 2. Biological responses to cellular stresses
(Adams, 1992; modified by Sugahara, 1994).

Changes	Agents
A. Biological properties	
Increase of metastatic potential	UV-irradiation TPA <u>γ-radiation</u> hypoxia
Growth/mitogenic stimulation	glucose starvation and acidosis H_2O_2 and t-butylhydroperoxide ($10^{-8}M$) UV-radiation Low oxygen concentration (2.5%) Adriamycin ($10^{-9}M$)
Drug resistance	<u>γ-radiation (10Gy)</u> hypoxia
B. Expression of macromolecules	
Xanthine Oxidase/dehydrogenase ratio	hypoxia and glucose starvation
Enrichment of HSP 70 transcripts	UV irradiation hypoxia
Increase of haemeoxygenase	hypoxia UVA, H_2O_2 and sodium arsenite heat shock
Increases of PKC activity/transcript expression	<u>x- and γ-irradiation</u> UVA
Depletion of topoisomerase II	Chronic anoxia and glucose starvation
C. Expression of protooncogene transcripts/gene products	
fos and/or myc	<u>x-irradiation</u> <u>γ-radiation</u> heat shock UVC hypoxia
D. Apoptosis	
Thymocytes	γ -radiation
Stem cells in intestinal crypts	"

radiation effect induced by the DNA damage.

So the problem is this: We start originally from the DNA damage, and this is an original idea. But now we show that some such as adaptive responses are of an epigenetic nature. But the problem is how this epigenetic nature is fixed as genetic change observed in cancer. And another problem is that, if we have two kinds of completely different responses, one genetic and another epigenetic, what is the proportion at different doses and dose rates? So we still have two problems, two questions, for which we have no answers yet. But I think

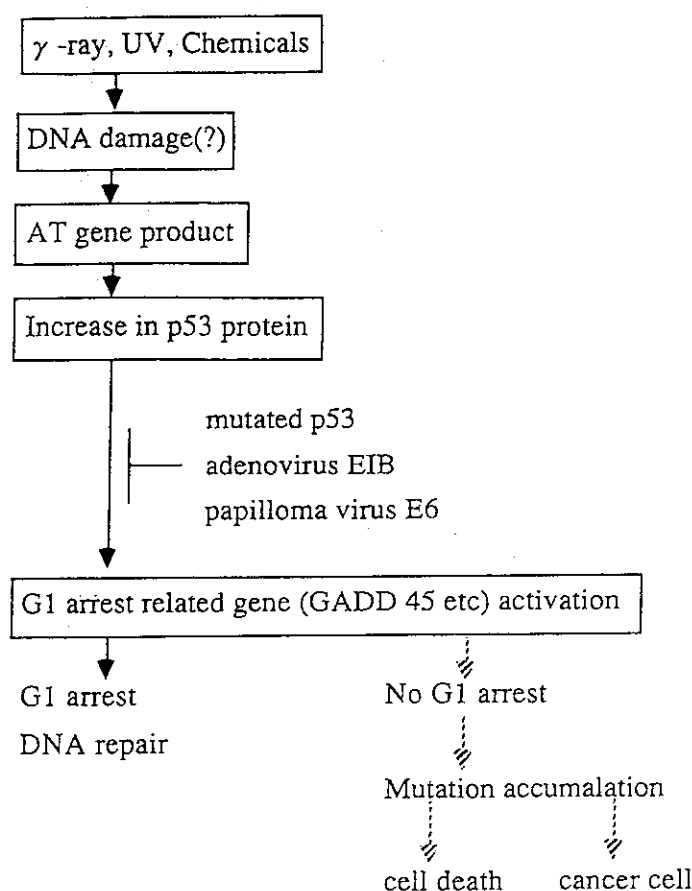
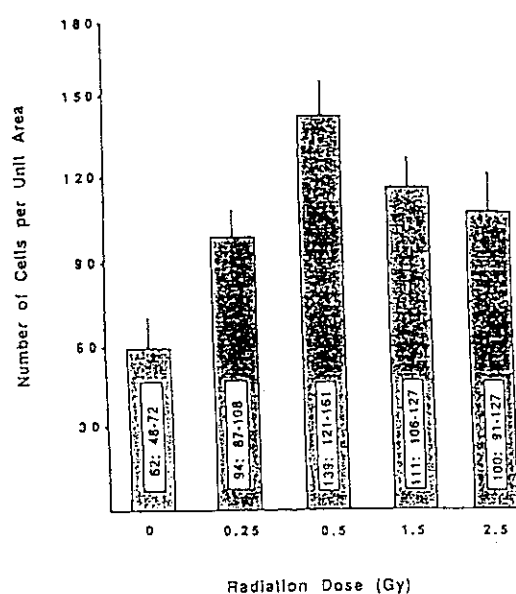


Fig. 5. Signal transduction model for G1-S checkpoint via p53 (Shiio, 1993; modified by Sugahara, 1994).

B16 cell adhesion to fibronectin in vitro



B16 cell experimental metastases in C57BL/6J mice

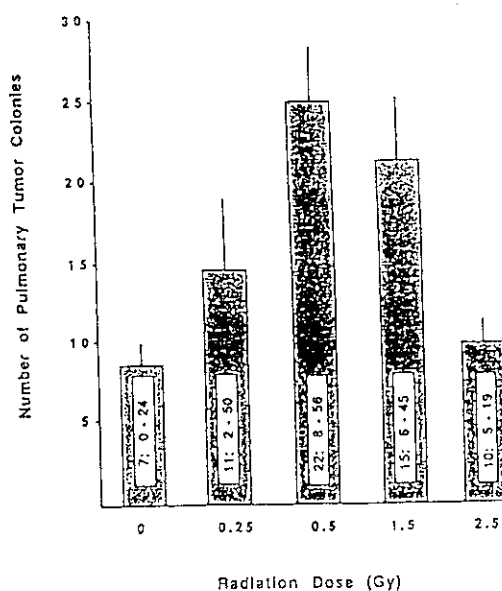


Fig. 6. Effects of γ radiation on B16 cell adhesion to fibronectin and on B16 cell experimental metastasis (Onoda, 1992).

an important point to be emphasized is that now you have to realize that radiation can induce some epigenetic response. And so I don't know at the present moment answers to those two question. I will show you some brief suggestion on this point.

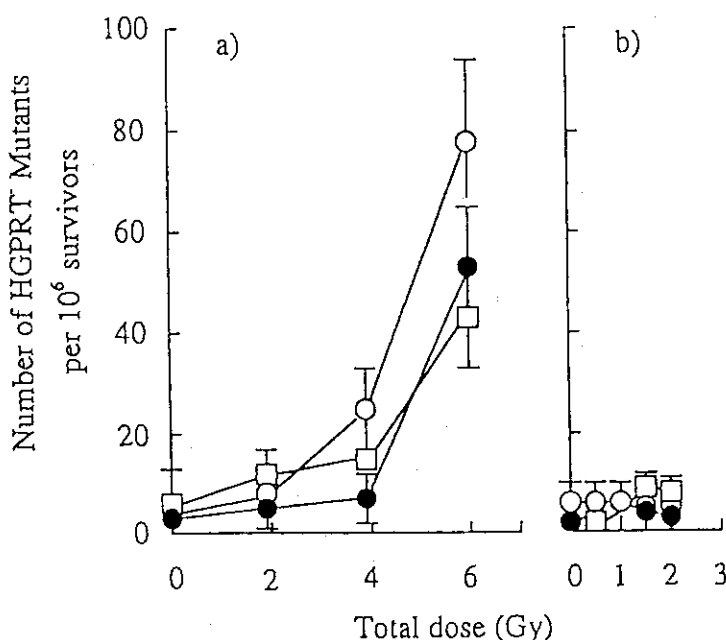


Fig. 7. Frequency of mutants at HGPRT locus in human embryonic fibroblasts (●, HE4, ○, HE6; and □, HE7) irradiated with single dose (a) or multiple doses of 7.5 cGy of ^{137}Cs gamma-rays (b). Each symbol shows the mean and standard deviation of three independent determinations (Sugahara and Watanabe, 1994).

