Fukushima and Health: What to Expect

Proceedings of the 3rd International Conference of the European Committee on Radiation Risk

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Lesvos, Greece

Edited by

Chris Busby, Joseph Busby, Ditta Rietuma

and Mireille de Messieres

European Committee on Radiation Risk
Comité Européen sur le Risque de l'Irradiation

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Edited by:
Christopher Busby, Joseph Busby, Ditta Rietuma and Mireille de Messieres

(from left) Inge Schmitz-Feuerhake, Hagen Scherb, Carmel Mothershill, Sebastian Pflugbeil, Alfred Koerblein, Guide, Shoji Sawada, Yuri Bandashevsky, Interpreter, Andreas Elsaessar

ECRR 2009 Edward Radford Prize awarded

by

Mrs Jennifer Radford

to

Prof Yuri Bandashevsky

Belarus

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Editor's Foreword

First we should apologize for the length of time it has taken to produce the proceedings of this 3rd International Conference of the European Committee on Radiation Risk. I am writing this introduction in October 2011, some six months after the Fukushima catastrophe. The resolution of the dispute over the validity of the Radiation Risk model has never been more urgent. The ICRP risk model has been falsified by many studies, and now in addition, at the 2009 ECRR Lesvos conference, by the presentations collected here in these Proceedings. The stark revelations of illness following exposure to the fission products and uranium released by the Chernobyl accident are *absolutely applicable* to the illnesses which will develop inevitably in northern Japan following the Fukushima catastrophe. As Edmund Burke said "Those who don't know history are doomed to repeat it". The problem is that the nuclear industry and its powerful lobbies have so covered up the real effects of Chernobyl that no-one knows the real history of the effects of the widespread radioactive contamination. Many of these effects are to be found here. The Fukushima cover-ups are also the same: the same focus on external dose rates at the expense of internal exposures, the same talk about radiophobia, the same misleading (and absent) data, the same dreary sequence of nuclear industry spokespersons talking down the evidence, and bit by bit disappearing from the media slots as the true horror of the situation became apparent.

What we have seen is the disappearance of the ICRP from Sweden following the resignation of its Scientific Secretary Jack Valentin. In this collection I have included a short exerpt from a videoed discussion I had with him just before the 2009 conference. The full video discussion is now available on the internet. It is clear that Valentin had decided to back off from the ICRP and its risk model. The ICRP has relocated to Canada with a new secretary, an individual with a MSc in Health Physics. But the writing has been on the wall for the ICRP for some time. The effects of Fukushima will act as a final proof of the total bankruptcy of its obsolete approach. There is no doubt about the health effects of the Fukushima catastrophe. All the Chernobyl effects presented here were caused by exposures to the same substances that now contaminate northern Japan. The cornerstone of Science Philosophy is the Canon of Agreement, which states that the antecedent conditions of a phenomenon, when repeated, will produce the same phenomenon. Let no one doubt that the Chernobyl experiment, repeated in Fukushima, will cause the same result, a result reported in these proceedings in all its terrifying clarity
Chris Busby,
Riga, September 2011

The Credibility of the ICRP

Partial transcript of conversation between Professor Chris Busby, Scientific Secretary of the European Committee on Radiation Risk, and Dr Jack Valentin, Scientific Secretary Emeritus International Commission on Radiological Protection. Part of a public meeting in Stockholm, 22 April 2009 marking the 23rd anniversary of Chernobyl.

CB: As scientists we ought to look at all sources of information, but ICRP has never cited any one of the many articles that falsify [ICRP] or which show your levels of risk are in error. Why?

JV: This puts me in a slightly difficult position, of course, because I tend to agree with you — we should have quoted some of your stuff because since we don't agree with what you are saying we should then have said why we don't. […] If you've got the Scientific Secretary of ICRP you press a button on its back and it says what it's supposed to say but I'm retired so I can say what I like. But not many people are greatly impressed by the evidence that you bring. It would have been much wiser in that situation to state more clearly why we are not impressed, thus giving you a chance to come back again. [Then we could have a debate and understand why we don't agree with each other.]

CB: [cited as an example the 2006 ECRR publication *Chernobyl 20 Years On* and a "Russian studies" section of the 2004 Minority report of the UK Government Committee Examining Radiation Risks of Internal Emitters, CERRIE] … hundreds of references from the Russian language literature showing extraordinary effects from radioactivity - on genomic instability, genetic effects in plants and fish which cannot suffer from radiophobia — an enormous document which has been entirely ignored, suggesting bias.

JV: I have already agreed [ICRP, UNSCEAR, BEIR should not ignore these findings] But we're not talking here about individual results but on most of them I believe my colleagues would make technical comments [on individual results].

CB: Don't the leukaemia clusters near nuclear sites falsify ICRP?

JV: but there are other clusters around sites which were proposed for nuclear power stations but the reactors were not built.

CB: That study is confounded by the unused sites being on previously contaminated sea coasts and in areas of high rainfall [and high weapons fallout].

JV: We're now talking about confounders — that's the problem we have with all of your [epidemiological] studies. You have insufficient controls. ICRP has no official position on this but in principle people don't agree and will point to [epidemiological] studies where you get quite contradictory results, for example lowered cancer. Bernie Cohen and radon is the most famous, falsely showing a health benefit of radiation.

CB: These arguments about confounding disappear in the case of infant leukaemia after Chernobyl. The babies were in the womb. The same results from 5 groups in 5 countries published in different journals with doses calculated in microSieverts but statistically significant excesses. How do you explain that?

JV: I can't, but I don't think you have enough explanations either. I honestly don't think you can convince me that you are right. There are technical arguments. We should have emailed reports and gone them slowly and thoroughly. That would be a clever way of continuing a discussion between ICRP and ECRR.

CB: Yes and no, but to get here we have had to be robust, chaining ourselves to nuclear power stations, writing in the literature and using every possible method of publicising that your risk model is bankrupt. Otherwise we wouldn't be here.

JV: Are you sure you wouldn't have had more success if you just came up friendly like and talked to the people at the Health Protection Agency? [UK radiation protection advisers]

CB: [refers to long and well known experience of bad faith in various dialogues including by the Chairman and secretariat of CERRIE and the UK government departments involved.]

JV: Yes and I have heard many stories not very favourable to you. It's a mistake to look back and argue about who did things wrong. Can't we look forward and be more constructive?

CB: Yes, I agree. I have a question here that I was asked to put to you. It is "Can the ICRP model be used by Governments to predict the consequences of a nuclear accident, in terms of cancer yield?"

JV: Basically no, because the uncertainties we are talking about would be too large; one order of magnitude. You are talking about two orders, but even at the one order I am talking about it's not useful for that sort of prognosis.

CB: What's the point of it then?

JV: We're talking of the upper limit of course. Your most likely number of cases would be X but ten times X cannot be excluded.

CB: Ok, ok, ok, and that means it *is* useful. So would the Government be formally reasonable, using ICRP risk models to calculate the risks — the cancer yield — from some hypothetical explosion at Barsebeck for example, even if they'd have to say it might possibly be ten times that predicted figure? Formally?

JV: It would automatically be misused by both camps and that therefore is why it is not … you don't do it like that. You look at individual doses — the highest individual doses and calculate which is the sort of area where people should not live — which is the sort of area where they should have special needs — quick evacuation in case of emergency so this number exercise. I think it's just silly. It serves no good purpose whether you're in your camp or a pro-nuclear camp or an ICRP camp.

CB: Well in this case I'm in a political camp […] there are questions that politicians need to know the answer to. When you build new nuclear power stations, or [consider] any nuclear policy, you need to know what would happen if something went wrong. You need some kind of model, and at the moment they are using your ICRP model. Are you saying they should be or they shouldn't be? You seem to be saying they should use no model at all. Is it guesswork, or what?

JV: Well I certainly wouldn't say they should use your model because …

CB: ECRR gives the right answer

JV: … no it's the wrong answer, leading to large expenditure that would not be sensible and could be used to save lives in other [ways]

CB: The draft ICRP Recommendations said that for many internal exposures the concept of absorbed dose was not valid. We would agree with that of course, but it disappeared from the final report. Why?

JV: In fact there is a whole section of the Biological annex which talks about the difficulties. I don't know exactly why the specific statement disappeared but a person reading those paragraphs in the annex will be able to see there's huge uncertainty.

CB: We're not talking about uncertainty but about the impossibility of using absorbed dose for internal nuclides.

JV: ICRP's position is that it's possible to use it albeit with large uncertainties.

CB: How large is large?

JV: Two orders is a very large uncertainty.

CB: So it could be in error by two orders for some internal exposures — so we agree?

JV: (laughing) I'd hate for you to go home and say "Jack agreed with me"

CB: but I need an answer

JV: Then the answer is I don't agree with you. (laughing)

CB: but you just said *Two orders of magnitude* …

JV: Yes but you can find, I'm sure you can find, an exceptional case, a specific case, where there would be that sort of uncertainty but remember it can go in another direction, and I'm sure that you can find in most cases there are uncertainties which are less than one order of magnitude, which you would find normally. If we look at the existing evidence I don't think you have enough evidence to prove your case.

CB: The existing evidence is three orders of magnitude, if we take the childhood leukaemia clusters around nuclear sites; three orders.

JV: That's what you are claiming on the basis of a handful of cases.

CB: I'm claiming it on the basis of the German study, Aldermaston, Sellafield, Harwell and many others […] #

The full meeting was videotaped and can be seen on:

www.youtube.com/watch?v=minY5smeLGKw

Shortly after this meeting Busby addressed the Swedish radiation protection institute SRM. Deputy Director Carl Magnus Larsson said the ICRP model cannot be used to predict the health consequences of accidents. He added that for elements like Strontium and Uranium which bind to DNA national authorities would have the responsibility to assess the risks. Another SRM member said that the Secondary Photoelectron Effect was well recognised, also that in 1977 the ICRP had considered a weighting factor "n" for elements which bind to DNA but had not implemented it. Carl Magnus Larsson was sent to Australia where he still (Oct 2011) is.

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Radiation Risk: the present and the future. Requirements for a comprehensive and accurate model

Prof. Christopher Busby

Scientific Secretary: European Committee on Radiation Risk ECRR
UK Ministry of Defence Depleted Uranium Oversight Board (DUOB)
UK Dept of Health Committee Examining Radiation Risks from Internal Emitters (CERRIE)
Leader: Science/ Policy interface; Policy Information Network for Child Health and the Environment (PINCHE; European Union).
Guest Researcher: Julius Kuehn Institute, German Federal Agricultural Laboratories, Braunschweig
Visiting Professor, Faculty of Life and Health Sciences, University of Ulster, Northern Ireland

The ICRP radiation risk model, developed in 1952 and currently still the basis of legal limits has failed the human race and is now embarrassing in its manifest error. It is based on simple assumptions that in the great majority of cases fail to hold. Born in the statistical analysis of cancers in the Japanese A-Bomb victims, it firstly assumes that the risk of cancer is proportional to the *absorbed dose* or *equivalent dose*, in Joules per Kilogram – and that every cell within the organism receives the same ionisation, as the dose is simply divided by its mass. Secondly, it assumes a linear progression in risk (double the dose, double the risk of cancer) with no threshold, and thirdly it assumes that internal exposures can be accurately or sufficiently modelled as external exposures – that there exist no biochemical or local enhancements of the ionising effects of radiation at the scale of the target for radiation effects, the chromosomal DNA or other nanosized organelles. There are political and military dimensions which support the use of this model even when it is clearly incorrect – and these assumptions are manifestly incorrect. The epidemiology shows effects which occur at 'doses' which the model predicts are far too low to show any effect.

Theory and Experiment

External and internal isotope or particle doses confer hugely different ionisation density at the DNA level. Epithelial tissues and organelles concentrate certain isotopes due to biochemical or biophysical affinity. The resulting high levels of local

ionisation can make double strand breaks and so these effectswhich follow from this damage should be proportional to Dose squared. This is a simple kinetic theory argument since *Second Event* decays can intercept the repair mechanism, with obvious damaging effects.

- DNA binding; membranes. Z4 (high Z elements uranium).
- The dose response is not linear and can be biphasic.
- No inclusion of ionisation density enhancement near DNA from Auger or transmutation.
- Genomic and bystander effects mean non-cancer effects and possible field cancerization

The epidemiological effects of low-dose ionisation are clear, but causality is denied on the basis of this false model. The effects of the Chernobyl disaster and the health following irradiation are clear in the ex-Soviet union and in children born across northern and western Europe. Cancer clusters, both adult and child exist around power plants, weapons laboratories and waste processing plants.

Let me give some examples out of many. Many are listed in the ECRR2003 report and were discussed by the UK CERRIE committee but since then others have appeared which vindicate the model which we presented in ECRR2003. I list some of these in Table1.1 below.

Problems in the basis of radiation epidemiology

Epidemiologists increasingly employ regression methods, and regression methods do not work if there is not a continuously increasing dose response. The result is that they give the answer that there is no association. Epidemiological results are routinely dismissed even by the epidemiologists on the basis that doses are too low to account for the effects, but Dose itself cannot be used for internal risk due to anisotropy. It has been noted that the dose response for many radiation studies, of health effects, in animals, in cell cultures and in biomarkers is often biphasic (Fig 1.1). One example in the real world is the rate of infant leukemia in those exposed to the Chernobyl fallout [3]. In this cohort, which was extremely tightly described, the increases in leukemia were not a monotonic function of the estimated dose. The yield was largely biphasic, and very similar to that shown in Fig 1.1 There are two theoretical plausible reasons for such a response, both discussed in ECRR2003 [4].

Table 1.1. Some examples of the development of cancer and other ill health in populations exposed to internal radionuclides which the current radiation risk model of the ICRP fails to predict or explain

Example	Effect	Error factor	Note
Global atmospheric tests	Cancer epidemic, infant mortality, heart disease	300-500 for cancer	Cancer increases easily seen in populations of Wales and England [1,3]
Chernobyl	Infant leukemia in Germany, Greece, Scotland, Wales, Belarus	400	Published in two journals, discussed by CERRIE [2,3] No other explanation
Chernobyl	Cancer in Sweden	600	Study by Tondel et al [6] shows increased cancer risk of 11% per surface contamination of $100kBqm^{-2}$. Effect predicted by ECRR model [3]
Chernobyl	Global health effects	Vary. Many effects not predicted by current models	Report by Yablokov et al in New York Academy of sciences [4]
Nuclear Test veterans	8-fold Child congenital anomalies	Not predicted by current models	Similar high congenital anomalies in Fallujah Iraq due to Uranium weapons [9, 10]
Uranium effects in Iraq Gulf veterans, Balkans peacekeepers	Very large increases in cancer and birth defects	1000 to 10,000	Cancer in Gulf veteran now (2009) linked to DU exposure by a coroner jury in UK [11]
Childhood cancer nuclear sites	Sellafield and many others. Most recent is KiKK study	1000 to 10,000	No other explanation
Irish Sea coastal contamination	Sharp increase in cancer risk near coast	1000 to 10,000	Very high statistical significance. Inhalation of particulates

But if the effect is a result of exposure to the fallout, we note that a regression approach would fail to find any statistically significant correlation. This is because the problem with regression is that it has to begin with an assumption of the relationship that is being tested, and the assumption is always that as the dose increases, the effect does also. But we know this isn't true for many relationships. Take the stretching of a wire as a result of increasing tension. We know that stress is proportional to strain only until the elastic limit and after that the wire breaks. This is also true for the fetus, exposed to radiation, and no doubt also to other systems. There only have to be two sensitivities of cells, or of individuals and a biphasic dose response results. The Youngs Modulus analogy in a living system would perhaps be the induction at lower doses of repair mechanisms and their overwhelming as the dose was increased.

A second problem arises in retrospective epidemiology, the method of many studies of the effects of radiation exposure. It is now clear from, studies of Chernobyl exposed populations that exposure to radiation causes increased death rates from a wide range of causes, heart disease and strokes being among them. Since cancer is a disease mainly of old age, the competitive death rates from non cancer illnesses result in a reduction of the cancer rate in those populations exposed, since many die of other causes before they become old enough to develop cancer. I have found this recently in a re-examination of Thorotrast and Radium studies. In one Japanese study of Thorotrast exposed individuals there was a loss of almost 20 years of lifespan in women compared with Japanese national deaths rates. This may be why these studies show only liver cancer effect in the very old. The destruction of bone marrow tissue and the likely resultant effects on health were drawn attention to by the head of the Medical Research Council, J F Loutit in 1970 and he specifically noted that these problems would affect the interpretation of the epidemiological studies of Radium Dial painters by Robley Evans and later researchers who employed retrospective analysis with cancer as an end point [7].

What we know and what we would like to know

The Japanese A-Bomb studies are insecure because the control groups were exposed to internal radioactivity. For external exposures at least, the ICRP model cannot be too far in error: otherwise there would be large observed effects from medical exposures and from background radiation. Other external exposure studies do not show large differences except in the case of foetal exposures, and these are accepted. We do not know the effects of fractionation or multiple exposures occurring inside the cell repair timescale, and we do not know how the effects of repair system variation alter the epidemiological conclusions.