In Fig. 7 there are three kinds of human embryonic cells exposed to single or fractionated irradiation. They are normal cells, not cancer cells, and the panel a) represents a single dose: so 2 Gy, 4 Gy, and 6 Gy. Panel b) represents a multiple dose of 7.5 cGy per week, and the total dose is 1 or 2. And here you can see a big difference. The ordinate is the incidence of mutant at HGPRT locus. And here you can see, at single doses, the increase in the incidence of mutation corresponding to dose, but in the case of fractionated irradiation at cGy order, we can see no increase. Very few. But still we can find some mutation here. So we can compare the molecular basis of these mutations in panel a) and b). And to compare this, we checked the increase of cells lost all exon at HGPRT locus; i.e. a very large deletion (Fig. 8). So the ordinate shows the percent of mutants lost all exons. Here you can see that in acute irradiation the changes observed are very small. And no increase in total exon loss with these doses was observed. But in case of fractionated irradiation, the incidence of all exon loss is increased depending on the dose. So the pattern is completely different. So what does this mean? Probably at single doses we can see very high incidence of chromosomal aberrations, and at fractionated irradiation, the chromosome aberrations, i.e. structural chromosomal aberrations, are very few. But we can see the complete loss of one chromosome at fractionated irradiation. So the pattern is completely different. So my suggestion is that in the case of acute irradiation we can see the direct effect of ionizing radiation, but in the case

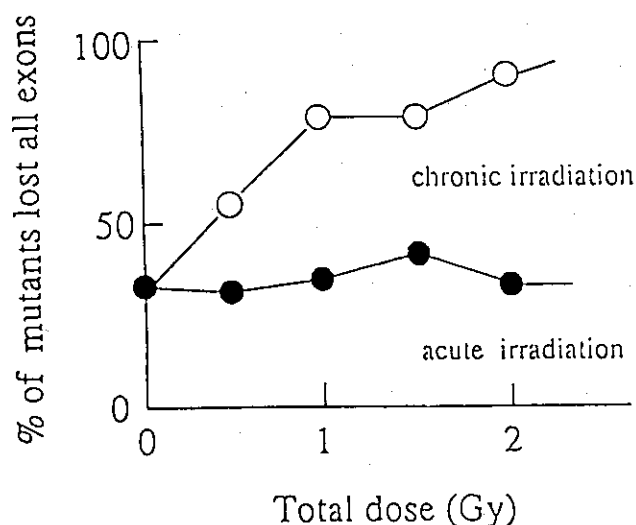


Fig. 8. Increase of cells lost all exons at HGPRT locus in mutants induced by chronic gamma-irradiation analyzed by multiple-PCR (Sugahara and Watanabe, 1994).

of chronic irradiation, some intervening biological event must be there between the ionizing radiation and the effects observed. Recently Dr. Kondo gave us a hypothesis. He proposed a "wound healing error hypothesis". After irradiation, not random but adaptive mutations which promote wound healing will be induced. Some of the adaptive mutations may result in uncontrolled cell growth. And this may be the basis of some genetic change observed in cancer. But our hypothesis is different. Our work was carried out in cooperation with Dr. Watanabe in Nagasaki University, and we assume that genetic instability is induced by ionizing radiation. This instability induces mutation and selection, and it may go to cancer. So this is still quite a hypothesis. But I think if you are a biologist, we have to look at whether there is any epigenetic response observed after ionizing radiation, and what is the proportion of the direct DNA damage and mutation, and of the epigenetic response. And we have to find out how the epigenetic change finally results in genetic change. And so in this respect I am very happy that IAEA has this kind of training course to stimulate research in this field.

Dr. T. Sugahara: So shall we start our second round? But first, are there any questions on the panelists' presentations? Please nominate the person for whom you have a question. Are there any questions? Yes, please.

Mr. Y.L. Aksu (Turkey): I have a question for Dr. Stather. The limit for a pregnant woman is 2 mSv. What happens if a pregnant woman goes to a high radiation area where she may exceed this limit?

Dr. J.W. Stather: Well I believe there is a difference between radiation that is a result of somebody working and which can be controlled and radiation that is due to natural circumstances. The ICRP limits are concerned with occupational exposure that are additional to these due to natural radiation.

Dr. Sugahara: Anyone else? Between the panelists you can have questions.

Dr. J.W. Stather: I should add that there is always a balance to be struck between protecting the fetus and not necessarily wanting to discriminate against women. That's always a difficult situation. So the limits that are suggested by ICRP must take account of these sorts of considerations.

Mr. Y.L. Aksu (Turkey): It is a recommended limit also. Our regulations are based on the ICRP, and I think there will be a big argument if we put this limit in our legislation or law, and a pregnant woman never chances to be exposed to more than 2 mSv.

Dr. J.W. Stather: I think the problem does come down to not wanting to discriminate against women. So ICRP is recommending, until pregnancy is diagnosed, that men and women should be treated broadly as equal. But once pregnancy has been confirmed, then the fetus is being treated broadly as a member of the public. The only way to be sure of not exposing the fetus at all is to stop women working with radiation, and that is, of course, not a sensible thing to do.

Mr. O. Garcia (Cuba): Yes, in this case, most women do not like to work more with radiation. They are not wanting to reach any limits of exposure. In our country, this is a difficulty. When a woman's pregnant, she continues to work.

Dr. J.W. Stather: Well, in England, I think in the vast majority of cases, if a woman became pregnant, then she would be moved away from work where radiation levels were relatively high. I assume the same would be true in Japan. Is that right?

Dr. S. Kobayashi: Right.

Dr. S. Okada: Well, if they found out after pregnancy, what would the U.K. do? No, the pregnant woman was found to be exposed before knowing about the pregnancy.

Dr. J.W. Stather: There will be situations where the fetus is exposed as a result of occupational exposure of the mother. In the U.K., average doses to workers are now about 1.5 mSv a year, so worker doses are really quite low. So, generally doses to the fetus in the first month or two would be expected to be very small.

Dr. S. Kobayashi: May I? What Mr. Aksu asked, is that, I am just interpreting, in Turkey you may have a very high background area. Is this right?

Mr. Y.L. Aksu: No.

Dr. S. Kobayashi: No, that's not. I see. So in that case your question does not concern us. But if there is a high, very high background area, and people are living there, and there is a chance of a pregnant woman receiving a natural dose exceeding 2 mSv, what would you do? That is the essential question you asked, is that right?

Mr. Y.L. Aksu (Turkey): Yes. But I think a pregnant woman who flies overseas may be exposed to more radiation. And is this comparable to 2 mSv?

Dr. S. Kobayashi: So, apart from the regulation, your question is what we would do under

these circumstances. Is that right? Okay.

Dr. S. Okada: Do you have any — ? What would you do?