1% of cells are actively dividing and 200-600 times more radiosensitive than non-dividing cells

Predicted dose-response relationship for mutation in animal with two types of cell sensitivity sub classes: high sensitivity replicating cells and low sensitivity quiescent cells. Sensitive sub-class are first mutated then killed as dose increases.
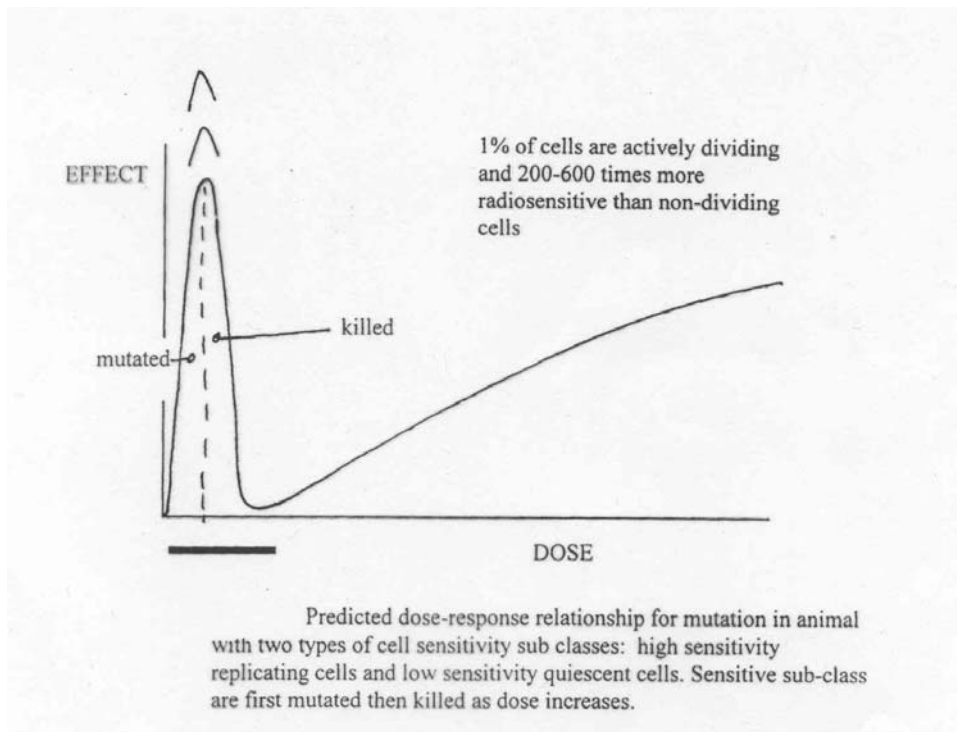
Figure 1 - Predicted dose-response relationship for mutation Biphasic dose response: due to induced cell repair, sub classes of cell sensitivity, deaths of individuals,

Although we do know the organ affinity (bone, prostate, muscle), we *do not know* the in vivo affinity of major radioactive elements for DNA; notably, uranium, barium, strontium, tritium, plutonium, radium. This is an extraordinary lack of knowledge in 2009.

- *We do not know* the ionisation density at the DNA due to decays of various types and RBEs from internal elements located at different distances from the DNA.
- *We do not know* the importance of membrane doses or the membrane affinity of major risk elements e.g. Cs-137.
- *We do not know* what happens and what ionisations occur at the position of transmutation decay of an element bound to DNA e.g. Sr-90---Y-90.
- *We do not know* the effects of multiple decays.
- *We do not know* the local doses from Augers or Z4 elements bound to DNA.
- *We do not know* the ionisation density near massive sub micron particles either radioactive or passive photoelectron amplifiers.

Thankfully, both to the ICRP and others we do understand the bio kinetics of internal isotopes and tissue half-lives. We know the decay energies and mean absorbed doses to (large masses of) tissue, and the dose coefficients based upon these quantities. But it is not enough.

The ICRP phantom

For the ICRP and other current risk models the body is modelled as a bag of water, radiation is assumed external. Therefore, the *ABSORBED DOSE* is *ENERGY* divided by *MASS*, Joules/Kg = Gray. This method would give the same dose for warming yourself in front of a fire as eating a hot coal, and this is clearly problematic.

Fig. 1. Some irradiation geometries with an anthropomorphic phantom.
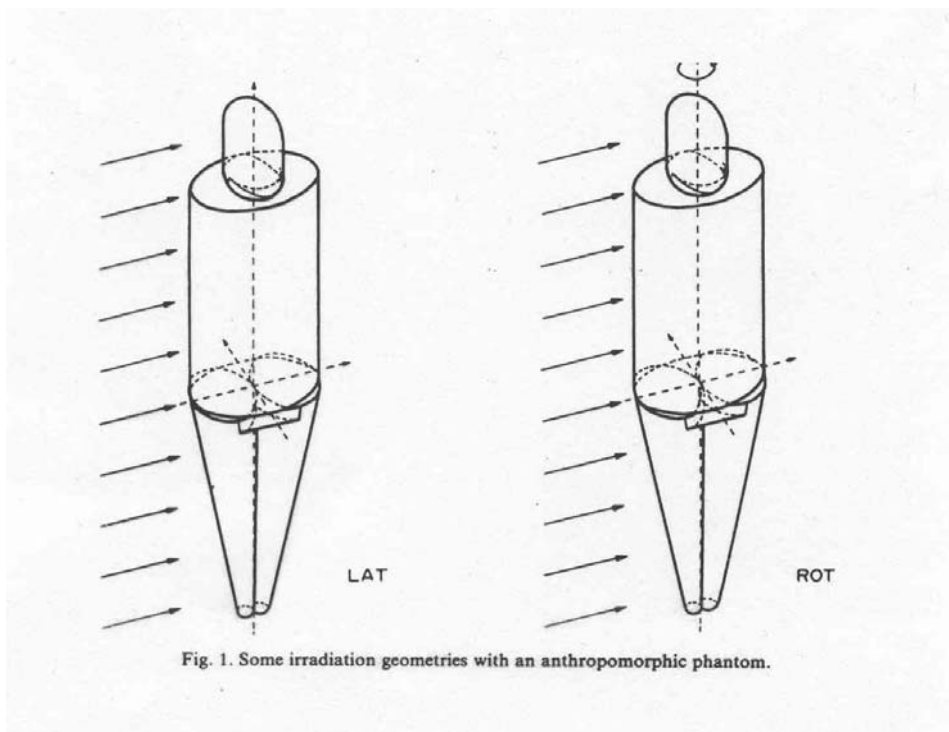
Figure 2 - *Irradiation Geometries*
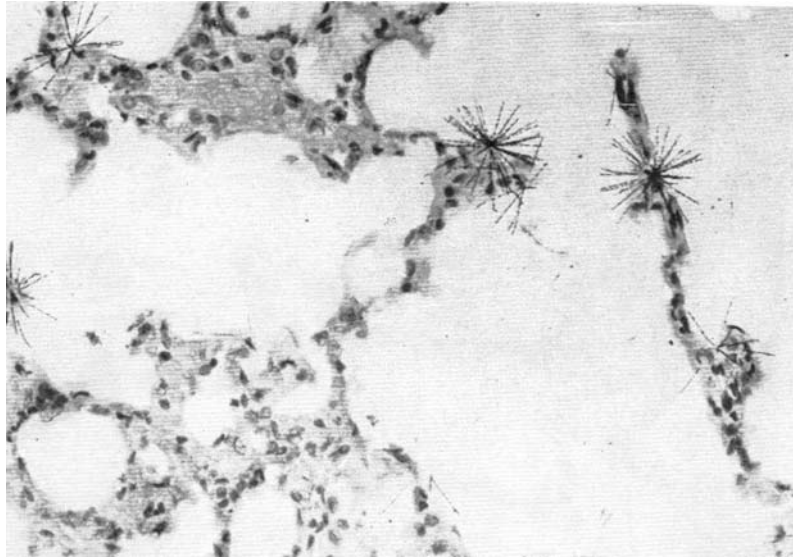
Figure 3 - *Alpha particle decays – Micron diameter particles of Plutonium in a rat lung: 'Alpha Stars'*
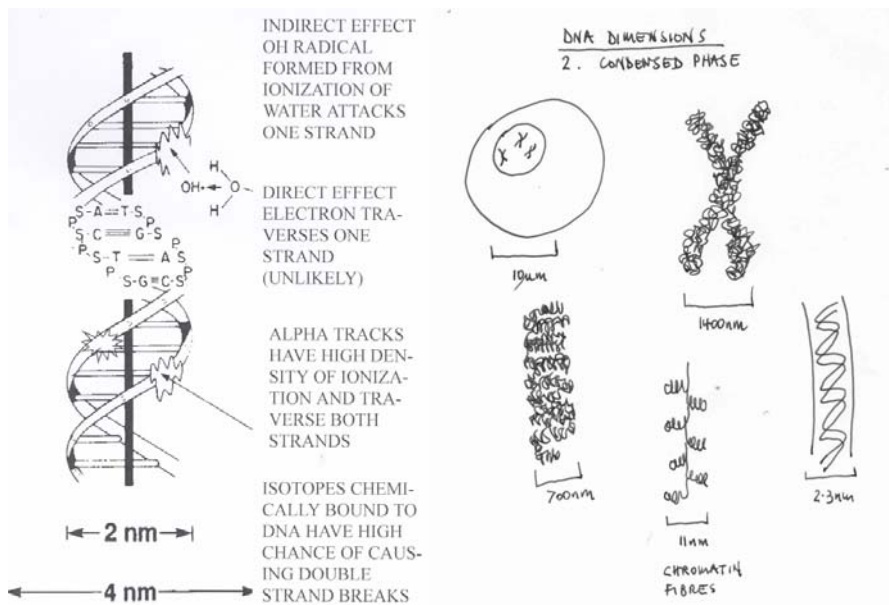
Figure 4 - *Some DNAP dimensions*

The internal doses to human populations from various processes have been calculated and are listed in the literature, e.g. UNSCEAR reports. One obvious way forward is therefore to employ weighting factors for the different internal exposures: this was the approach taken by ECRR2003.
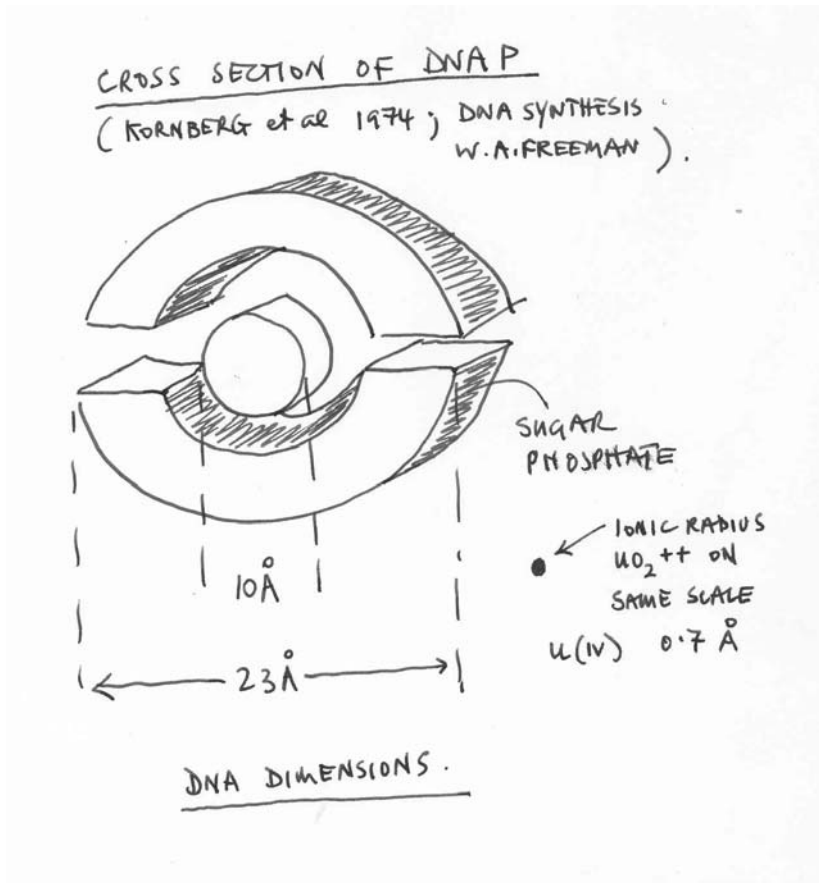
Figure 5 - Cross Section of DNAP with Uranyl ion on same scale

We know from experiments with Auger emitters bound to DNA (e.g.I-125) that DNA is the target for the effects of ionising radiation (Fig 6). Therefore a rational way forward would be to attempt to calculate the ionisation density at the DNA for all radiation exposures. For high ionisation density we can employ second order kinetics and increase the risk accordingly. At minimum, even one such approach would put the current ERCC model on a more secure footing.

It is an interesting thought experiment to consider the effects of the weak beta emitter Tritium. Tritium is afforded a RBE weighting factor of 1.0. But since the range of the beta emissions from Tritium are a few nanometres, it is clear that for uniform distribution of HTO in the body, in the cytoplasm, most of the beta energy cannot intercept the DNA and is effectively wasted. This means that the very small fraction of HTO that happened to be near the DNA is the cause of all the genotoxic effects.
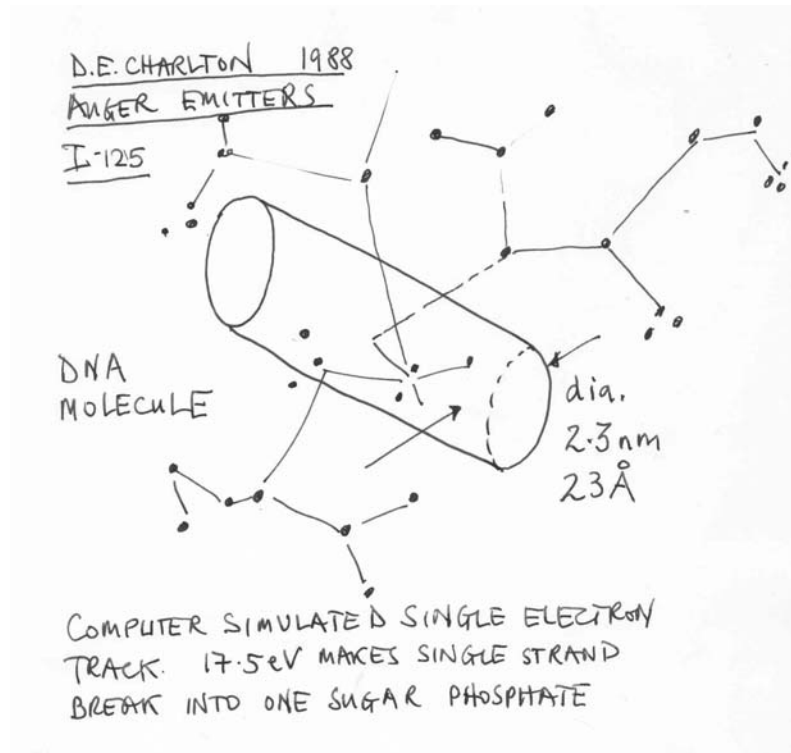
Fig 6 - *Auger emitters*

Moving forward

A secure radiation risk model must be based upon empirical data which compares similar exposures, and be able to explain all of these observations. It must be able to predict the outcome of specific exposures. It must not make unsupportable assumptions, and it must be able to employ historic exposure data to re-examine historical exposures and their effects. One avenue of progress is to develop the ECRR weighted risk factor approach to modelling internal exposures. At the same time, we must develop a way of comparing internal elements on the basis of their ionisation density at the DNA in order to support the semi-empirical approach. This is based upon the epidemiological results of internal exposures to mixed fission products which routinely give an error factor of 300 to 600 times for risk based on ICRP doses. This range, two to three orders of magnitude, explains all the observations of anomalous cancer yields following internal exposures to fission products and uranium. The Chernobyl accident exposures are a very valuable source of information, since they have isotope maps and in principle might yield health effects which can be tied to different isotopes.

In general, exposure has been assessed in terms of Cs-137 as this can easily be measured, but in fact, Sr-90 is potentially a much more serious hazard. However for now, good news is around the corner.

ICRP and Jack Valentin

As many of you know, the mainstay of the ICRP is their Scientific Secretary, Dr Jack Valentin, from Sweden. Valentin is the editor of the latest version of the ICRP model [8] and has been involved in collating and publishing most of the ICRP works since the 1990s. He recently resigned from his position and was asked, just after this, by the Swedish anti nuclear organisation MILKAS to debate the issue of the two risk models, ECRR and ICRP in Stockholm. The meeting took place only a week or so ago, on 22nd April (2009). The format was that we each gave an outline of our respective case and then there was a session where we asked each other questions. As a result of my questioning him, he made two extraordinary statements. Both were captured on video by Ditta Rietuma and have been put on the internet. The whole session was also recorded on digital media. These are the statements:

1. The ICRP risk model cannot be used to predict the levels of cancer in populations exposed to ionising radiation. The reason is that there is too great an uncertainty about the risk coefficients for certain internal nuclide exposures. The uncertainties could be as high as two orders of magnitude.