Dr. J.W. Stather: Within Europe, there are moves to measure radiation exposure during flights, and to give advice on what doses might be received by the aircrew. The intention is not to measure individual members of the crew. As you know, I'm sure, a captain of an aircraft can receive maybe 7 or 8 mSv a year, compared with maybe 2 mSv a year from natural radiation at ground level.

Mr. Y.L. Aksu (Turkey): You said 7 mSv?

Dr. J.W. Stather: 7 or 8 mSv for a pilot or member of the flight crew who flies a lot.

Mr. Y.L. Aksu (Turkey): But I think that a German scientist from GSF said overseas captains and stewardesses (inaudible) possible, if (inaudible) and then a problem will be presented whether these persons are radiation workers or the public, because the doses they receive are in excess of the public limits.

Dr. J.W. Stather: Yes, there will be situations where flight crews receive relatively high doses. I think the first stage is to look at what doses are. Whether you would want to control the number of hours a pilot flies, I don't know yet. I think it hasn't reached that stage.

Mr. E.K. Osei (Ghana): (inaudible) the woman is pregnant, the lower abdomen that amount of dose.

Dr. J.W. Stather: ICRP recommended 2 mSv to the surface of the abdomen, which means in practice 1 mSv, roughly, to the embryo and fetus.

Mr. E.K. Osei (Ghana): And after that tell us about treating the pregnant woman. Is there any other way?

Dr. J.W. Stather: Well, before pregnancy is diagnosed, there are no special restrictions.

Mr. E.K. Osei (Ghana): And after pregnancy is diagnosed?

Dr. J.W. Stather: After pregnancy is diagnosed, then the dose to the surface of the abdomen should be no more than 2 mSv. And the intake of radionuclide should be less than a twentieth of an ALI. In the U.K., NRPB has recommended that after pregnancy has been diagnosed the dose to the fetus should be kept to < 1 mSv, both from external radiation and intakes of radionuclides.

Mr. E.K. Osei (Ghana): (inaudible; further question about pregnant women and exposure to the fetus) and we are considering the fetus to be a member of the public.

Dr. J.W. Stather: Well, I'm saying broadly as a member of the public. There's a balance to be struck between treating the fetus strictly as a member of the public and at the same time not wanting to discriminate against women.

Mr. E.K. Osei (Ghana): (inaudible question about pregnant women) or maybe transferring her to a place where the radiation level is very low.

Dr. J.W. Stather: That is what would happen in the U.K. Yes.

Mr. E.K. Osei (Ghana): That's what is happening there? Okay. And in doing that you're not discriminating against pregnant women.

Dr. J.W. Stather: She'd still be employed, and she'd still be receiving the same salary, but the dose to the fetus would be reduced.

Mr. E.K. Osei (Ghana): You don't discriminate? Okay. And let me ask another question. In your opinion, if a pregnant woman, after she finds out she is pregnant, is exposed to an acute dose of very high radiation, would you advise maybe abortion or...?

Dr. J.W. Stather: This would be a medical decision made at the time. There is always the problem of working out exactly what is the risk. I believe it would have to be quite a high dose before termination of pregnancy would be recommended. What that would be would depend very much on the circumstances.

Dr. T. Sugahara: I see. Concerning this point, my question is: How does the policy of dose limit handle the variety of natural background radiations?

Dr. J.W. Stather: It's additional.

Dr. T. Sugahara: Even if it is very high?

Dr. J.W. Stather: Yes, it's still additional.

Dr. T. Sugahara: Is exposure in flight artificial or natural?

Dr. J.W. Stather: Well, it's an artificial circumstance, but it's natural radiation. Some thinking still has to be done in regard to how we treat air crew receiving high doses. What happens in Japan?

Dr. S. Kobayashi: We have nothing that determines any reaction to it.

Dr. J.W. Stather: A problem we are tackling in the U.K., and that ICRP is also tackling, is radon. There is a report coming out from ICRP looking at how we tackle exposures to radon both in the workplace and in homes. This will be in Publication 65. But with radon, it's an interventional situation. It's not a new practice that's producing exposure.

Dr. T. Sugahara: Are there any other questions?

Ms. G. Nesterenko: I would like to know your opinion about late effects from internal exposure to radionuclides (for example cesium-137) due to contaminated foodstuffs.

Dr. J.W. Stather: You mentioned cesium, but the interesting situation is for thyroid cancer in Belarus, which is quite different from Russia, and apparently different from the Ukraine as well. In some areas of Belarus there have been a significant increase in the number of cases of thyroid cancer, but this is not being observed in the Ukraine. There is interest internationally, and obviously in Belarus, about the reason for the difference. It might be a result of better medical checks on individuals, or there may be a real increase due to radiation exposure. We don't know the answer yet. I think this is one area where a lot of the work could go on trying to understand the reason for these observed differences in thyroid cancer incidence. One thing that makes the difference difficult to understand is that the latent period for thyroid cancer is thought to be four or five years, and yet we are seeing thyroid cancers really quite early. Most of the dose is due to iodine-131, which is short-lived, but there should be some long lived radionuclides such as iodine-129, which may give a scope of dose reconstruction based on environmental measurements. I think that is the sort of help that maybe would come from international organizations. Clearly it's expensive to do, and it would need international support. Cesium can be measured in whole body counters, but the dose is probably quite low now.

Dr. S. Okada: In Japan, we take lots of iodine in seaweed.

Dr. J.W. Stather: Yes, that's right.

Dr. S. Okada: But in Russia (both men talk at once) some areas have very low iodine intake rates, right?

Ms. G. Nesterenko (Belarus): You are right.

Dr. S. Okada: They take up iodine very easily, quickly.

Ms. G. Nesterenko (Belarus): In order to understand the effects of internal exposure to cesium-137, we've started the examination of children with high levels of internal exposure by means of whole body counters. For this purpose we also use ultrasonic, endoscopical and other diagnostic methods. We've observed some changes in the health state of these children, for example changes in their stomach's mucous membrane. But it's too early now to say about the results of this examination. We need more time.

Dr. J.W. Stather: Cesium would not selectively irradiate the stomach, because it's very quickly absorbed. It gives a more or less uniform dose to all tissues. Even if a small amount of cesium is swallowed, it wouldn't just irradiate the stomach. You must have had some estimates of the body content of cesium in these areas that go back some years. Have you got some estimates of doses?

Ms. G. Nesterenko (Belarus): No, we only started to study one year ago.

Dr. J.W. Stather: You haven't tried to make any estimates of what the radiation doses from the intake of cesium might have been, have you?

Ms. G. Nesterenko (Belarus): We haven't.

Dr. T. Sugahara: Another topic? May I give you, Dr. Okada, a new question about the hormesis?

(Inaudible discussion for a short time)

Dr. S. Okada: I guess to start with — we still don't know whether radiation hormesis is really acting on the health effects of radiation. I'd like to hear yes or no from this side, hormesis or not.

Dr. T. Sugahara: My idea is that hormesis includes something to be evaluated. But the problem is: Is there any hormesis in radiation carcinogenesis? In the 1992 meeting on low dose effect in Kyoto, all participants accepted adaptive response, though it was not sure whether it is universal or not. But we had no agreement on hormesis for carcinogenesis at low doses.