2. The ICRP and UNSCEAR were wrong to ignore the evidence from Chernobyl that their risk model was wrong and to ignore the evidence advanced by the ECRR that their risk model was wrong.

When asked why he was saying these things now, Valentin said that when he was employed by ICRP he was unable to, but now he was no longer employed he was free to do so.
I do not want you to imagine that Valentin is on our side, as it were. He made it quite clear that he did not agree with my position or that of the ECRR. What he did say is that the ICRP model was not safe for the purposes of analysing the outcome of exposures in the event of a nuclear accident, and that (inevitably) was incorrect when analysing the effects of the Chernobyl accident.

Uranium effects and Court Cases

It may be that the resignation of Jack Valentin has to do with some other recent developments in which I have been involved and which have had a significant

impact on the acceptance of the ICRP model as a gold standard for radiation risk assessment. The first is the case of Uranium genotoxicity. As you know, Uranium, U-238, is considered a very low level hazard by ICRP. This is because its half life of some 4.5 billion years means that it has a very low specific activity, about 12MBq/kg. The ICRP risk analysis provides the military with an excuse to employ uranium weapons for tank armour penetration and the uranium mining companies to avoid conceding that the many increases in ill health in those native Americans living on Uranium mine waste are a consequence of their exposures. Like most of the arguments in this area of radiation risk the absorbed doses are calculated and shown to be too low for the observed effects.

However, there is one way in which Uranium exerts an influence on absorbed dose that has been entirely overlooked by the ICRP model. My PhD student at the University of Ulster, Andreas Elsaessar, will be addressing this later in the programme but I will say something here about it. I first pointed out in 2003 that since physics tells us that gamma radiation is absorbed by elements in proportion to the fourth power of their atomic number Z, internal contamination by high Z elements will attract natural background gamma radiation into the body. This radiation will be mostly converted to photoelectrons of almost the same energy as the gamma. Photoelectrons are, of course, identical to beta particles or any other energetic electrons that are produced in the body following gamma irradiation. If the Uranium contamination is relatively low, this would just increase the absorption of gamma rays, the absorbed dose, by a tiny fraction. But this is not all. It turns out that Uranium, as the UO2++ ion has an enormously large affinity for DNA, binding to the phosphate backbone. The affinity constant is 10E+10 per mole. It follows that in the body, most of the soluble Uranium is bound to the DNA, including germ line DNA, mitochondrial DNA and chromosomal DNA. It follows that nanoparticle Uranium has a very high local absorbed dose due to photoelectrons. Its intrinsic radioactivity is not relevant here: this is a secondary photoelectron effect and would occur with other high Z particles like platinum and gold. Indeed, recently this effect has been employed to destroy tumours by injecting them with gold nanoparticles and then irradiating with X-rays. I have applied for a patent to use uranium in the same way, not nanoparticles but uranyl ion, which, I argue will stick to the tumour DNA at Urranium doses which are quite low and within the range found not to cause significant health effects in human populations. Of course, the effects of this discovery, are to demonstrate a plausible mechanism for the clear ill health effects manifested by Uranium in places like Iraq, and other battlefield areas, and also of course, in those who became contaminated at the nuclear bomb test sites.

In the last three years I have providing evidence in court cases as an expert witness for a number of individuals who have suffered cancer as a result of earlier exposures. Many of these have been veterans of the nuclear weapons testing carried

out by the UK in Australia and Christmas Island. I have to say, that so far, I have persuaded the courts in every case that the ECRR model is more accurate than the ICRP model, and this despite opposition from expert witnesses from the defence side. The cases have thus been won, and in some instances very large settlements have resulted. So there is some light at the end of the tunnel. If we can take our arguments to the courts, and advance our evidence, it quickly appears that unbiased legal minds and juries, presented with this evidence, immediately see that the ICRP system of belief is a house of cards, built up in the cold war, and no longer credible in the light of modern scientific tests and evidence emerging in the last ten years. Much of this evidence has emerged as a result of work by you and our colleagues, for which the world should give thanks, and eventually will.

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2

Non cancer illnesses and conditions in areas of Belarus contaminated by radioactivity from the Chernobyl Accident

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The ecological environment influences the health of people and regulates the development of human society. Ignoring the considerable overall global progress in the business of protection of the environment (and therefore the health of people) there are countries in which there are serious environmental problems. First of all are the countries of the former Soviet Union. The aspiration to catch up and overtake the military and economic development of Western countries forced the former Soviet Union administration to introduce new industrial technologies that left a fatal impact on the environment and therefore the health of people. First of all, it is necessary to consider the Nuclear weapons tests of the USSR.

Pollution by radioactive elements of huge territories in Belarus, Lithuania, Latvia, Estonia, the Ukraine and Russia since the 1960s is the direct consequence. The population of these countries had no information on the existing radiation factor, and it could therefore not naturally protect itself from its influence in any way.

The Radio-ecological problem in Belarus

Since the beginning of the 1960s there have been a great number of Cs-137 radionuclides found in foodstuffs consumed by the inhabitants of these Soviet states for many years [1]. Although the contamination of Belarus by the Chernobyl catastrophe is well known (Fig1) what is less well known is the prior contamination by the weapons test fallout. I present a number of pieces of evidence of the contamination of areas of the USSR in Figures 2.2-2.4. Fig 2.2 shows how, prior to the Chernobyl disaster, Cs-137 levels were high in the 1960s and fell regularly after the atmospheric bomb tests were banned in 1963. For example, cow's milk is one of the basic products containing high levels of Cs-137 radionuclides for inhabitants of Belarus and the Baltic lands. A "Milk-Caesium Map" was created – the largest Cs-137 radionuclides contained were observed from 1967 to 1970 in Gomel region of the Republic of Belarus.
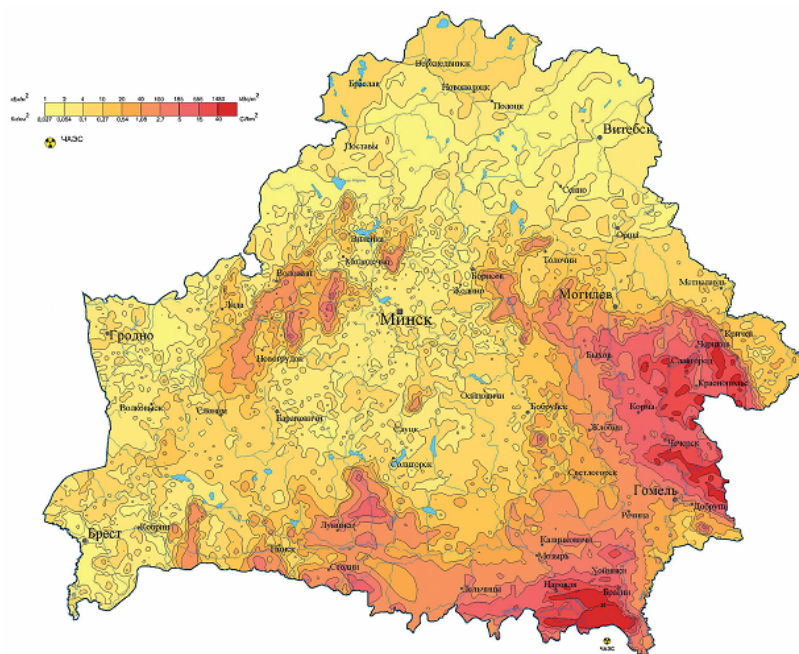
Fig 2.1 *Cs-137 pollution in territories of Belarus in 1987*
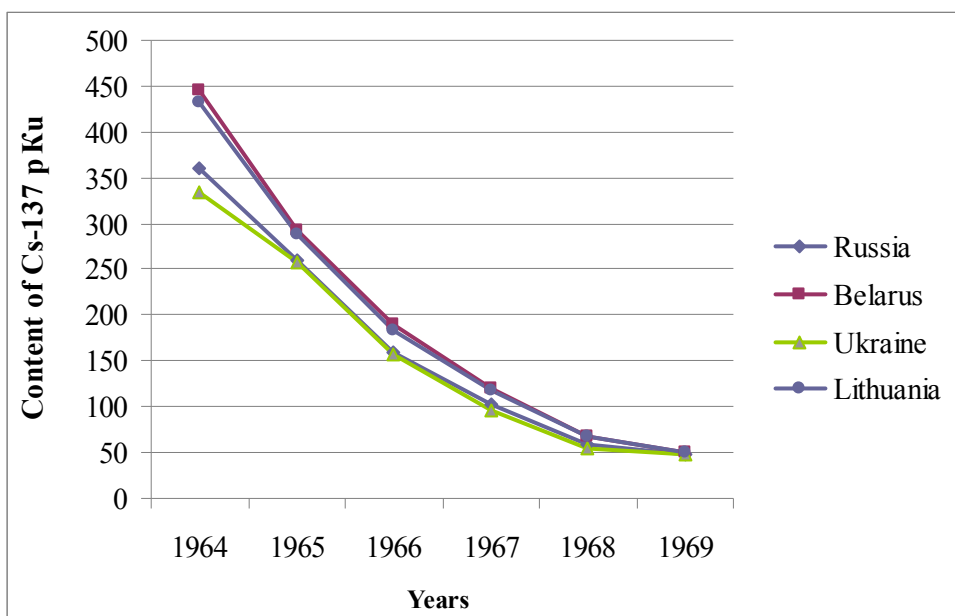
Fig. 2.2 - *Cs-137 contents in villagers' daily food allowance in pCi (Marey A.N. and co-authors, 1974)*

Fig. 2.3 *Cs-137 contents in cow's milk (pCi/l) from different districts of Belarus in the 1960s (Marey et al 1974).*

The Chernobyl accident of 1986 intensified a lot the already existing radiation effects on the population of many European countries, focusing on the Republic of Belarus. The map of Cs-137 radionuclides deposition in the territory of Belarus after the Chernobyl accident in 1992 (Fig 2.1, Fig 2.4) almost corresponds to the map of such radionuclides deposition in the territory of Belarus in the sixties (published in 1974 (Fig 2.3; Marey A.N. et al. 1974.). It was only due to western public interest that after the Chernobyl accident in 1986 it became possible to speak about the influence of radiation on the health of people in Belarus and another countries. Judged by its scale and consequences, the Chernobyl accident on April 26 1986 is considered to be the largest man-caused catastrophe in human history. Its social, medical and ecological consequences require detailed study. Above all European countries, Belarus was the worst affected. About 70% of the radioactive substances released to the atmosphere as a result of the accident at the 4th block of the Chernobyl NPP landed in and contaminated over 23% of the territory of the Republic. At present in this zone there live close to 1.4 million inhabitants, including 260 thousand children. The radiation situation in several affected regions is still difficult today. The greatest danger is represented by the consumption of the foodstuffs containing radioactive elements Cs-137 and Sr-90. The contribution of these radionuclides to the internal dose reaches to 70 to 80% (Busby and Yablokov 2009). The increases in death and reduction in birth rates in Belarus have shown as a negative trend in the demography index since 1993: 2002 -5,9‰, 2003 -5,5‰, 2005 -5,2‰.
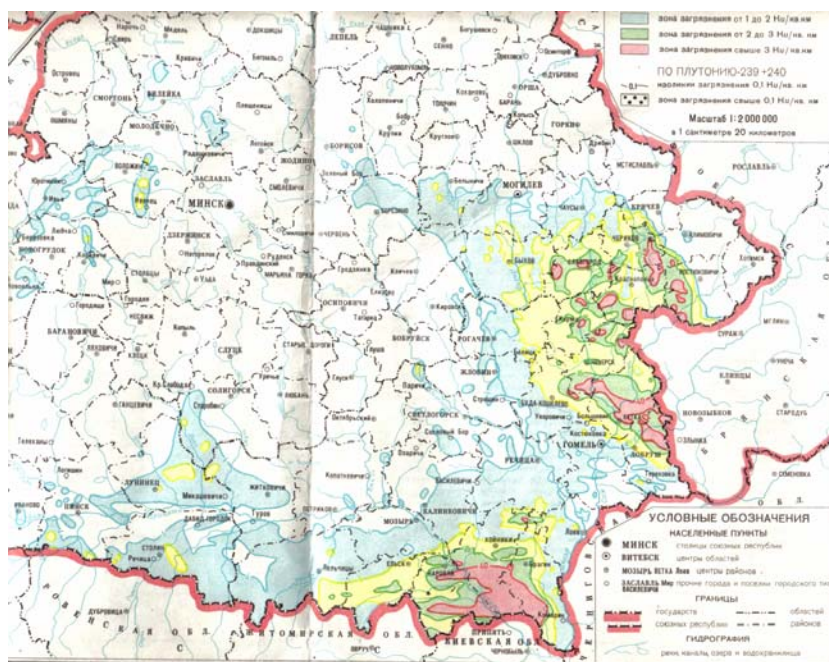
Fig 2.4 *Map of Cs-137 deposition in the territory of Belarus in 1992*
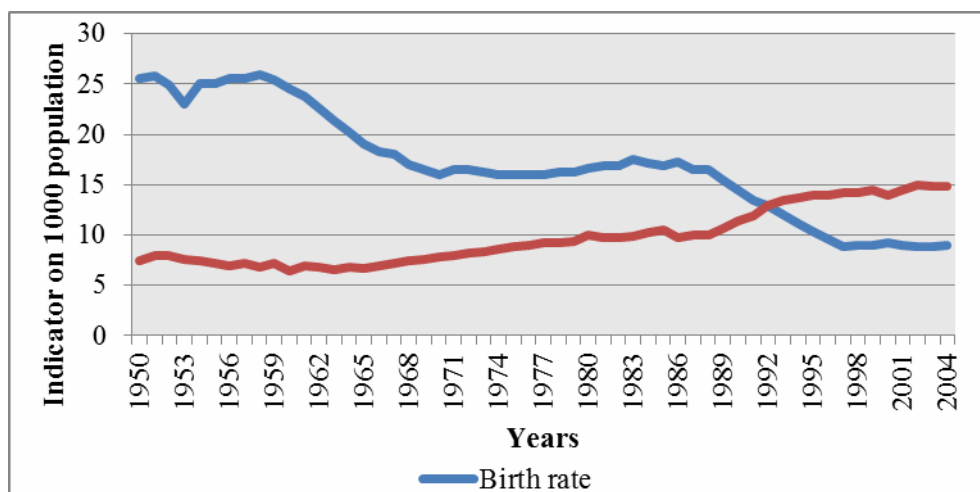
Fig. 2.5 *Indices of the death-rate and the birth-rate (per 1000 inhabitants) in the Republic of Belarus*
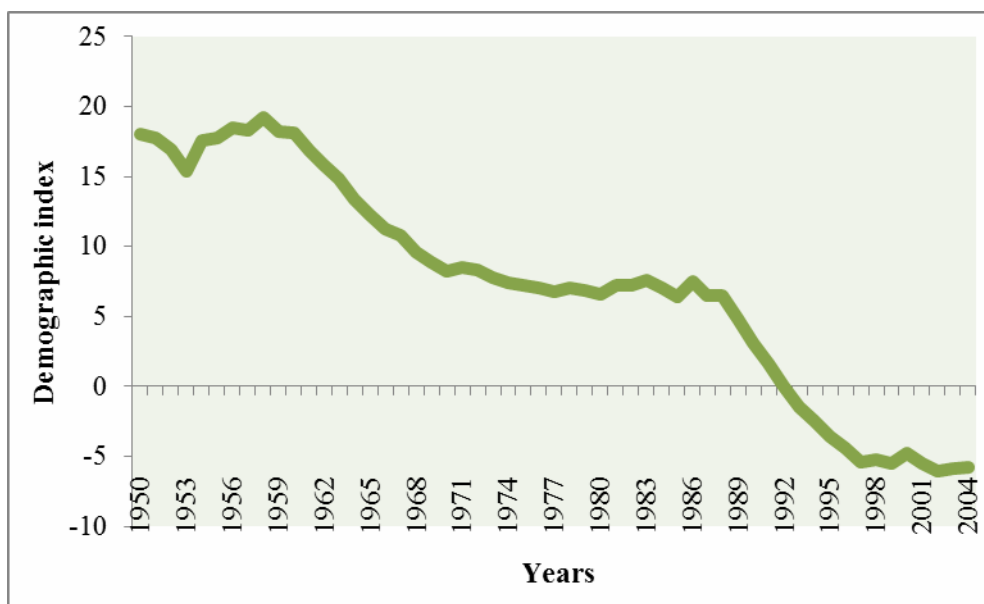
Fig 2.6 *Demographic index for the Republic of Belarus, 1950-2004*
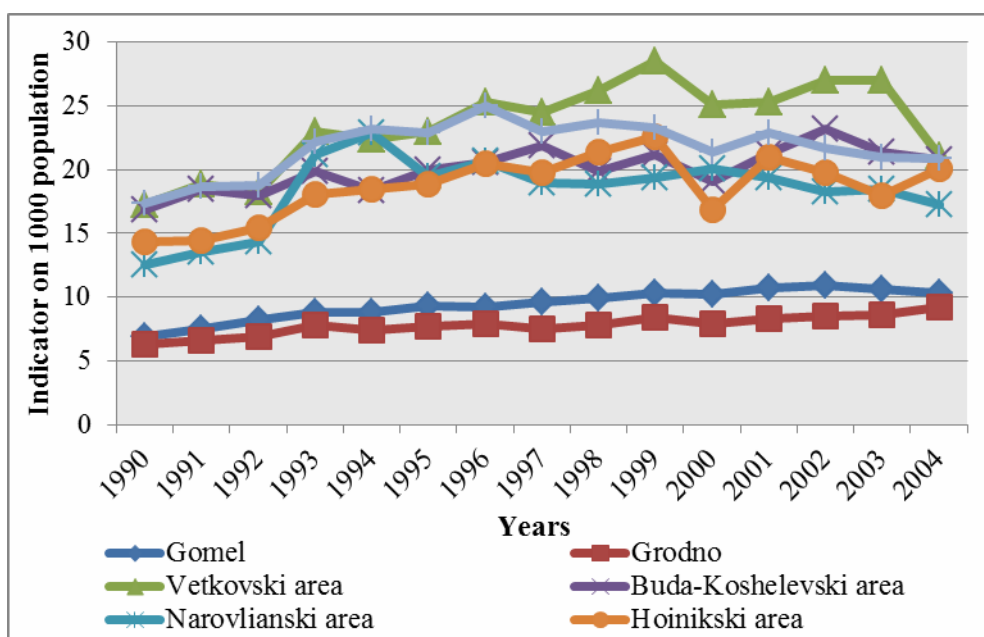
Fig 2.7 *The dynamics of the death-rate of the population in different districts of Belarus*
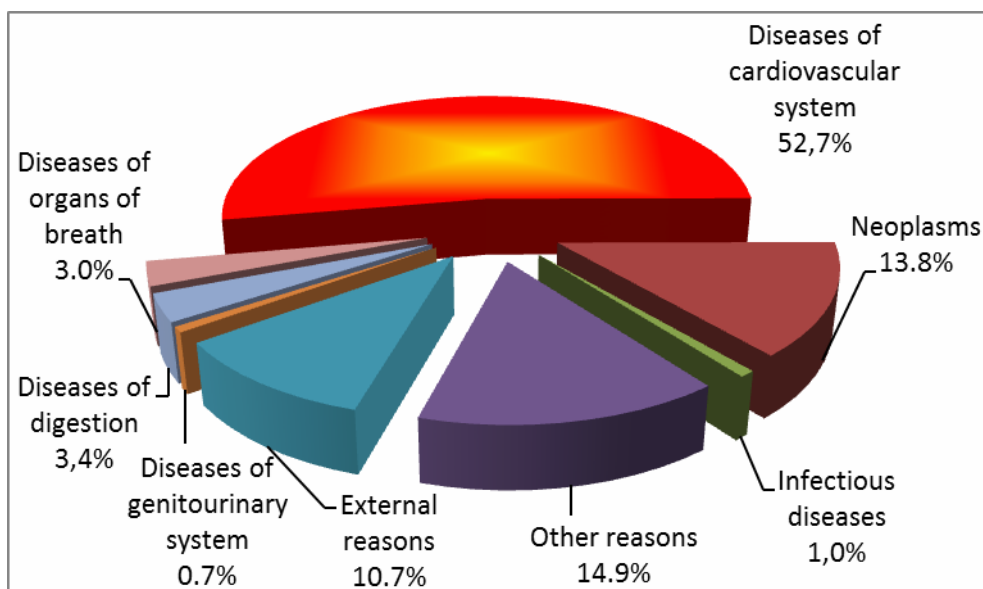
Fig 2.8 *Structure of the causes of death in Belarus, 2008*

Among the causes of death of the inhabitants of Belarus, cardiovascular and oncologic diseases take the dominant place. The statistically significant increase in the primary incidence of diseases of the cardiovascular system, especially amongst those who dealt with the consequences of the Chernobyl nuclear accident is cause for anxiety (Fig 2.9).

Cs-137 radionuclides under conditions of permanent chronic intake in food are accumulated in vitally important organs: thyroid gland, heart, kidneys, spleen, cerebrum. This affects these organs to different extents.
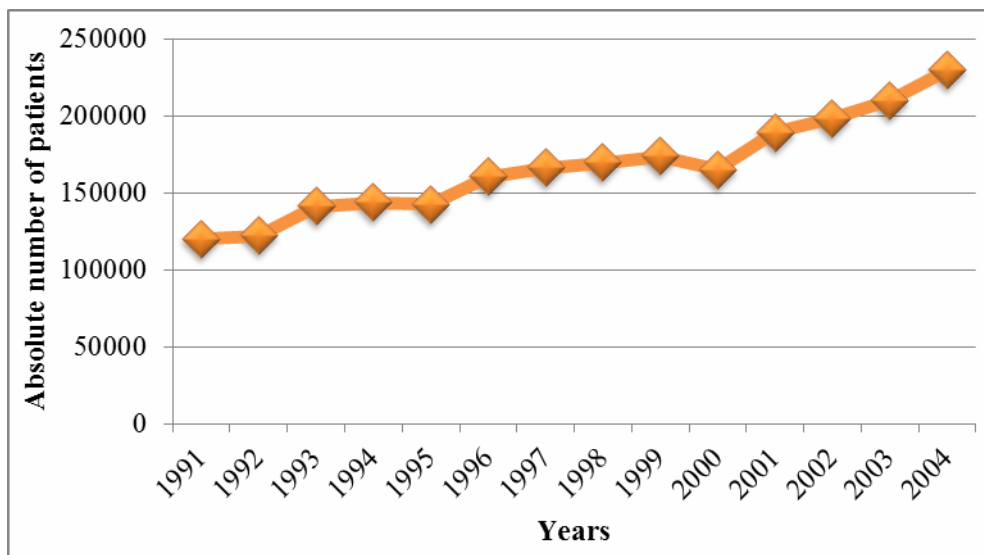
Fig 2.9 *The dynamics of cardiovascular diseases in the Republic of Belarus*
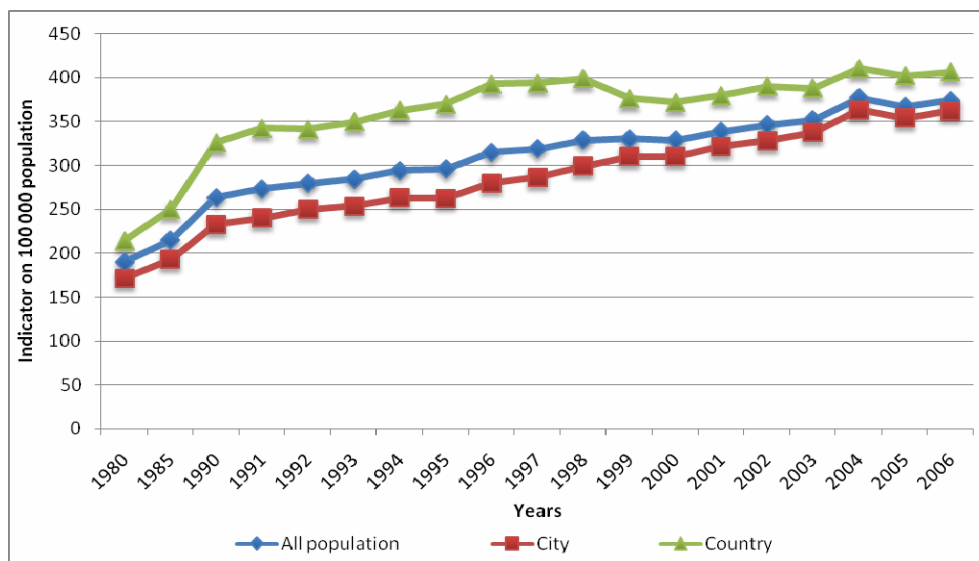
Fig 2.10 *Incidence in the population of the Republic of Belarus of malignant neoplasms (per 100,000 inhabitants)*
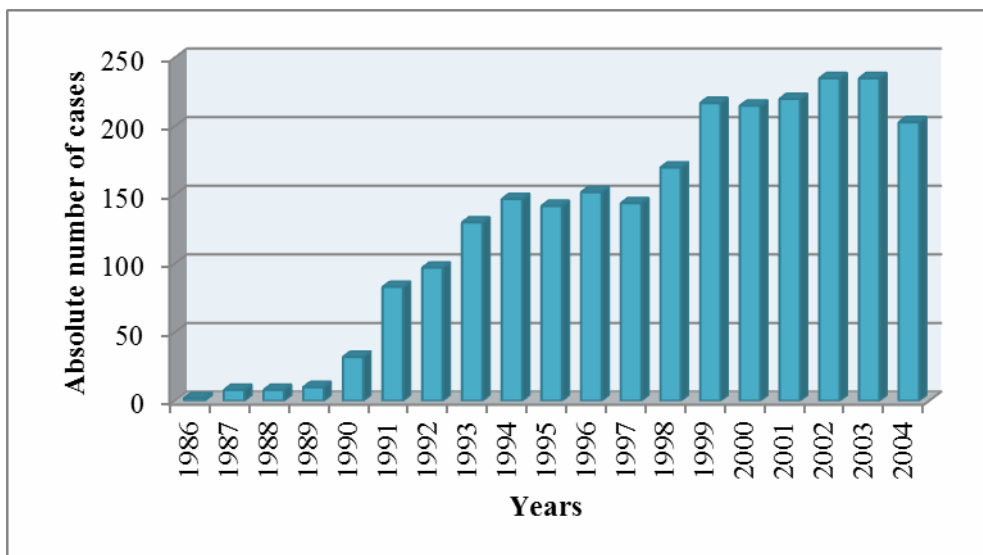
Fig 2.11 *The dynamics in the absolute number of cases of thyroid cancer detected for the first time in Belarus*
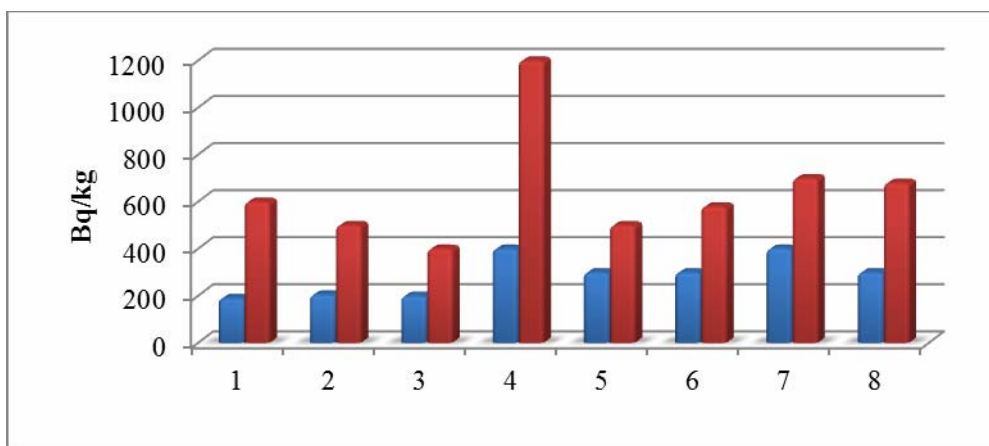
Key: 1 – myocardium, 2 – brain, 3 – liver, 4 – thyroid gland, 5 – kidneys, 6 – spleen, 7 – skeletal muscles, 8 – small intestine

Fig 2.12 *Cs-137 contents in adults' and children's viscera according to the data of radiometric measurements of the autopsies of inhabitants of Gomel region in 1997 and 1998 (Yu. I. Bandazhevsky, 1999, 2003)*

Cs-137 incorporation leads to metabolism disorders in highly differentiated cells and dystrophic and necrobiotic processes in development. The degree of disorder is the function of the Cs-137 concentration in the organism and in the organs mentioned above. The more intense the process, the higher the degree of disorder. As a rule if several organs are subjected to the radiotoxic effects simultaneously, this provokes general metabolic dysfunction. It should be noted, the organs and tissues with the negligible or absent cell proliferation (e.g myocardium) under physiological conditions suffer to the greatest extent. Cs-137, accumulated in the organism, seems to block the metabolic processes and affects membrane cell structures. The process provokes structure and function disorder in many vital systems but primarily the cardiovascular system. Structural, metabolic and functional modifications in the myocardium correlate with radiocesium accumulation and demonstrate its toxic effects. The energetic system and mitochondrial systems are violated. Deep and irreversible changes (due to the increase in Cs-137 concentration) lead to the necrobiotic processes in a cell. Suppression of the enzyme creatine phosphokinase appears as a consequence of energetic instability (Fig 2.14).

Fig 2.13 - *Accumulation of the rat cardiomiocytes mitochondria with radiocesium incorporation 45 Bq/kg Uv. 30 000*
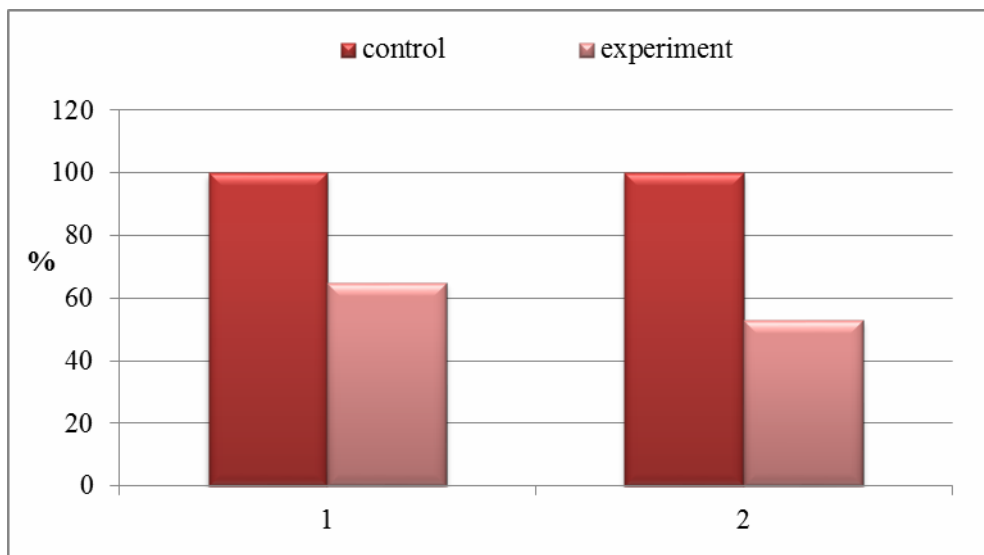
Key: 1 - alkaline phosphates, 2 - creatinphosphokinase (p <0,05)

Figure 2.14 *Variations of activities of enzymes in myocardium tissue among experimental animals (% versus control)*