Dr. J.W. Stather: UNSCEAR, of course, prefers to use "adaptive response" which seems to me more appropriate. And you know from this morning's presentation that a document has been prepared from UNSCEAR covering the subject. I was at the UNSCEAR meeting last week. The committee has accepted the document for publication. The only significant change was to modify the conclusions. The committee is saying that there are scientific data that indicates there can be an adaptive response, but largely it's from cellular studies and often short term, although there are some animal studies. You might interpret some of the epidemiology as being suggestive. The feeling of the committee was that there was really little that could be done yet in terms of using information on adaptive response in assessing risk estimates, and hence in setting dose limits. So it's presented as a scientific review of the subject, but with a note that at present the information cannot be used in setting standards for protection or influencing risk factors. I think that was the main conclusion.

Dr. S. Okada: I have a question. Do you think an epidemiological study will prove or not prove the existence of hormesis, or what do you think?

Dr. J.W. Stather: Well, one of the talks I gave described the U.K. National Registry of Radiation Workers and the first analysis was published in 1992. This showed for the first time in a worker study a significant increase in the risk of leukemia in people who are occupationally exposed, and a suggestion that the risk of solid cancers is increased. The difficulty with all these occupational studies, there are a number going on now, is that they lack statistical power. And I think what we'll see ultimately is the U.K. study combined with a Canadian study that has yet to be published, and with the U.S. studies that have been published which show no significant increase in risk of cancer. As I explained in my talk, if you combine the U.S. study and the U.K. study, you end up with a risk factor that's very similar to the risk factor ICRP has recommended for workers ($4 \times 10^{-2} \text{ Sv}^{-1}$). I expect to see worker studies extended with longer follow-up and gaining in statistical power. Most of that work is being coordinated by IARC, The International Agency for Research in Cancer, based in Lyon (France), and supported by the CEC and other organizations. I think this is one way things are going to develop to get better information on risks at low doses.

Dr. S. Okada: So you think larger populations or longer observation periods will give better answers?

Dr. J.W. Stather: Yes, it will narrow the confidence limits. But I think for quite a long time to come our risk estimates must be primarily based on the high dose studies. Here one of the questions is about the problem of having to project risks into the future. And really, only following populations for longer is going to provide the necessary information. There is still the question of transferring risks from one population to another. We need to look at how we might transfer the risks for the particular cancer types between one population and another. This could be done by comparing different study populations.

Dr. S. Okada: Reproducibility and consistency have to improve?

Dr. J.W. Stather: Yes, that's right. The more you can get from a number of epidemiological studies which are comparable, then the stronger the case is. As time goes on we should see information on more detailed risks for individual tissue types from the Life Span Study. We don't get anything yet from the Japanese population on fatal thyroid cancers or skin cancers, liver cancers, or bone cancers.

Dr. S. Okada: Do you think we'll be able to solve all of these problems?

Dr. J.W. Stather: No, but on the other hand, I'm sure in ten years from now we will do better than we can do now. I think for the Life Span Study the main question, to my mind, is what's going to happen to the youngest age group. Are we going to see a constant relative risk, which seems to be the case at present, or is that relative risk going to decrease at long times after exposure? I think there's good information from a number of other epidemiological studies to suggest that the relative risk may start to decline at long terms after exposure. We could be overestimating the risks in the younger age group. Maybe another ten years will give us a much better understanding of how the risks in those young age groups are changing. They are now reaching the ages at which we start to see cancers really developing in some numbers in the 40 to 45 age group.

Dr. T. Sugahara: Dr. Kobayashi, do you have comments on this?

Dr. S. Kobayashi: I have many points that I would like to touch. Firstly, regarding thyroid cancer in Belarus and the Ukraine. There are arguments saying that it cannot be due to irradiation. That is one point. One, some people say that, but others say still it is an observed fact. And so we have to accept the fact as it is, and we should explore possible explanations for this. And as you mentioned, I think multifactorial agents exist in the induction of thyroid cancer, especially in the pre-existing pathological conditions, plus radiation may enhance the incidence as well as shorten the latency period, which so far has not been experienced. So we have to accept this fact; and I would rather like to support the findings that say it is true. That is regarding the incidence of thyroid cancer after the Chernobyl accident. And another factor is that it may be modified by nutritional and eating habits in Belarus. There was some indication that Professor Sugahara and his group made a preliminary study to improve the health condition of the heavily irradiated population, not the population exposed to lower doses, after the Chernobyl accident by supplying certain specimens of food, a kind of food, so-called functional food, which is made from chlorella, and there was a marked improvement in the

health condition of the people who were given this provision. And we are not sure yet whether it is really due to the nutritional effect of this chlorella, or whether it is due to the psychosomatic effect of taking something good for their health, and that this improved their mental condition, which is then reflected in the improvement of their gastrointestinal or cardiovascular situation. And that is then reflected in their overall health condition. And all these things have to be taken into account. That is one comment.

And another thing, as I mentioned, is the great variety of cancer incidence by type, and by country. Even in the case of lung cancer, there is a danger of one to four cases per 100,000 for the incidence of lung cancer by country, and also in the case of leukemia, there is a two or three times difference by country. So the final risk estimates may be different from country to country. That is my second comment. Thank you very much.

Dr. T. Sugahara: Are there any other questions?

Ms. G. Kozak (Syria): I read some articles which indicate that the rate of chromosomal aberration increases with age. To what extent can radiation contribute to this increased incidence? Can we consider radiation the essential factor that causes this increase?

(Japanese panelist and participant speak at the same time.)

(British panelist and Chair speak at the same time.)

(Many people are speaking and laughing at the same time.)

Dr. T. Sugahara: I'll give an answer. In Japan, we had a very large number of studies done on chromosomal aberrations. Dr. Tonomura in Tokyo Medical and Dental University studied about 10 or 20 persons, each 20, 30, 40 and 50 years old, and so on, and he demonstrated a very clear increased incidence of unstable chromosomal aberrations with age. But the problem is that, if it is induced by background ionizing radiation, the incidence may be different in this area and the Osaka area. Because background radiation is not double, but about fifty percent higher in the Osaka area. So we expect the slopes to be different in Tokyo and Osaka. But it was not. Dr. Tonomura followed these chromosomal aberrations, but found no difference. But quite recently, and it's still quite preliminary data, we have observed the incidence rate in China, in a higher background radiation area. There the increase in chromosomal aberrations with age was higher in the high background area than in the control area. So some part of the aberrations may be related to background radiation, but some part may be different. So at the present moment, we have no clear answer as to how much background radiation contributes to this increase in the incidence of chromosomal aberrations with age.

Dr. S. Okada: The study in Hiroshima and Nagasaki also showed micronuclear incidence going up with age. And also glycophorin A mutations go up with age. So not only chromosomal aberrations, but several other biological indicators are showing an increase with age. I don't know if it's due to background radiation. Maybe something else is associated with some kind of upper aging.

Dr. T. Sugahara: Any other questions?

Ms. C. Panlaque-Aguilar (Philippines): My concern is about workers who are occupationally

exposed to radiation. These include paramedical staff employed in hospitals engaged in nuclear medicine, diagnostic and cobalt therapy, personnel in research establishments who are involved in the application of radiation, industrial radiographers and other individuals who are occupationally or accidentally exposed to radiation. Now, I would like to know your opinion on having a prescreening or preemployment examination before they begin to work in these establishments which may indicate any pre-exposure to radiation, such as chromosome aberration analysis, micronucleus test or more sensitive tests maybe on the molecular level that would indicate DNA damage, so that for the period of time that these personnel are employed in these establishments, any incidence of radiation-induced condition/sickness/disease can be explained.

Dr. T. Sugahara: Explained?

Dr. J.W. Stather: I would think a better way of monitoring radiation exposure is through physical measurements. A good estimate of radiation exposure will not be obtained using chromosome aberration techniques, at least for low doses to which most people are exposed. Another difficulty is that with the conventional technique of assaying chromosome aberrations, the damage observed decays quite quickly with time. With FISH techniques, it might be possible to obtain some estimate of cumulative exposure for higher doses, but it is a very expensive technique.

Dr. R. Mukherjee: But after all you are concerned with the biological effect.

Dr. J.W. Stather: I think part of your question was about whether you can identify people who may be more or less sensitive to radiation, and I think we can't do that yet.

Ms. C. Panlaque-Aguilar (Philippines): How about the probability of having cancer in the future? Maybe a more quantitative evaluation of the potential risk to the health of these people before they begin to work in these establishments must be initiated.

Dr. J.W. Stather: I don't think we can do that now. I think in the future, with the way mechanistic work is going, we may well be able to identify people who are more sensitive to radiation-induced cancer than others. Then there will be difficult questions to be answered. For example, would you exclude some people working in radiation, would you operate at different dose limits? I just don't know the answer. But right now, of course, there are still differences in sensitivity between people. As we have seen, women are rather more sensitive than men, but we apply the same dose limit. Young men are more sensitive than older people, but we apply the same dose limit. We develop our risk coefficients for populations that probably do have individuals with differences in sensitivity, but we also apply them to a population. We're not trying to pick out individuals in doing that. I think, you know, if you can really identify somebody, and say he's much more prone to cancer, I think that is very, very difficult. If differences of a factor of about 10 or more are identified, then action may need to be taken in the future.

Dr. S. Okada: There have been studies of radiation workers in more than ten different establishments in the U.K and the U.S., and if their mortality rates are compared with those of the general population (SMR), the radiation workers' are always 20 to 30 percent lower.

Dr. J.W. Stather: But that's a different issue. That's a different issue. (laughter) If you're a worker, you must be healthier than the population at large, just because you're working.

Dr. S. Okada: That is called healthy workers effect, because when they pick those workers, they carry out a health examination, they try to get the healthy people as compared with the general population, and that's one reason why.

Dr. T. Sugahara: Concerning the sensitivity to radiation of individuals, there is a different problem. Many studies have been done on the Hiroshima and Nagasaki A-bomb survivors. For example, the colony formation assay or chromosomal aberration incidence and micronuclear incidence by giving the exposure to the peripheral blood, or some to the skin fibroblasts in cultures were studied. There was some variation, not very large variations in sensitivity, but no correlations was found in the incidence of cancer and this sensitivity. My idea is that probably the criteria are not good. I mean that only what we can observe is chromosomal aberration or big genetic damage or colony formation. These criteria may be different from the cancer susceptibility. So we should find new ideas to find out what kind of sensitivity test is good to identify the higher sensitivity for cancer induction. But at the present moment we have no answer yet.

Dr. J.W. Stather: There's a third advantage of having a medical check-up, of course. If somebody has cancer, then it is likely that it will be detected before the start of employment. It would be possible to be sure that it was not due to radiation at work. That's probably a safeguard for the employer rather than the employee, though.

Dr. S. Kobayashi: Certainly.

Ms. I. Gyuleva-Angelova (Bulgaria): I would like to receive some more information about the effect of low-dose radiation on cell membranes and cell membrane receptors of the lymphocytes and other cells, because more of your investigation concerns DNA damage. But most cell membranes are also very radiosensitive. I hope to understand some more about cell membranes.

Dr. S. Okada: Well, I guess the membrane problem has been going on since the 1940's and 50's, and still we don't know yet. But now we are getting more and more sophisticated methods, so we might be able to pinch holes someplace on the membrane.

Dr. T. Sugahara: Concerning this, I'll show you the experiments on metastasis. This is an intergrin receptor expression, and this is not activation, but just a shift of the receptor. Originally it is inside of the cell membrane. But after irradiation, it comes up through the membrane, and receptor activity is increased. So this kind of study is related to the membrane change.

Dr. S. Kobayashi: Some 15 years ago, one of my colleagues did experiments using erythrocytes, where she measured the transport of sodium and potassium, and these transport systems were clearly inhibited by radiation at a minimum dose of 25 rads at that time. So if you call 25 rads a low dose, you can say that in the in vitro system, cell membrane systems can be affected.

Dr. S. Okada: Dr. Sugahara, one of the questions you asked us was whether there is a threshold or non-threshold in radiobiological response. And I made up one OHP film. And I would like to show it (an OHP slide was cut). I'd like to hear your opinion. For this non-threshold hypothesis, linear hypothesis, they say that even the smallest doses are risky. And if you take dose response, they show a linear response, but much data is pointed here, and no data is available at a really low dose. So some people question. But anyway, DNA damage, mutation, chromosomal aberration at low doses may be. And all of these carcinogenesis, especially solid tumors except leukemia, in Hiroshima and Nagasaki, in the time after exposure, started the cancer age, and the higher doses showed a constant relative ratio. So the higher the dose, the ratio is going up like this. And the dose-response of solid tumors shows linear response. Now if we come to the threshold hypothesis, there are several experiments. One of them, Dr. Tanooka's experiment, showed this — the time after radiation, at a low dose, it goes up with the radiation field quite slowly, and the higher the dose, the latent period becomes shorter and shorter. So if you take the latent period this way, against the radiation dose, with higher dose it is shorter, but the smaller the dose, with latent period going up, at some point lifespan is crossed. So if a person will die before developing cancer, then he has a threshold. So in that way you get threshold response. The other one is the example of thymic lymphoma in the animal experiments. These are the fraction of cells that have been killed, and the rest of the cells are still there to divide, and that is very important. Cell division is very important. In that case, with a low dose related to cell killing, there is no stimulation of cell division. But as you increase the starting dose, it starts to stimulate cell division, and then the incidence of cancer goes up. So in these two cases, you have thresholds. So it is the difference of mechanisms. And it's not only one or the other, but, I think, both that are correct. And then the other case is this repair hypothesis; I don't know if you call this threshold or hormesis. This is questionable too, but anyway these two have to be examined in the future. But I would like to hear what you think of it, or whether you can think of other mechanisms.

Dr. T. Sugahara: I have a question. In your left panel (Fig. 3a), in leukemia, it looks like hormesis but your conclusion is that, because this is not significant from a background level, you generally apply the LQ model. And in your right panel (Fig. 3b), all cancer except leukemia, still at a dose less than 0.3 Gy, there is no significant difference, but you give a straight line. Why?

Dr. S. Okada: Why not? (laughter)

(Several people speak at the same time.)

Dr. T. Sugahara: But we are concerned about low dose.

Dr. J.W. Stather: Well, yes. But if you're asking why people fit a linear quadratic to leukemia and a linear model to solid cancers, it's because of data points at higher doses. Until of course, a killing effect becomes apparent.

Dr. S. Okada: We are not talking about high doses. But what I'd like to point out is that this is 86,000 people — 45,000 control and 40,000 residents — a population. You can never do this kind of animal experiment.

Dr. J.W. Stather: In the low dose group, how many excess solid cancers occur in the lowest dose group? There aren't very many radiation-induced cancers in total.

Dr. S. Okada: The number is here. Right here (Fig.3). All cancers total several thousands.

Dr. J.W. Stather: But the excess due to radiation is very small, isn't it? Less than 400.

Dr. S. Okada: Very small. Right. (Two people speak at the same time.)