The effects of Cs-137 are most extreme in the cardiovascular system of the developing organism. Radiocesium concentration over 10 Bq/kg leads to the violated electrophysiological processes in the myocardium of children. Those born after 1986 and continuously living on the Cs-137 affected territories with concentration above 15 Ci/km^2 suffer serious pathological modifications of the cardiovascular system, manifesting itself clearly both clinically and electro cardiographically. Cs-137 radionuclides incorporation in schoolchildren causes the disorder of electrophysiological processes in cardiac muscle shown by the disorder of cardiac beat rate. There found to be a clear dependence between the radionuclide content in the organism and the cardiac arrhythmia rate (Fig 2.15).
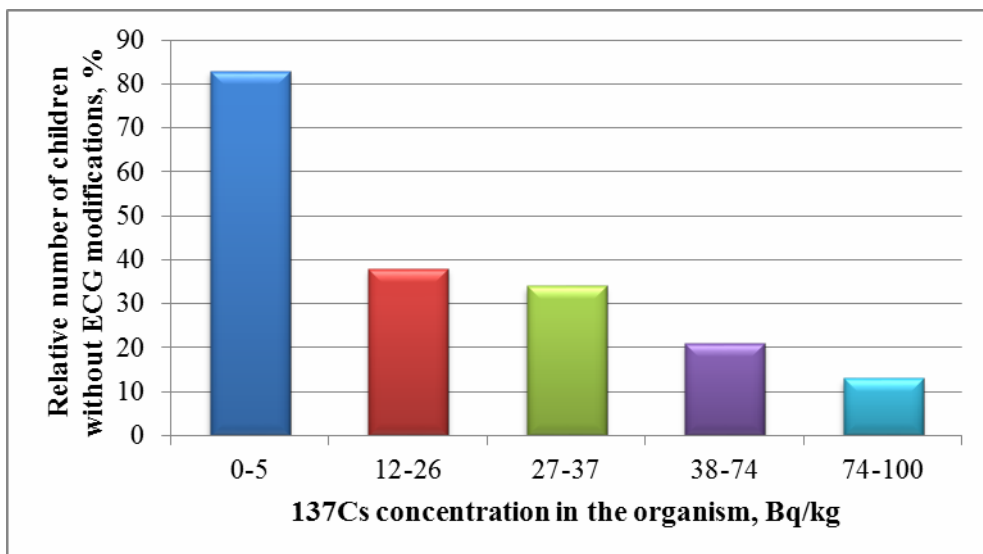
Fig 2.15 *Number of children without ECG modifications as a function of Cs-137 concentration in the organism (Bandashevsky and Bandashevsky).*
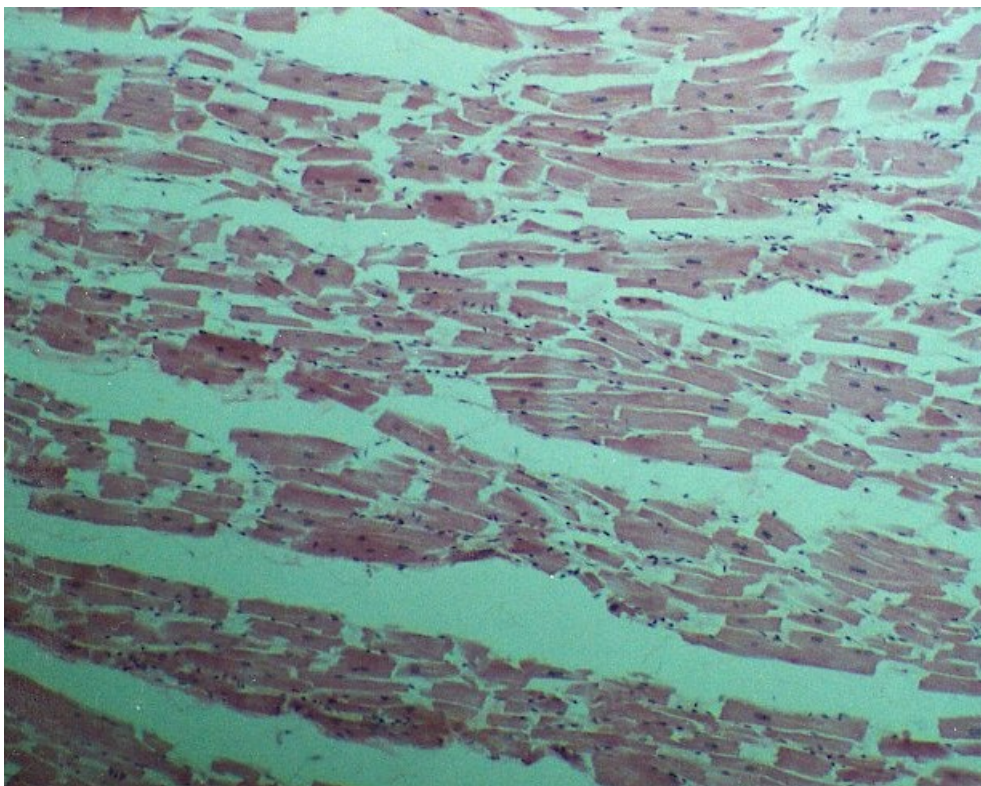
Fig 2.16 - *Histological myocardium composition of a 43-year-old Dobrush resident (sudden death case). Radiocesium concentration in heart – 45,4 Bq/kg. Duffisious myocytolis. Intermuscular edema. Fragmentation of muscular fibers. Colored by hematoxylin and eosin. Uv. X 125*
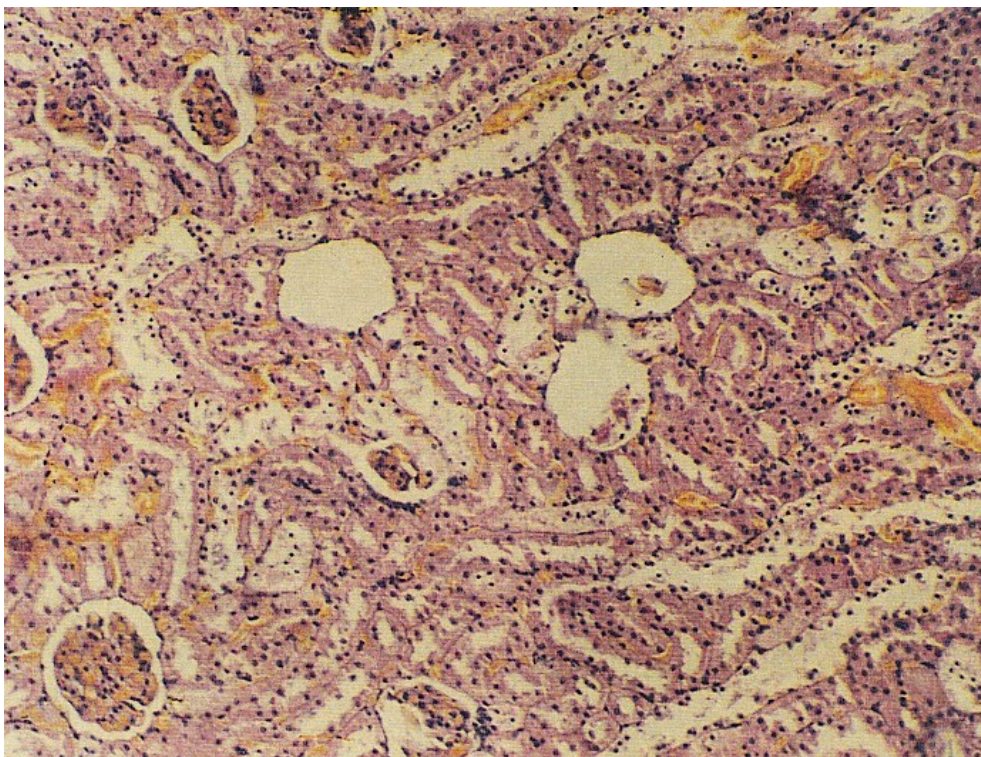
Figure 2.17 *- Histological kidney composition of an albino rat with radiocesium concentration 900 Bq/kg. Necrosis and glomerulus fragmentation with cavity formation. Necrosis and hyaline-dropping dystrophy of the canaliculus epithelium. Colored by hematoxylin and eosin. Uv. X 250*

The situation is quite organ specific. Fig 2.17 shows the effect in the kidney. Due to the microscopic architecture of the blood supply the radiation induced pathology of the organ has its own specific features. The radiation disease of the kidney is seldom accompanied with nephrotic syndromes, but is more severe and quicker in character when compared to the ordinary chronic glomerulonephritis. The latter is characterized by frequent and early development of the malignant arterial hypertension. Already after 2-3 years radiological kidney damage leads to the development of chronic renal failure and cerebral and cardiac complications**.** Kidney destruction is one of the main effects of Cs-137 in addition to the products of metabolic accumulation in the organism and their toxic effect upon the myocardium and other organs and also of the arterial hypertension. If the cases of sudden death in Gomel are considered, 89% of these are accompanied by this kind of general organ destruction, this state being not registered during their life time. Serious pathological

modifications of the liver are also noteworthy. The progress in toxic dystrophy of the liver with prevailing destruction of the cellular protein and metabolism transformation, results in formation of fat-like substances which contribute to such severe pathological processes as fatty hepatosis and cirrhosis (Fig 2.18).
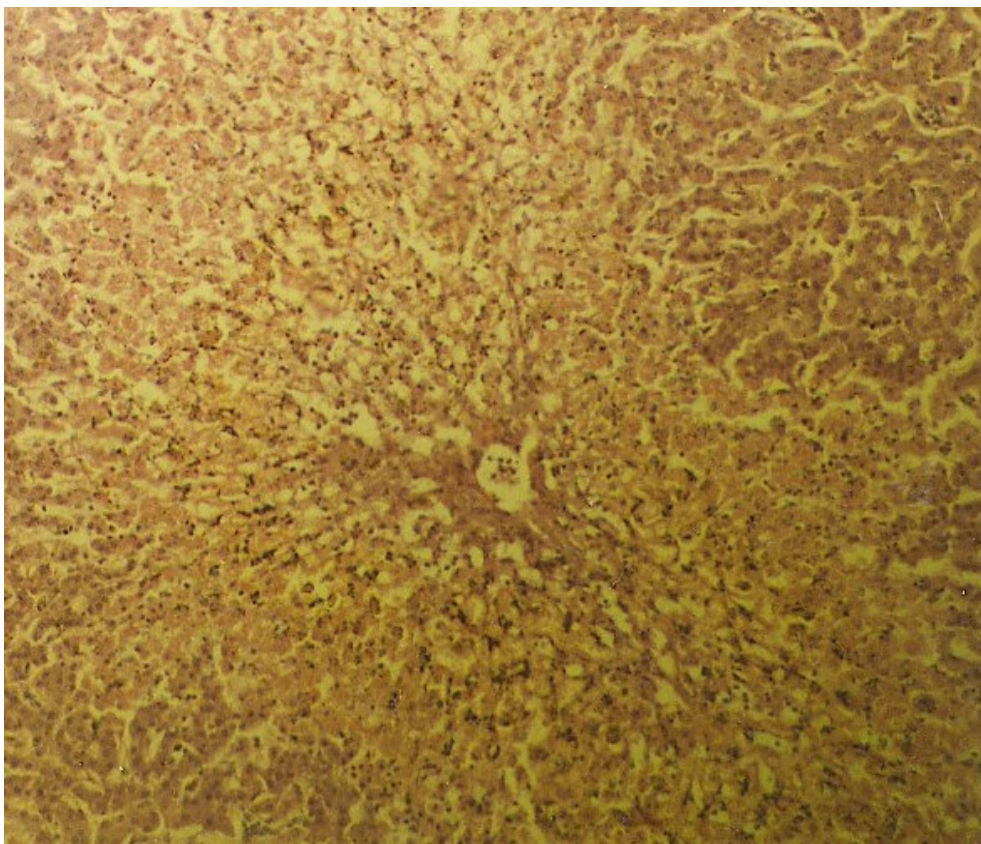
Fig 2.18 - Histological liver composition of a 40-year-old Gomel resident (sudden death rate). Radiocesium concentration in the liver – 142,4 Bq/kg. Fatty and protein dystrophy, hepatocytes necrosis. Colored by hematoxylin and eosin. Uv. X 125

The endocrine system is also exposed to influence of incorporated Cs-137. The adrenal gland also appear affected by the incorporated radiocesium, the level of cortisol being a function of the radiocesium concentration in the organism. The modifications in cortisol production are especially noticeable for the neonates, their mothers having accumulated considerable Cs-137 concentration in the organisms (mainly in the placenta) (Fig 2.19). These children are famous for their ill-adaptation

to the intrauterine existence. The effect is seen in rats whose mothers were fed Caesium 137 (Figs 2.19, 2.20).
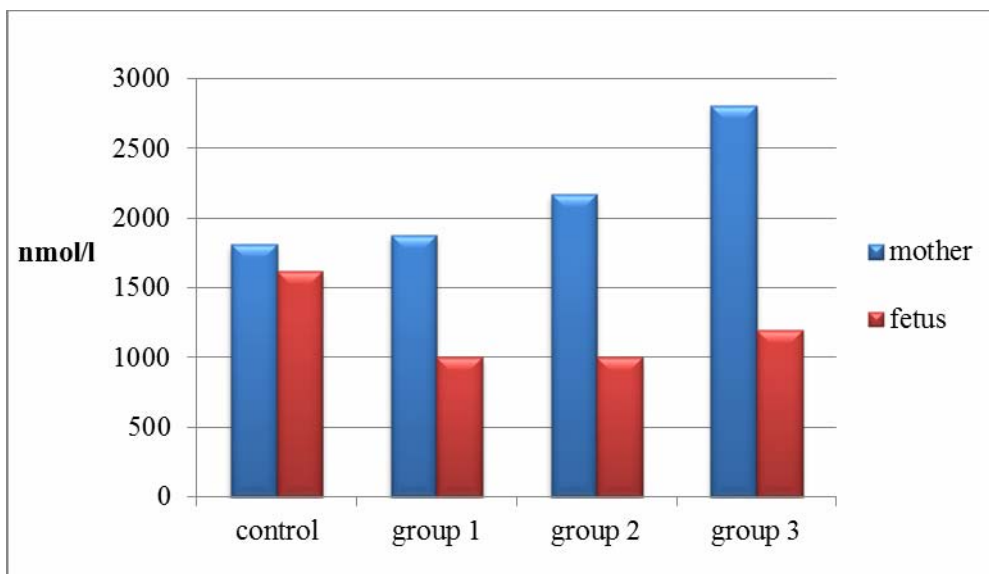
Key: Cs-137 concentration in placenta: Group 1 – 1-99 Bq/kg; Group 2 – 100-199 Bq/kg; Group 3 – >200 Bq/kg.

Figure 2.19 - *Cortisone concentration in mother and foetus blood in control and test groups*

Pathology of the female reproductive system is a product of the violation of endocrine functions. Radiocesium is also responsible for the imbalance in the progesterone-estrogen with women of fertile age in different phases of the oestral cycle, and this is a key factor for the infertility. Radiocesium incorporation in placenta and other endocrine organs during pregnancy gives rise to hormone disorders both in the mother organism and foetus. In particular, the Cs-137 concentration rising, the testosterone contents increases as well as the thyroid hormones and cortisol in blood. Distortion of hormone statues in the mother-foetus system due to radiocesium leads to extended pregnancy time and childbirth and postnatal child evolution complications. In case of natural feeding, radiocesium penetrates the child's organism. Thus, the mother's organism purifies itself, while that of a child's becomes Cs-137 contaminated. Many systems being formed in this period, radiocesium has an extremely negative effect upon the child's organism. The nervous system is the first to respond to the radioisotopes incorporation. Cs-137 incorporation within 40-60 Bq/kg, which is due to the 28-days animals feeding with

oats, causes distinct imbalance of the biosynthesis of monoamines and neuroactive amino-acids in different compartments of the brain, in particular, in the cerebral hemispheres, which is characteristic of mean lethal and super lethal radiation doses. This is reflected in time of various vegetative disorders.

Fig 2.0 *Rat foetuses from mother fed Cs-137*

The increase of the cases of cataracts in schoolchildren living in the radio contaminated areas should also be mentioned – the frequency of detecting this pathology is like the other conditions found to be in direct relation to the quantity of Cs-137 radionuclides in the organism (Fig 2.21).
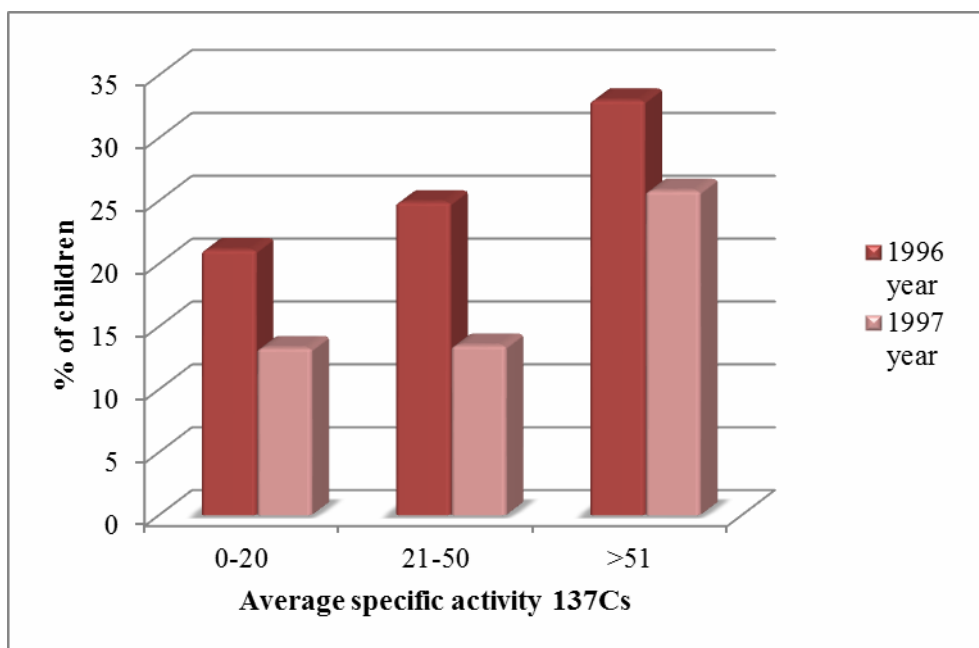
***Fig 2.21**- The dynamics of the increase of the cases of cataract in the children of Vetka district of Gomel region depending on the level of the average specific activity of Cs-137 (Bq/kg) in the organism (Yu.I. Bandazhevsky and co-authors, 1997, 1999)*

To summarise, the long-living radioisotope of Cs-137 affects a number of the vital organs and systems. As a result, highly differentiated cells are adversely affected, the process being dependent on the radiocesium concentration. The basis of the process lies in destruction of the energetic mechanism, leading to protein destruction. In this connection, the characteristic feature of the Cs-137 effect upon the human organism appears a depressed metabolic processes in the cells of vital organs and systems, due to the direct influence and the effects of the toxic tissues (nitrogen compounds) and violation of tissue growth due to the vascular system disorders.