Dr. J.W. Stather: Of several thousand cancers in total, you're talking about maybe 400 that have been caused by radiation, of which some 80 are leukemias. That's across all the different groups. So there are very few caused by radiation.

Dr. S. Okada: Right. Right. Right. And that's the reason why (Two people talk at the same time.) we have been bothered with this kind of problem for years. Well, I guess everyone has to answer by himself.

Dr. J.W. Stather: Well, would anybody here set dose limits on the assumption that there might be a threshold, or would you do what ICRP has done and make the assumption based on the present, no threshold, approach. It's more than an assumption, that there might be some risk at any dose. Do you think it's a reasonable approach then? You obviously do. Clearly there are very interesting radiobiological phenomena and I think there is a lot more to learn about the way radiation interacts with DNA and cells in general. But I think there is still a long way to go before this radiobiology can be applied to protection.

Dr. T. Sugahara: But do you support radiobiological research?

Dr. J.W. Stather: Oh, very much. At NRPB three and a half years ago, I think, we took the decision that just epidemiology on its own was insufficient to answer the questions that are being asked about such issues as the effects of radiation at low doses; the effects of alpha particles; the question of dose rate. It will not be possible to answer all the questions with animal studies or epidemiological studies. You're only going to answer these questions by doing more fundamental work. So we've set up a group to look at the fundamental mechanisms of interaction of radiation with cells. UNSCEAR has also been interested in these new developments. In the 1993 report, there was an Annex on Mechanisms of Carcinogenesis, and at the meeting of UNSCEAR last week, they decided that that work would continue, and there would be another consultant brought in to develop the work looking at mechanisms of damage to DNA. It is seen as important to answer the questions that we're discussing now: What are the effects at very low doses?

Dr. T. Sugahara: So what is the idea of IAEA? IAEA also supported research. How do you stimulate this kind of fundamental research?

Dr. R. Mukherjee: This research support of course is understanding with more precision the radiobiological mechanisms, and that pertains to many other questions of radiobiological effects in terms of cancer production and all. But when this question of risk, estimation of standards and all that, of course we adhere to the international practices. But the approach is that with the availability of newer and newer more sophisticated techniques, you are inclined to go

deeper in understanding. So research support is primarily based on that and plus providing additional clarification of what the approach is, like this.

Ms. T. Galichanskaya (Ukraine): Now the main theme is the genetic effect of ionizing radiation, but I have a special interest in epigenetic effects such as syndrome stress because the Chernobyl accident caused serious stress. And many scientists think the health effects observed depends upon stress. Some commented.

Dr. S. Kobayashi: I have already made the point that stress is the main cause of a variety of diseases in modern society, not only in the developed countries, but also developing countries. Worries and anxiety in everyday life are the cause of many kinds of disease both mental and psychosomatic.

Dr. J.W. Stather: But I suggest it's not just stress; it's the things that people take to try and reduce the stress that cause the problem — alcohol, cigarettes, for example. They're the real problems. (Several people are talking and laughing at once.)

Dr. S. Kobayashi: It is another kind of stress. So anyway, all these problems in relation to the stress are the cause of anxiety and disease. So if we can find a way to deal with these problems, then we can control most of the problems of health risk that may be attributable to low dose radiation. If we can deal with these things properly, then we can forget about the effects of low dose radiation. Nothing to worry about anymore.

Dr. R. Mukherjee: Well, I would just like to add —, this reminds me of a few years back there was a meeting in, and Dr. Morimoto of Tokyo University presented data, and his end point for damage was (unintelligible). He grouped the people on the basis of stressful or less stress, and the habits, i.e. who takes breakfast in the morning or doesn't, or different daily living habits — he made study groups. It was very, very interesting, and the highlight of the meeting. He showed that with stressful situations, there were lots of damages; there was a correlation. So I don't know what the point of follow-up is, but it definitely has a point in population monitoring.

Dr. J.W. Stather: I might read something from this book. (laughter) It's not quite stress, but Dr. Kobayashi mentioned diet. Well, this is a book about Health Effects of Low-level Radiation by Sohei Kondo. There's a chapter in it about Zen Buddhism. A table here looks at diet and stomach cancer. The thing that strikes me is for a high consumer of green tea, the risk of stomach cancer is less than half the average. Whether that reduces stress, I don't know.

Dr. R. Mukherjee: I think a considerable amount of research information shows detection of anti-cancer factors in many of the dietary agents, so that is very, very important. Vitamin C, vitamin E, and all the antioxidants.

Dr. T. Sugahara: In this respect, I'd like to make some comments about the radiation-induced cancer and chemically induced cancer. And as far as experimental studies are concerned, chemicals, especially the mutagenic chemical carcinogens, induced cancer very rapidly in experimental animals. But the radiation-induced cancer, except leukemia, appears very late. Just like in human beings, when the animal aged, the solid cancer appeared. And so that the pattern is different. But the problem is that there are many studies concerning chemopreven-

tion, i.e. studies to prevent the cancer incidence by applying some chemicals or certain foods. And at that time the principal study was carried out using the chemical carcinogens. So my question is whether, radiation-induced cancer and chemical-induced cancer can be protected similarly.

(Some discussion between Dr. T. Sugahara and Dr. J.W. Stather.)

Dr. T. Sugahara: Yeah, yeah, yeah. When I was a Science Council member in RERF we sometimes discussed whether there is any possibility for protecting them from the increased incidence of cancer, but there are no studies at all. But for the incidence rate, we never acted. We just observed. But the problem is, as a human being, if we can find some way to protect against incidence of cancer, we should. But unfortunately or fortunately, I don't know. I have no special method to intervene.

Dr. J.W. Stather: You mean like stopping people smoking? (laughter)

Dr. T. Sugahara: Yeah. So it may be that if all the people stopped smoking, the incidence would be different.

Dr. J.W. Stather: Yes, very different. I mean if people are exposed to radon and cigarette smoke, the best thing is to stop smoking, isn't it? I might mention that at the recent UNSCEAR meeting they decided that another Annex that would be produced for the next report would look at combined effects of radiation and other agents and not just chemicals. They'll be looking at ultraviolet radiation and other factors that might interact with the ionizing radiation.

Dr. R. Mukherjee: Well, yes, the chemical counterpart of ICRP-type, International Commission on Chemical Mutagenic Carcinogens, ICCMC, that is working very actively on test systems for identification of potentially carcinogenic and mutagenic chemicals, and they are definitely using those too for standard setting. So lots of activities are too late, but it has started, and it's ongoing. They have test criteria and limit setting. So it is coming. And they are also correlating the chemical structure of the compound with respect to its mutagenicity, carcinogenicity. From all different approaches they are tackling this field. (Two speaker talk at the same time.)

Dr. T. Sugahara: In this respect, quite recently I got some preliminary data about the radiation-induced cancer in Chinese medical x-ray workers. In China, they still very frequently use fluoroscopy. Film is very expensive there, so they are still using the fluoroscopy for chest studies and so on. And we are collaborating with the Chinese scientists for the epidemiological studies on cancer incidence, and recently have had some very interesting findings that there are increasing incidences of skin cancer, breast cancer and thyroid cancer. That's acceptable. But there are increased incidence of esophageal cancer, but no increase in lung cancer. And also they have a higher increased incidence of liver cancer, but no increased incidence of stomach and intestinal tumors. So it's very strange. But you may know that there are some areas where they have a very high incidence of esophageal cancer because of their food. And also concerning the liver cancer, there is an epidemic of virus. So I sent a letter to China requesting that he immediately check this point. So if it is so, it is very interesting. The combined effect is very high in the case of this kind of chemical or virus.