The pathological modifications in the human and animals organisms caused by Cs-137 may be joined together into a syndrome which may be termed: "long-living incorporated radioisotopes". (SLIR). The syndrome appears in the cases of radiocesium incorporation in the organism (its degree being the function of the incorporation quantity and time) and the syndrome is characterized by the metabolism pathology, stipulated for the structural and functional modifications in the cardiovascular, nervous, endocrine, immune, reproductive, digestive, urinary excretion and hepatic system. The quantity of the radiocesium, inducing SLIR may vary, depending on age, sex and the functional condition of the organism. Children have been shown to have considerable pathological modifications in the organs and

systems with an incorporation level over 50 Bq/kg. Nevertheless, metabolic discomfort in the individual systems, primarily in the myocardium, has been registered with Cs-137 concentration amounting to 10 Bq/kg.

Conclusions

Twenty three years after the accident at the Chernobyl nuclear power plant, the inhabitants of the Republic of Belarus, living in the territory contaminated by radioactive elements and consuming these radionuclides for a long time, run the risk of the incidence by cardiovascular diseases and malignant neoplasms. The steady rise of this pathology within 23 years after the accident has led to a situation that is close to a demographic catastrophe when a death-rate of the population has begun to exceed a birth-rate by a factor of two times. The current situation requires the immediate decisions at State and international levels directed at the solution of the problem – protecting the state of health of the citizens living in the territories affected by the accident at the Chernobyl.

[1] (Marey A.N. and co-authors, 1974; Rusyayev A.P. and co-authors, 1974; Ternov V.I., Gurskaya N.V., 1974).

3

Bystander effects and genomic instability Part 1: From the gene to the stream

Prof. Carmel Mothershill, Prof. Colin Seymour
McMaster University, Hamilton, Ontario, Canada

Editors Note:

Prof Motherhill gave a powerpoint presentation and also later on a paper. Since the presentations and remarks at the conference were so interesting we reproduce the elements of the presentation as Part I and following this as the paper in Part 2

I will present our recent research on the phenomena known as **genomic instability** and the **bystander effect**. Many scientists now refer to these areas as Non Targeted Effects NTE. I will consider some aspects and findings relating to Non Targeted Effects:

- The fish model

- Case studies

- Serotonin

- DNA repair

- Legacy/ delayed effects

- Multiple stressors

- Implications

- Ecological

- Evolutionary

The old view of the introduction of genetic damage into somatic cells to cause cancer and other effects was that there was a fixed mutation, a hit, and this expanded through the normal replication of the cell to increase the number of descendants carrying this mutation. This was called the clonal expansion theory.

We now believe that this is not an important process and that genomic damage is introduced by a different mechanism (Fig 3.1).

Old view- clonal

Hit

New view-non-clonal, population-determined outcome

?Hit
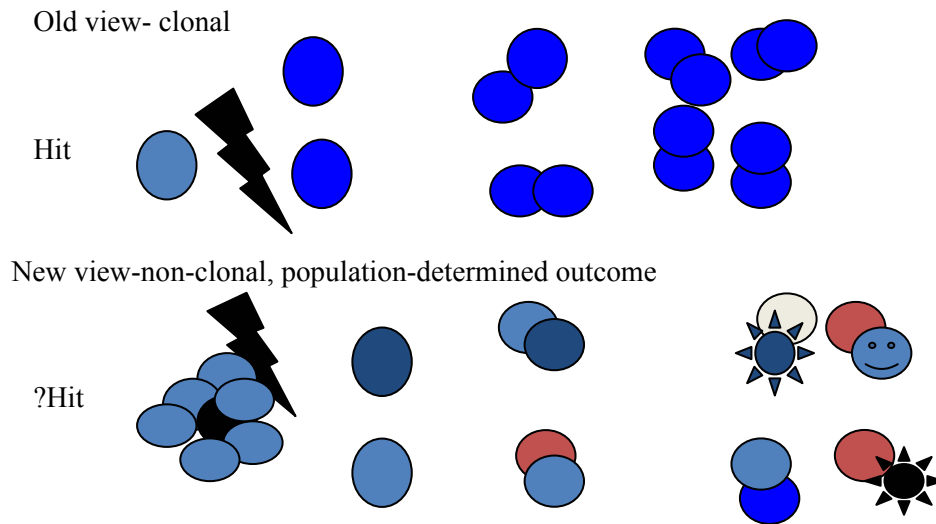
Fig 3.1 *The link between bystander effects and delayed instability*

Genomic instability and bystander effects are linked mechanistically. They occur even at very low doses (fully saturated at 5mGy acute dose), and are inducible in vivo and in a wide range of species (fish, crustaceans, molluscs as well as mammals). The effects are perpetuated in the progeny of those afflicted, and alter the chemical uptakes in the bodies. They are detectable by many different endpoint measures, including death, survival, proliferation mutation and transformation.

I will present some examples.

First, in Fig 3.2 we see that lymphocytes from Chernobyl affected populations demonstrate damage 20 years after the exposures.
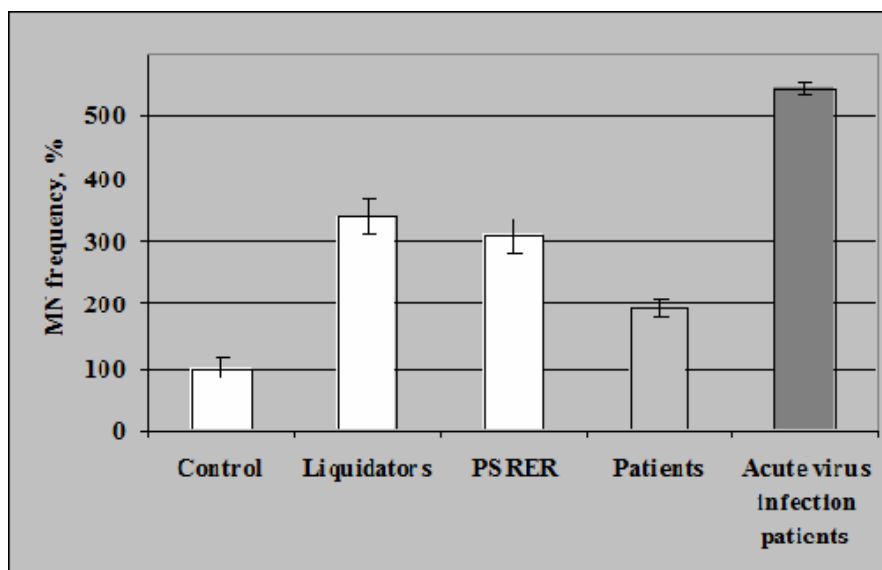
Fig 3.2 – *Damage in lymphocytes from Chernobyl populations 20 years after the accident*

Another example comes from experiments with mice. Mitochondrial membrane depolarisation effects are shown in Fig 3.6. Below (Fig 3.3 and 3.4) can be seen depolarisation effects in a medium from unirradiated and irradiated tissues from two strains of mice. In one (apoptosis prone) damaged cells commit suicide. In the other (cancer prone) a signal is initiated which promotes genomic instability.
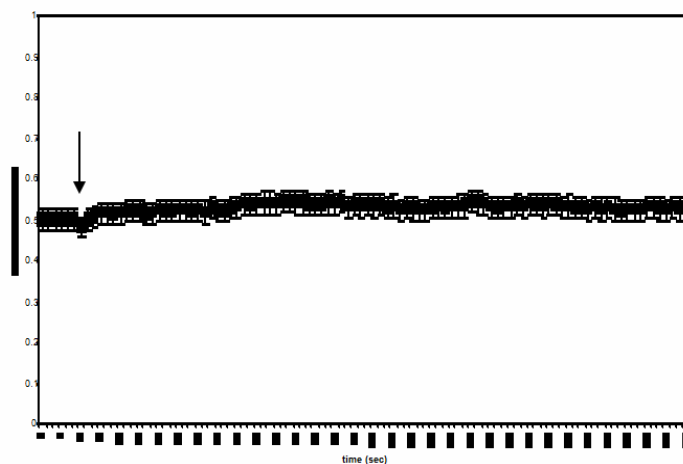
Fig 3.3 C57BL/6 apoptosis prone
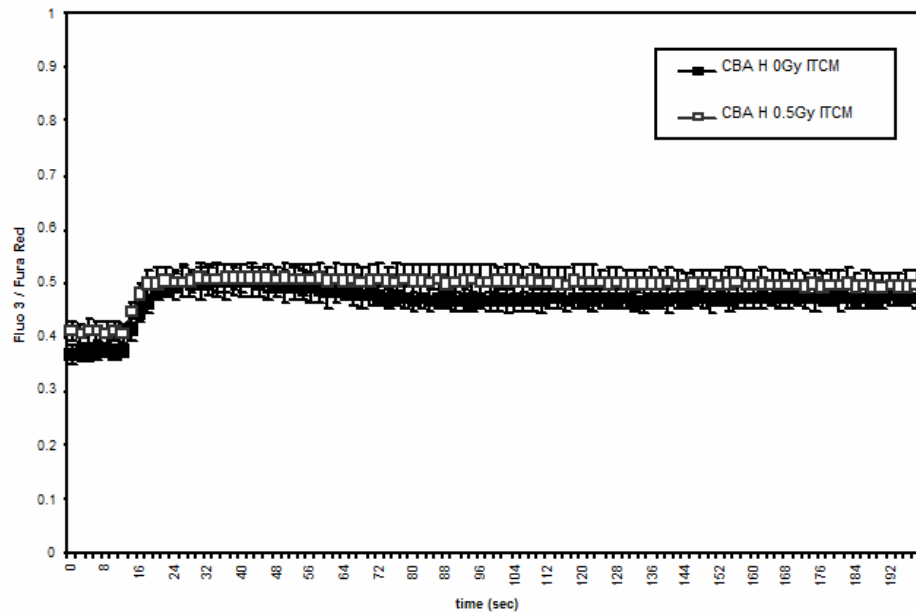
Fig 3. 4 *CBA/Ca cancer prone*
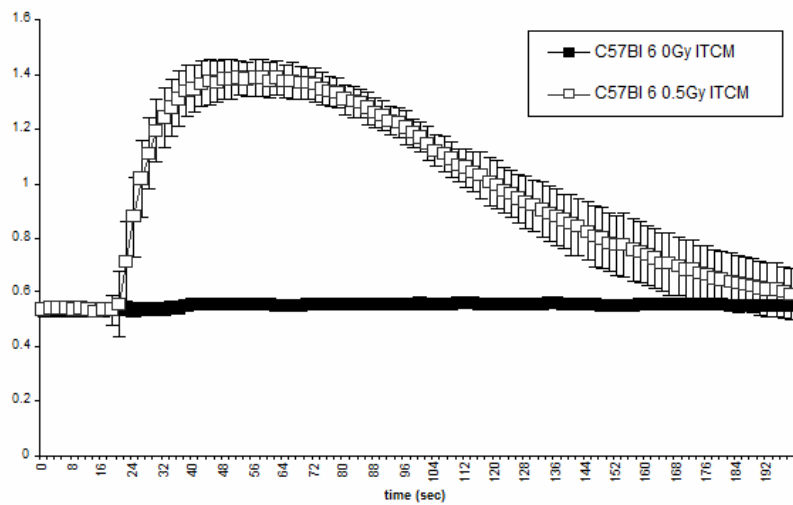
Fig 3.5 C57 *Apoptosis prone*
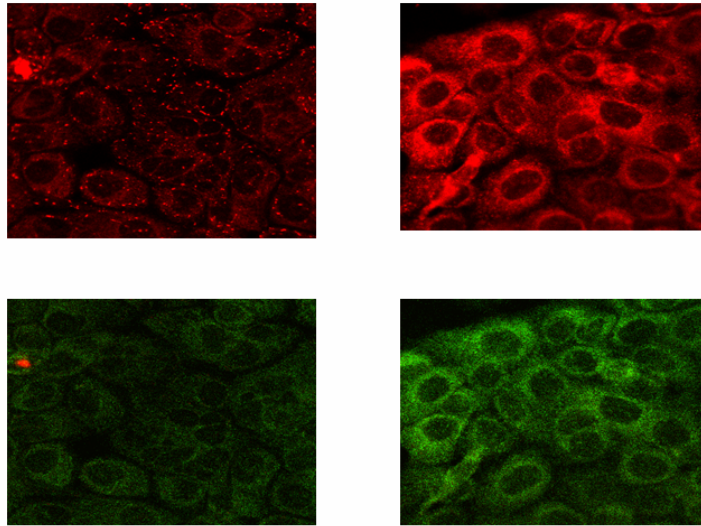
Fig 3.6 *Mitochondrial membrane depolarisation*
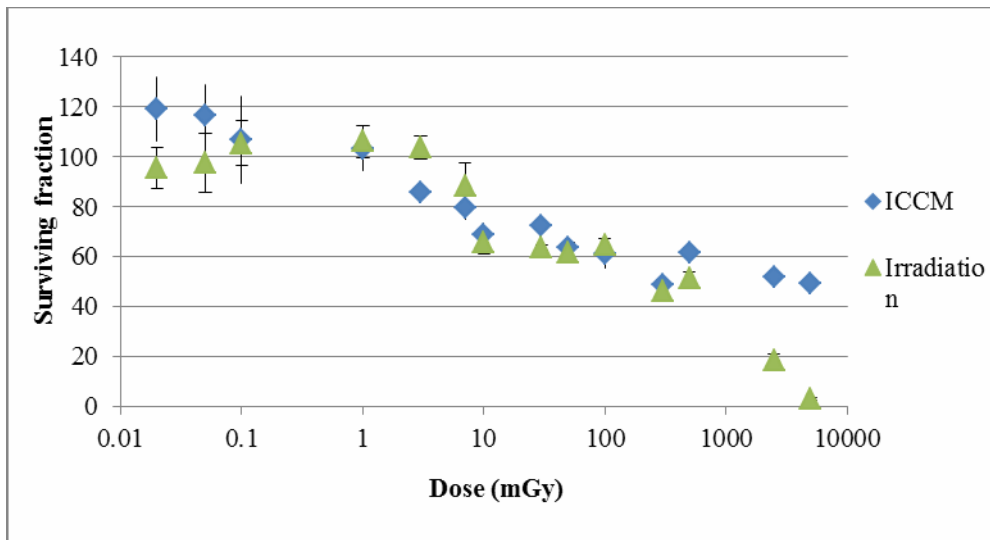
Fig 3.7 *Bystander and direct dose survival curves over six orders of magnitude ^{60}Co with calcium data*
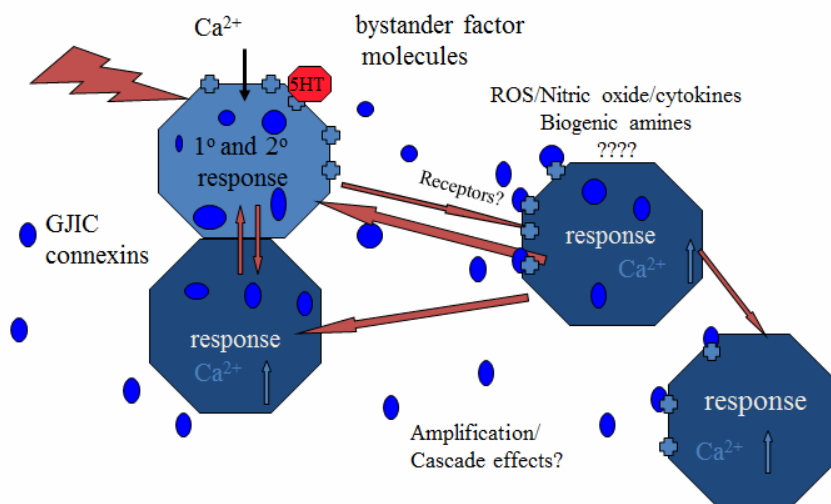
Fig 3.8 *The bystander effect*

It is clear from these findings that a number of questions must be asked. Firstly, can we see Non Targeted Effects in other species and can we see them at environmentally relevant exposures? Is it possible to see evidence of trans-generational effects or mixed exposure effects and finally if so what are the likely impacts and how do we deal with them?
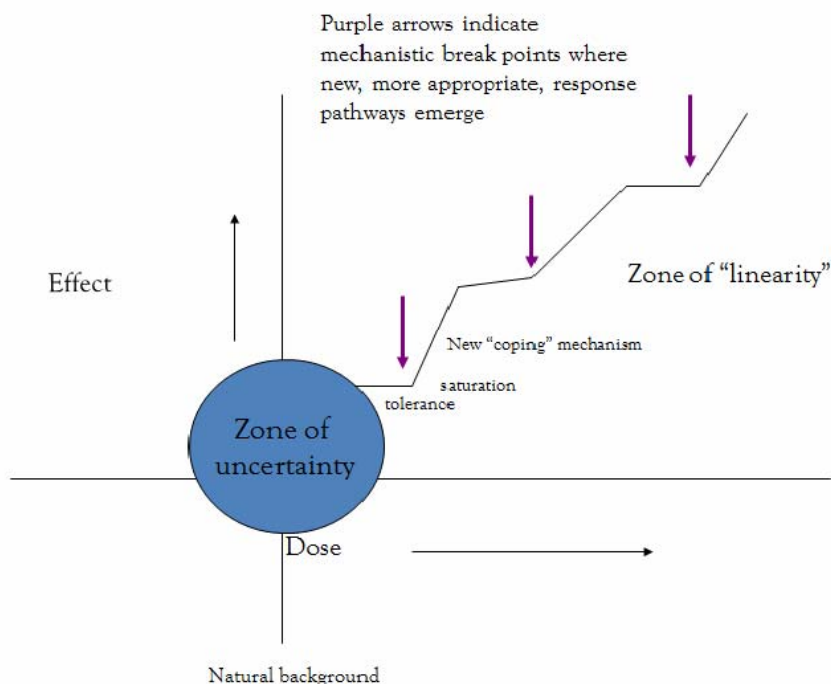
Fig 3.9 *Proposed dose response relationship for radiation induced biological effects*

Fundamentally, we must ask if low doses are less or more dangerous than an LNT model extrapolation would predict from high doses?

- Less adaptive response/selection

- Induced repair/tolerance

- More

- GI and bystander effects

An *in-vivo* explant model for mechanistic studies can be established. All tissues that we have so far tried to date from humans, rodents, fish, frogs, molluscs and prawns have yielded viable growing cells capable of producing and responding to bystander signals, expressing relevant proteins after irradiation and showing apoptosis and necrosis. This differentiation in 2D can also be seen.
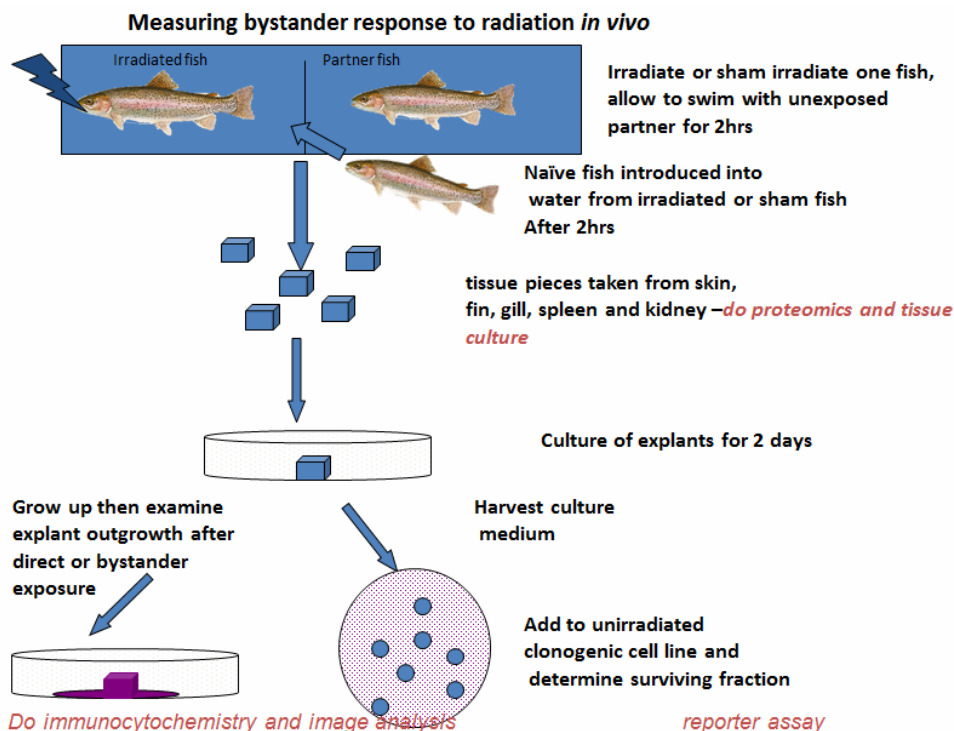
Fig 3.10 *Bystander response in vivo*

When these studies were carried out, a number of results pertain. The bystander effect was induced in three species of fish exposed to irradiated fish/or their water – modeling an evolutionary conserved mechanism. An attenuation of signal was only seen after the fish were removed for six hours from the water and live fish continue to emit signal for over twelve hours: **a stable water soluble signal**. The chronically exposed Medaka confer an adaptive response on reported cells: **The chronic radiation effect is different to an acute effect**. Multiple stressors appear to have sub-additive effects: this suggests **a saturable or antagonistic mechanism.** Bystander proteome and direct irradiation proteome lead to very different results – very important for understanding potential risk outcomes. The effect can be demonstrated in trout as early as the eyed egg stage and is still there in retested adults two years on: **it is a persistent effect once induced.** Finally, serotonin is involved in vivo and in vitro in fish and mammalian cells: **a conserved mechanism.**
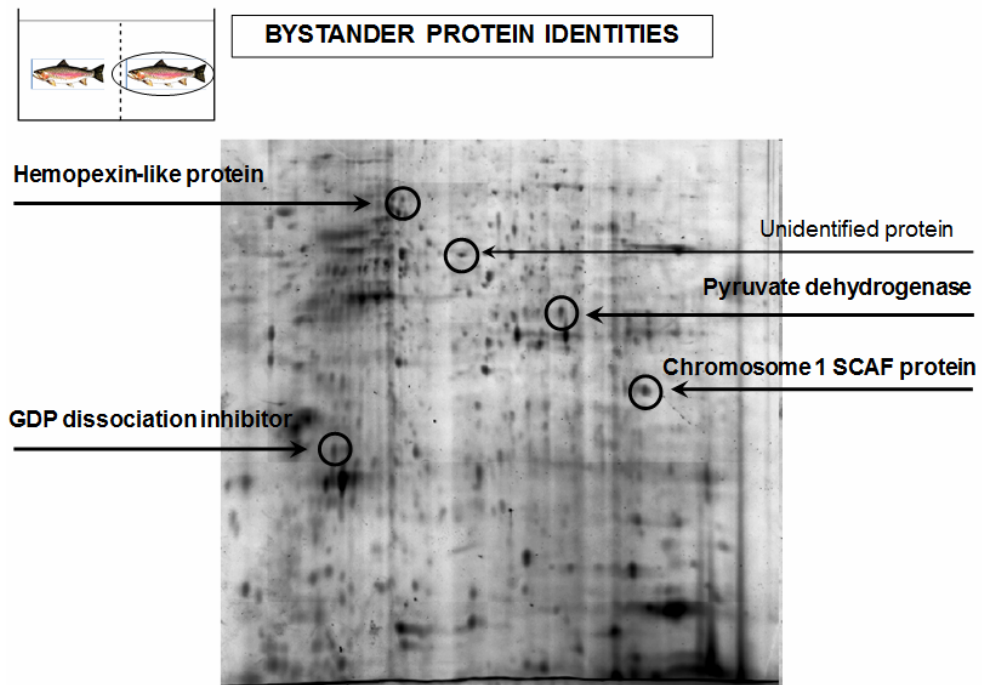
Fig 3. 11 *Bystander protein identities*

Fig 3.12 Proteomic responses to the bystander effect

Serotonin and DNA repair are critical factors in vivo and in vitro. DNA repairs deficient cell lines and transgenic Medaka both produce highly toxic bystander signals after low dose irradiation.
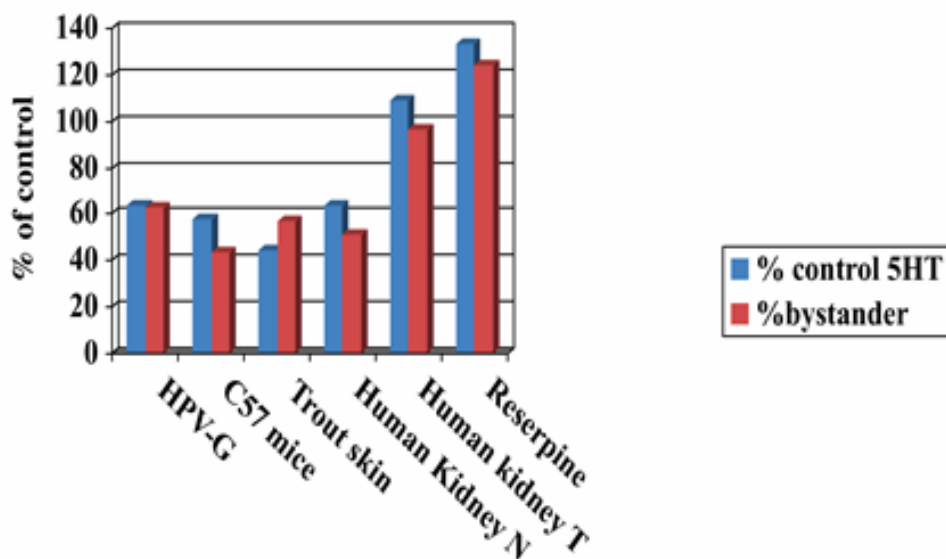
Fig 3.13 *Serotonin bound by irradiated cells in vitro, leading to calcium pulse*
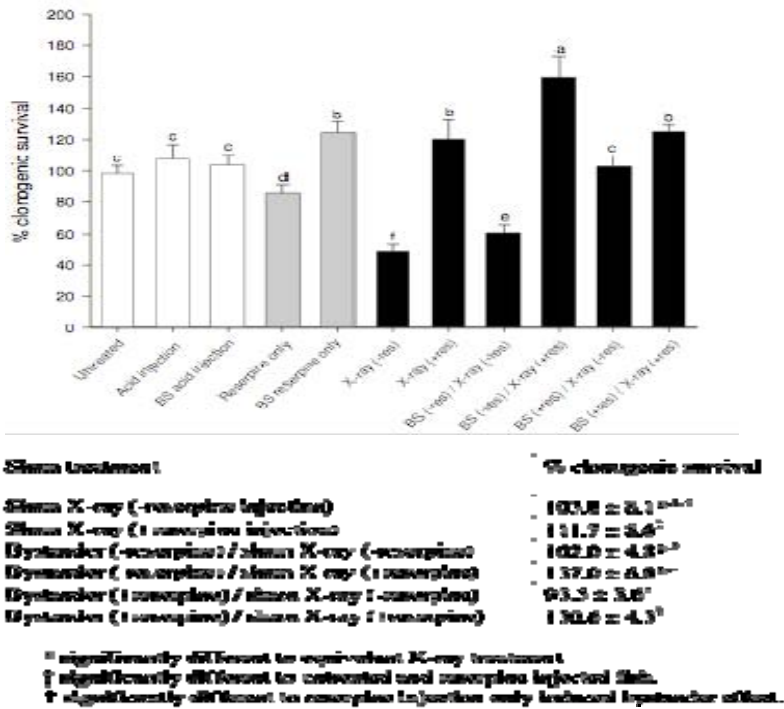
Fig.3. 14 *Reserpine inhibits bystander effect in vitro and in vivo*
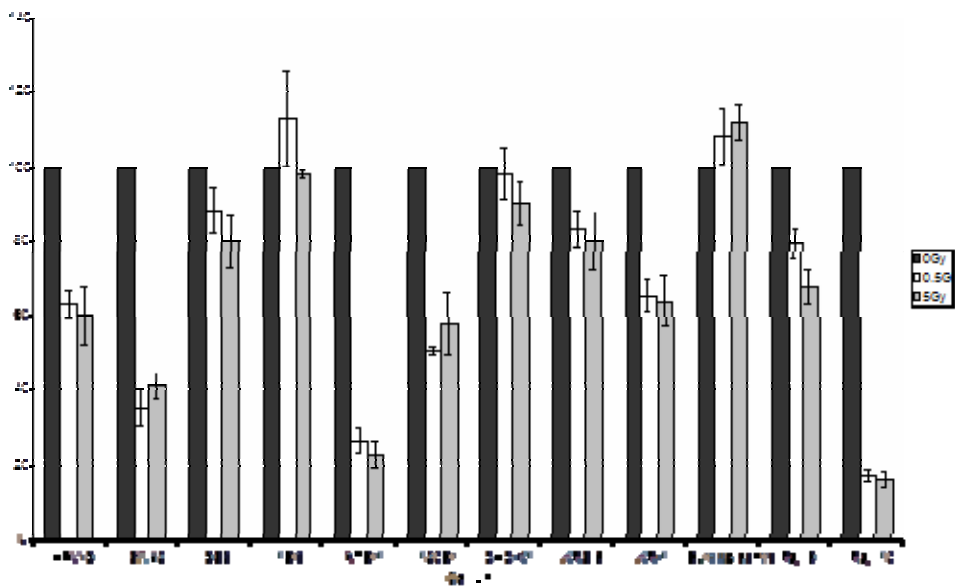
Fig. 3.15 - *Reduced reproductive survival in vitro*
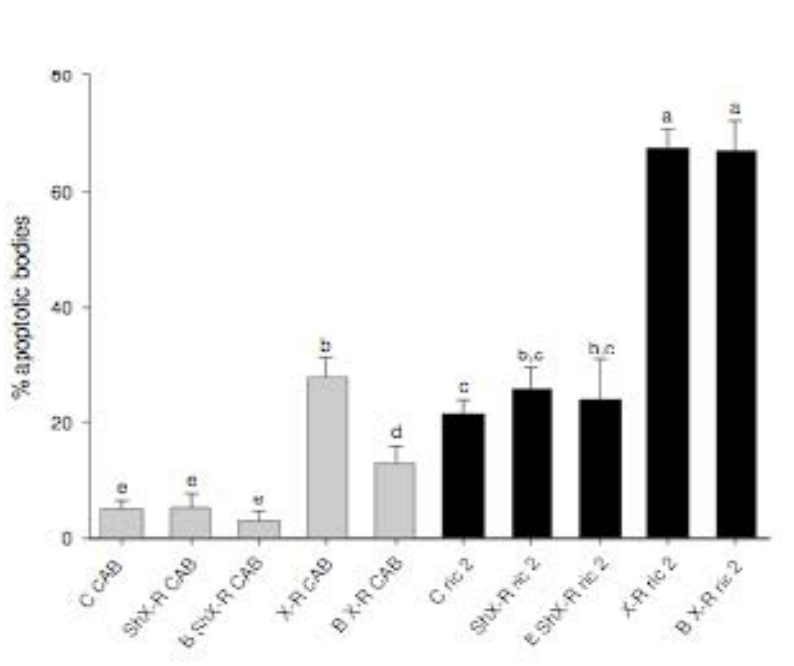
Fig 3.16 - *Increased apoptosis in vivo*
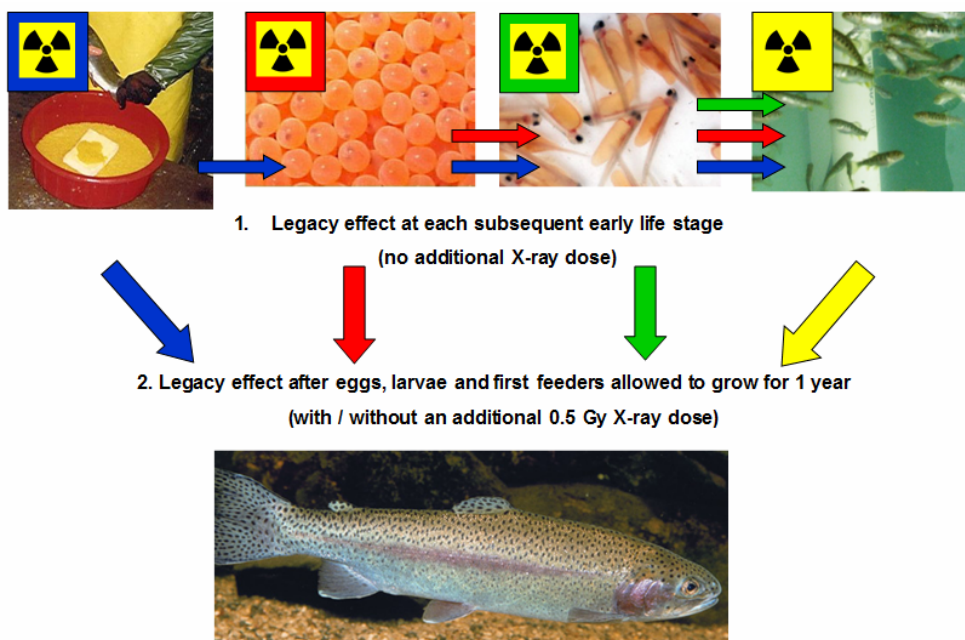
Fig 3.17 *Legacy of early life stage irradiation*