Dr. S. Okada: Also aflatoxin is —. (Two men speak at the same time.) Hepatic cancer in China and in Africa.

Dr. S. Kobayashi: May I add another point? That is, about ten years ago in the United States at Oak Ridge National Laboratory they made an experiment on mice, feeding a low calorie diet to see if the low calorie diet can influence the effect of radiation in cancer induction. And they clearly indicated that low calorie diet can reduce the cancer incidence. So in our institute at Chiba, NIRS, we did a similar experiment a few years ago on mice again, but for leukemia, not cancer in general. And we got a similar result, being that, by feeding the mouse lower calories, the incidence of cancer by irradiation is reduced, in contrast to the mice which were fed ad libitum, and could eat as much as they liked. We can add some conclusion to this if we also consider some epidemiological data on the American Indians living in Canada area, whose population showed a lower incidence of cancer across the spectrum, that is, incidence of all types of cancer are quite low in comparison to the white population there. So there may be some clue hidden in this observation that dietary control is very important. Not only this but as I said earlier the fact that we eat yellow and green vegetables as much as possible, and avoid eating fat and meat has some other connection in this regard.

Ms. B. Nasri (Morocco): Maybe if we control our appetite all day it will increase terror. (inaudible comments and general laughter)

Dr. S. Okada: You mean stress.

Dr. T. Sugahara: Low calorie diet is always a problem. If we apply this experimental data to human beings, what is the best food intake. And concerning this, in Hiroshima University, Dr. Yokoro made a breast cancer study in rats fed with different kinds of fat. And after irradiation, they had an increased incidence of breast cancer. When they were given animal fat the incidence increased. But when they were given fish fat, the incidence decreased. So even this, a kind of food, may be responsible for the incidence of breast cancer. And it can be modified even if it is radiation-induced.

Dr. S. Okada: Are we making propaganda of Japanese food? (laughter)

Dr. J.W. Stather: Anyway, any more questions on low doses? (laughter)

Dr. T. Sugahara: Before concluding, I would like once more to ask Dr. Stather. You asked the estimate by the ICRP method. And I think I agree with you that the estimate is okay. But I think sometimes because of the linear extrapolation the estimate for the protection is probably a little overestimated.

Dr. J.W. Stather: Well, it seems to be supported by the combined occupational studies from the UK and the USA. It seems to be a reasonable value. The National Registry of Radiation Workers gives a risk estimate of about twice the ICRP value for worker, and the US study doesn't find a risk. But if you combine the two, you end up with a risk of 4 to 5%/Sv, which is what ICRP recommends, but with wide confidence intervals, of course.

Dr. S. Okada: Well, one is so negative, and then you put them together. I don't know if combining them is ok.

Dr. J.W. Stather: But the NRRW is giving statistically significant increase in leukemia, although for solid cancers it's not significant.

Dr. T. Sugahara: But my question is, in that case also they have some high dose groups. And it may affect the slope of dose response.

Dr. J.W. Stather: It's looking for a trend with dose, yes.

Dr. T. Sugahara: What trend is that? At low doses there are no significant differences and then at higher doses we have significant differences.

Dr. J.W. Stather: It's a trend analysis. But you've always got the problem of assessing risk at the low dose end. At least they are workers exposed to low dose radiation, not bomb survivors who'll be exposed to up to a few Gy. I mean, they are at least workers. If you think ICRP has overestimated the risk, then by how much?

Dr. T. Sugahara: No! I think maybe it is okay for radiation protection purposes, but it may be a little overestimated.

Dr. J.W. Stather: How much?

Dr. T. Sugahara: I don't know. (laughter)

Dr. S. Okada: Could be 10%, 50%, 100%.

Dr. S. Kobayashi: It may relate to the dose rate reduction factor.

Dr. J.W. Stather: Possibly, but I think it's of interest that you can change the dose rate in animal experiments by a factor of a thousand and change the risk by a factor of only two or five. That's quite interesting, I think.

Dr. T. Sugahara:— this estimate at a very low dose, for example, just 1 mSv or 2 mSv per year. I think, that if you accept your risk estimate, we must have in the high background area a higher incidence of cancer. Significantly higher.

Dr. J.W. Stather: Yes, but then there are the problems of different diet in high and low background areas and other factors that can influence the result.

Dr. S. Kobayashi: So it is difficult to clarify which factor is to blame, so we cannot say whether the ICRP estimate is an overestimate.

Dr. J.W. Stather: But it does seem to me we're agreed that ICRP has taken a reasonable approach. Is that right?

Dr. S. Okada: (laughter) Well, yes. (laughter)

Dr. T. Sugahara: What do you think about that?

Dr. J.W. Stather: Is anybody going to disagree with that?

Dr. T. Sugahara: You've got a question?

Mr. E.K. Osei (Ghana): In the 1990 recommendation of ICRP, the Commission gave an annual dose of 20 mSv a year on average for the radiation worker and 1 mSv a year for members of the public. Natural radiation gives about 2 mSv a year, which naturally exceeds the ICRP limit for the general public.

Dr. J.W. Stather: Yes, but there are different issues. One is radiation that's, say, released from a nuclear site and exposing the local population, and the other is something that is present in the environment and you can't do anything about other than by intervention, or for radon.

Mr. E.K. Osei (Ghana): So—

Dr. J.W. Stather: Just to come back to what you said, it's 2 mSv effective dose, but of course the dose to most tissues of the body is 1 mSv. The lung gets a much higher dose from radon.

Mr. E.K. Osei (Ghana): So if (inaudible)—

Dr. J.W. Stather: Sorry, I don't understand.

Mr. E.K. Osei (Ghana): If somebody in the general public who is receiving at least 1 mSv from the natural background undergoes maybe one or two medical examinations in a year, he is going to exceed the limit set by the ICRP.

Dr. J.W. Stather: There's a different issue here. For medical exposure the assumption is that the benefits of the medical procedure are going to outweigh the disadvantages. If you have a broken bone or a tumor, then this will be diagnosed and treatment can be given. It's always necessary to weigh benefits and risks. But still the protection issues apply to medical practices. You still want to reduce the doses, but still provide the medical benefit.

Mr. E.K. Osei (Ghana): On the subject of adaptive response —, in low dose administration receiving low dose rates, there could be some immunity to radiation, while the possibility of getting cancer also exists at low dose rates. So what could you, in summary, say about these two issues?

Dr. R. Mukherjee: Well, as it stands with the current understanding of the adaptive response situation, as we have been mentioning, with some of the epidemiological studies, the data is equivocal. They are not, I mean, with respect to the overall, the whole organism, we cannot convincingly establish the effect. But with respect to the fine structure analysis of chromosome damage or gene expression, protein expression and all that, we really do not know yet what implication it has on the overall well-being of the organism. So you know that extrapolation of this effect to the whole organism context has to wait.

Mr. K. Takada: I am interested in the problem of whether there is a threshold in the radiation induced harmful effects, especially in cancer induction, because the subtitle of this panel

discussion is "Scientific findings and non-threshold hypothesis." From today's discussion I understand that there is no strong evidence verifying the existence of a threshold. Therefore, I think, in radiation protection practice, we should assume non-threshold response, and follow the risk estimates proposed by ICRP. By the way, Dr. Stather, chemicals are also important carcinogens. Do you think that there is no threshold in chemical carcinogenesis?

Dr. J.W. Stather: I don't think you can generalize, to be honest. It's a very wide question for a yes-no answer, isn't it?

Dr. R. Mukherjee: Well first of all, chemicals are so wide in variety—their action mechanisms, the dosimetry, their penetration, interaction—so many differences. So many differences in the chemical sphere compared to radiation sphere, so it is very difficult to make any comment.

Mr. K. Takada: Yes, but, please imagine a graph having chemical dose as the abscissa and cancer induction as the ordinate. Do you think that the curve passes through the origin? Please, assume that the chemicals at every dose level are brought into contact with critical cells.

Dr. J.W. Stather: Well, let's say I've never smoked a single cigarette, and I'm glad. I think, that the risk of smoking is broadly in proportion to the number of cigarettes you smoke, and the fewer the better. That is a chemical carcinogen.

Dr. T. Sugahara: According to my knowledge, WHO divided chemicals into two groups: one is mutagenic, the other non-mutagenic. And concerning the non-mutagenic chemicals, carcinogens, they have a threshold, and mutagenic chemicals do not. So they think that chemicals also act as mutagenics. So my point is that if the mutation, initial mutation, is an initial event, it's okay. But I presented this afternoon some epigenetic effects. Which is more important? So, from now on we should study comparisons, which are more important at low dose range.

Dr. S. Okada: Ames in the United States are saying that the mutagenics stimulate cell division. So even with smoking, the smoke will irritate your lungs and initiate cell divisions, and start cancer. Also old people get radiation burns, and the burns are very essential to develop cancers. So there again, the story is the same — the stimulating of cell divisions.

Dr. R. Mukherjee: That enhances the risk enormously.

Dr. S. Kobayashi: May I express my comment on in answer to this question? So up to this part the response (speaker goes away from microphone to blackboard, inaudible) we have here, and the question we are talking about, in this part. Now there is some observation, for instance, in Hiroshima and Nagasaki, regarding tumor induction, and Professor Okada mentioned (inaudible) indicative of (inaudible), and if we pick up the particular population whose age is very uniform and high, then we can observe the threshold response, of course, due to the latency of the cancer induction. So there may be this kind of phenomenon, including the adaptive response. And so many factors appear. So there may be difficulty (inaudible). But on the other hand, some years ago a report came from the United States indicating the increased sensitivity of cancer induction by certain physiological conditions including the allergic status. People who are allergic to some stimuli are more susceptible to

the cancer induction. Also there could be some people with a genetic component which is subjected to cancer induction by radiation, like AT, ataxia telangiectasia. So there may be such fraction of people in the large population. So overall my opinion is that it is a plus and minus (inaudible due to laughter). I would support the approach by ICRP. Thank you.

Ms. N.B. Nasazzi (Argentina): Imagine we can know something about thresholds or adaptive response, if we knew something existed, for example, what could be done from the protection point of view?

Dr. S. Kobayashi: It's a good question.

Dr. J.W. Stather: Well, I'm not sure what the approach would be. I've never liked the idea of using collective dose, which assesses very small doses over large populations and works out what the risk is in terms of numbers of cancer deaths. I think we should move away from that sort of approach. How you could use information on adaptive response in setting dose limits I do not know. That would depend on how clear-cut the information was.

Ms. N.B. Nasazzi (Argentina): Okay. It doesn't matter so much.

Dr. T. Sugahara: So my impression is that until now the ICRP developed a very good model, so we radiobiologists have nothing to do. But recently we have found two very important points that I mentioned, and that there is some epigenetic effect of radiation including the adaptive response and at the present moment it doesn't affect the ICRP proposal. But there is one new piece of biological evidence somewhat different from the ICRP model. And another one is the susceptibility. Is the cancer really random or not? I proposed this problem many years ago, but still I have no answer. But probably there is the possibility that cancer susceptibility is different in different people, and so only the susceptible people will have the cancer after irradiation. If the susceptibility to cancer induction is not really random, again the ICRP model will have to change because they assume a homogeneous population. But all these are still at a very preliminary stage of research. So I think that for ten or twenty years, the ICRP model will still be acceptable. But after we get the new data about these two points, ICRP will revise or modify their model, including our biological data. I hope.

Dr. J.W. Stather: I mentioned earlier that, although the assumption is that there is a homogeneous population, there clearly isn't. Men and women have different sensitivities, young people and old people are different, and, there will be differences between individuals. If differences between individuals by a factor of ten or so are found, we would then start to be concerned with the more sensitive group. But it certainly is a question for the future. I'm sure that ICRP and other organizations will have to tackle this in due course. It won't be just international organizations, it'll be national organizations, the regulators in individual countries.

Dr. S. Okada: And the person with radiosensitive genes might be discriminated from working in nuclear establishments.

Dr. J.W. Stather: And that's the problem.

(A comment by a participant)

Dr. T. Sugahara: So we have almost run out of time, do you have some comment for the future program?

Dr. R. Mukherjee: Well, nothing particularly. The question is whether research, with the deeper understanding of the biological effects of radiation on human health problems in general in the broad scope, will continue to be supported. And with the radiation protection aspect, this will give us an insight into the strategies in radiation protection implementation, but as to these protection standards and guidelines, it is not going to have any likely bearing or departure from—. That is my comment. I do not have anything else to add.

Dr. T. Sugahara: Is there any other members who want to add something before closing?

Dr. J.W. Stather: I thought I'd just mention the topics that UNSCEAR is proposing to tackle for the next five years. I've mentioned one or two. Obviously they've agreed to the document on adaptive response, which will be published later this year, as well as another document on epidemiology. The epidemiology document was not ready for publication last year, so it wasn't included in the 1993 report, so it will be published this year. So it will be quite interesting to have an UNSCEAR document with epidemiology and adaptive response in one document. There will be only two annexes.

Dr. S. Okada: One document?

Dr. J.W. Stather: Yes. For the future, they will continue to look at epidemiology. There will be more worker studies coming along, and a further analysis of the Life Span Studies. A consultant will be looking at genetics, particularly the problem of multifactorial diseases. We've mentioned already reports on looking at combined effects of chemicals and other agents with radiation. I think that's the important issue. I've also mentioned mechanisms. UNSCEAR are very interested in mechanism and radiobiology and so they will have a document examining damage to DNA and related issues. And as well as these documents, there will be the standard analyses of doses from medical exposure, occupational exposure, natural radiation, and to an extent these will depend very much on a review of the approach used to collect data. One of the key effects on the physical side will be to revise all the models they use for calculating doses from the release of radionuclides into the environment. The models UNSCEAR has used are getting to be quite old now, and lots of national organizations have developed better models. UNSCEAR is going to use better models for the future. It will also review the effects of the Chernobyl accident. So UNSCEAR, as the main international body considering biological effects, has got quite a full program for the next few years.

Dr. T. Sugahara: I am interested in this panel discussion as a radiobiologist. And a biologist is always challenging. I am challenging ICRP. So I think for radiation protection in daily work, you have a very good standard. And you can follow it. And now today, you can understand their principle. But if you are a radiobiologist, you have a very challenging problem. Radiobiology has many interesting problems to challenge to produce a new system of radiation protection. And this may be very much concerned about carcinogenesis. In this respect this panel discussion I think intends to make a challenge to all the ideas, and I hope you understand much better through our discussion what is the real situation of low dose radiation effects. And so I would like to close this panel discussion. Thank you very much for your coming.