From eyed egg onwards rainbow trout are affected by a 0.5 Gy X-ray dose and an X-ray induced bystander effect. Exposure of the egg, larvae and first feeding stages results in a legacy of these effects which extends to 1 year old fish. The natures of these responses (pro- / anti- apoptotic) are dependent on when the radiation dose was administered. We propose these results have implications for the radiological protection of the aquatic environment
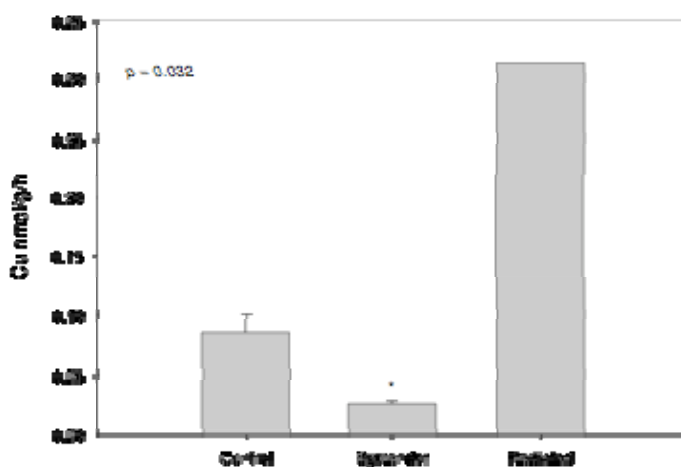
Fig 3.18 *Legacy effects on copper uptake: Fish exposed to 5mGy acute dose in November 2006 as juveniles*
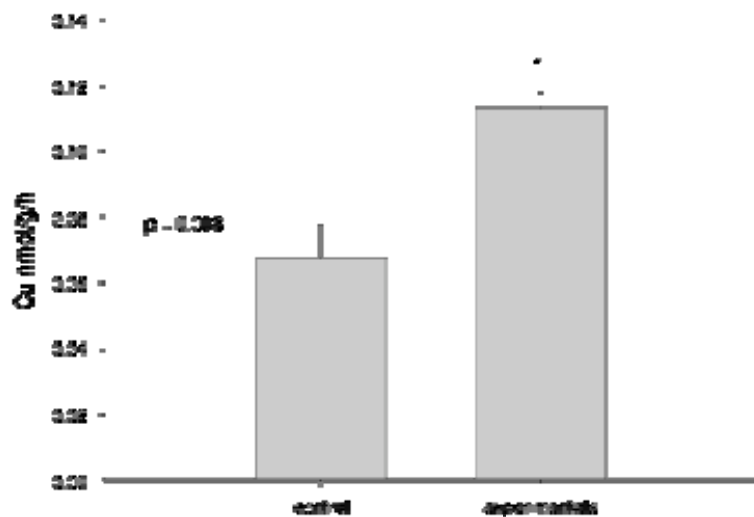
Fig 3.19 *Legacy effect of 5mGy 2 years ago at egg stage on copper uptake today*
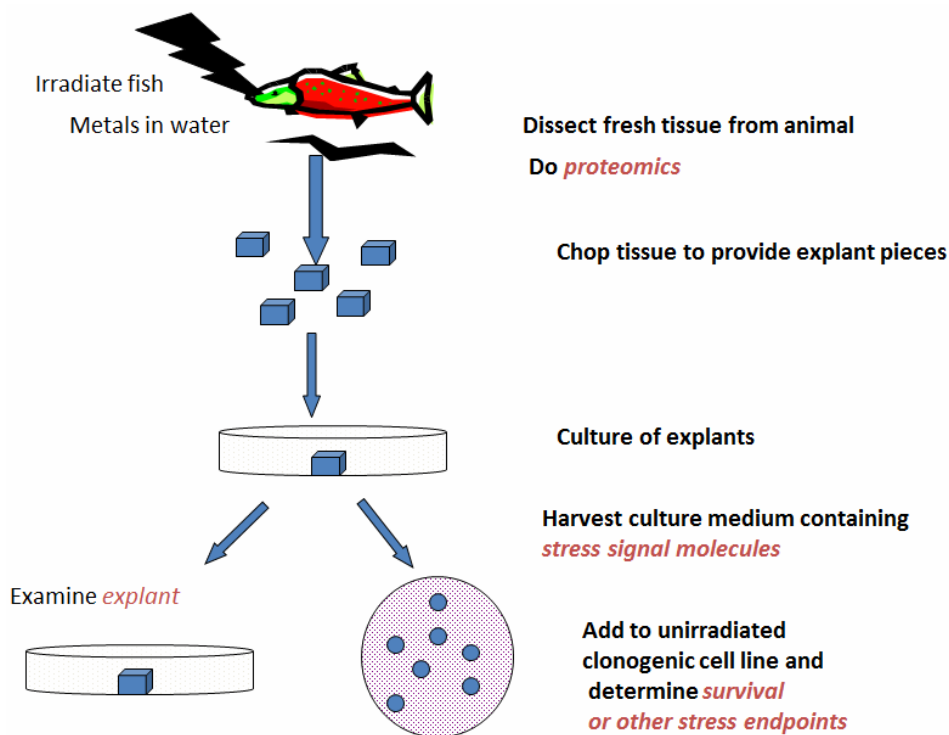
Fig 3.20 *Measuring radiation induced multiple stressor response in vivo*

A number of multiple stressor fish experiments were carried out (with Norwegian collaboration). They offered the conclusion that stress (bystander) signals are produced in vivo by salmonids in response to acute or chronic low doses of radiation (4-75mGy), and that Al, Cu and Cd all show complex effects when combined with low doses of radiation (4-75mGy). Furthermore, tissue specific differences are seen with gills being more sensitive than skin.
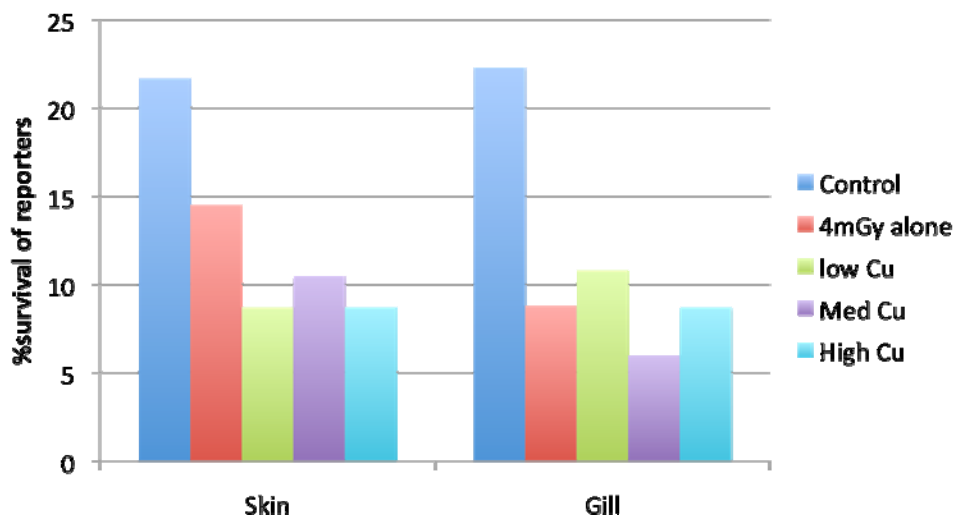
Fig 3.21 *Effect of 4mGy radiation in the presence of copper ions on bystander signaling*

But what about some more complex scenarios? Radiation induces a cell to undergo apoptosis, removing it from the potentially carcinogenic pool. Substance 2 (eg Cd) interferes with the signaling cascade and the cell lives – survival assay suggests that there is a protective effect to the interaction. If radiation induces an adaptive response in population A, a further stressor has little effect but a pristine population B with no adaption is devastated by the same stressor. This effect is clear, but it is our response to it that is flawed. Our current approach to risk assessment is dose driven, mono-agent and mainly mutation centered, and does not and cannot accommodate much of the low dose exposure data available for radiation or chemical pollutants. We need an effect (or no effect) driven risk assessment with careful regard to predictive value of our chosen reporters. We must learn to extrapolate: from effect to harm, harm to risk, individual risk to population risk and from population risk to ecosystem risk. We must learn how to regulate with an acceptance of uncertainty. However, more than this, there are issues with radiation protection studies such as these. Endpoint assays are usually snapshots at best and we need lifetime studies and a mechanistic understanding and modeling of factors in order to develop a more holistic understanding. This will allow us to validate these endpoints across time, and understand the effects of multiple stressors. The new non-targeted effects field suggests that low dose effects can fluctuate – so how do we live with and regulate in an environment of uncertainty? We must refuse our initial desire to cry "no effect", but ask "what effect" and "is it important?".

I finish with a final plea: we must realize that biodiversity (not only of biota) is important because we do not fully understand the mechanisms by which stress and evolution combine to produce new adaptations.

4

Part 2: Human and Environmental Health Effects of low doses of radiation

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Abstract

The last 15 years have seen a major paradigm shift in radiation biology. Several discoveries challenge the DNA centric view which holds that DNA damage is the critical effect of radiation irrespective of dose. This theory leads to the assumption that dose and effect are simply linked – the more energy deposition, the more DNA damage and the greater the biological effect. This is embodied in radiation protection (RP) regulations as the linear-non-threshold (LNT) model. However the science underlying the LNT model is being challenged particularly in relation to the environment because it is now clear that at low doses of concern in RP, cells, tissues and organisms respond to radiation by inducing responses which are not predictable by dose. These include adaptive responses, bystander effects, genomic instability and low dose hypersensitivity and are commonly described as *stress* responses, while recognizing that "stress" can be good as well as bad. The phenomena contribute to observed radiation responses and appear to be influenced by genetic, epigenetic and environmental factors, meaning that dose and response are not simply related. The question is whether our discovery of these phenomena means that we need to re-evaluate RP approaches.   The so called "non-targeted" mechanisms mean that low dose radiobiology is very complex and supra linear or hormetic responses are equally probable but their occurrence is unpredictable for a given individual. Issues which may need consideration are synergistic or antagonistic effects of other pollutants because RP at present only looks at radiation dose but the new radiobiology means that chemical or physical pollutants which interfere with tissue responses to low doses of radiation could critically modulate the predicted risk. Similarly, the "health" of the organism could determine the effect of a given low dose by enabling or disabling a critical response. These issues will be discussed.

What are "non-targeted" effects

Within conventional radiobiology as accepted in the 1950's continuing through to the 1990's there was little consideration of epigenetic effects, because the traditional concept of radiobiology was based on target theory (Timofeeff-Ressovky et al. 1935, Osborne et al. 2000). For an effect to occur, radiation had to hit a defined target within the cell, assumed to be DNA. Assumptions about the number of targets hit could then be made from measurements of dose and dose rate (Elkind and Whitmore 1967, Alper 1979). The evolution of non-targeted effect (NTE) radiobiology meant that at low doses the previous assumptions needed to be reconsidered in the light of the existence of non-DNA mechanisms (Morgan and Sowa 2006, Mothersill and Seymour 2006, Hei et al. 2008). The mechanisms underlying radiation effects are not constant with respect to dose and it would now be generally accepted that low dose effects are mechanistically different to high doses effects. This is not to say the mechanisms are necessarily mutually exclusive but it does mean that NTE's will contribute more to the overall outcome at low doses where targeted effects are small. Targeted effects will predominate at high doses and in situations where NTE's have been inhibited or otherwise prevented. In terms of the progression of radiobiological thinking in this field, disease caused by radiation no longer had to be exclusively genetically based, but radiation could promote or exacerbate systemic disease. This disease could have been caused for example by a chemical mutagen (Preston 2005, Baverstock and Rönkkö 2008, Gundy 2006). Equally, the radiation could facilitate a non-mutation based inflammatory type disease (Kusunoki and Hayashi 2008, Lorimore and Wright 2003, Manton et al. 2004, Little et al. 2008). These concepts, although largely accepted theoretically by the radiobiology community, have been difficult to prove epidemiologically because of what are generally called "confounding variables" such as smoking, drinking, age, gender, or concurrent past or future exposures to the same or a different pollutant (Sigurdson and Ron 2004, Prasad et al. 2004). These factors actually reflect the futility of trying to assign causation, as defined in epidemiology, to one agent when the doses are low! Others argue that radiation and many chemical "pollutants" might actually boost the immune system and be good (Calabrese and Baldwin 2000, Sakai 2006, Boonstra et al. 2005). The hormetic argument has many interesting applications but is unproven with regard to multiple pollutants. This adds to the confusion and controversy surrounding low dose

exposures. The essential point is that there will be huge individual variation due to involvement of epigenetic and non-targeted factors in the response (Wright and Coates 2006, Pinto and Howell 2007, Fike et al. 2007). At any one time we are as unique epigenetically as we are genetically. Epigenetic differences are linked to gender and lifestyle. In theory therefore a low dose of radiation could cause any number of effects ranging from beneficial to death-inducing disease depending on the context of the exposure and the interplay of factors such as cell communication, microenvironment, tissue infrastructure and a whole host of systemic variables which influence outcome from a cellular track of ionizing radiation (Wright 2007, Gault et al. 2007).

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Is radiation unique or is it one of many stressors??

Key developments leading to the current widespread acceptance of low doses of ionizing radiation as having similar mechanisms to other stressors include
(1) The development of sensitive techniques such as m-FISH, for detecting chromosomal abnormalities. (Pinkel et al. 1988, Speicher et al. 1996, Hande and Brenner et al. 2003, Edwards et al. 2005)
(2) Studies showing that delayed or persistent sub-optimal survival (reproductive death) could be seen in surviving progeny of irradiated cells. (Seymour et al, 1986, Mothersill and Seymour 1997, Stamato et al. 1987, Coates et al. 2005)
(3) The emergence of genomic instability as a mechanism by which low doses of radiation could cause delayed or persistent damage to chromosomes (Kadhim et al. 1992, Little and Nagasawa 1992, Marder and Morgan 1993, Ponniaya et al. 1997, Watson et al. 1997).
(3) The accumulation of knowledge of "bystander effects" whereby chromosome damage, death, DNA damage and various other consequences occur in cells receiving signals from cells irradiated with low doses of radiation (Hei 2004, Lorimore et al. 1998, Brenner et al. 2001, Schettino et al. 2005, Weber et al. 2005, Lui et al. 2006).
(4). Criticism of the epidemiological research undertaken after the Hiroshima and Nagasaki bombs as ignoring the damage from residual radiation and fall out (Sawada 2007, Mossman 2001).
The NTE paradigm emerged initially as a result of re examination of firmly held beliefs and some odd results in the laboratory which did not fit the DNA paradigm. Proof of the new hypotheses required the techniques such as molecular imaging, M-

FISH, and SKY as well as the development of tissue culture techniques for human *normal* tissues which permitted functional studies to be performed (Freshney 2005). Older studies tended to use high doses on a limited number of cell lines or highly inbred animal strains. These tended to thrive in the laboratory but were often unrepresentative of tissues in the outbred human or non-human (Elkind 1988, Hornsey et al. 1975, Alper 1973).

Important consequences for radiation protection and risk assessment: of newly discovered low dose effects

1. Life is organized in hierarchies of organisation

Hierarchical levels stretch from the individual "down" (organs – tissues – cells – organelles –genes) and "up" to populations (multiples individuals/ single species (multiples species – ecosystems). Confusion in the low dose exposure field (both radiation and chemical) arise from lack of consideration of this concept. Most of the arguments about whether radiation is "good" or "bad" fail due to lack of consideration of the level at which the effects occur and because most of the arguments are really only able to rely on human cancer incidence or deaths for data. For example cell death is seen as a "bad" effect but if it removes a potentially carcinogenic cell from the population of cells in a tissue it could prevent cancer starting and could be seen as "good". Survival of cells is seen sometimes as "good" but if they survive with unrepaired or wrongly repaired damage, they could start or facilitate development of a cancer. Similarly in the non-human populations – death of radiosensitive individuals which cannot adapt to the changed (now radioactive/chemically polluted) environment, could be "good" for the population in evolutionary terms depending on the life stage and reproductive status when the effects manifest, although death will always be "bad" for the individual. It is only by considering responses in context, that any conclusions can be drawn about risk or harm.

2. Concepts related to time and space

There are two aspects to this – one is simply, the age of the organism at the time of irradiation and the deposition pattern of the ionizing energy (its linear energy transfer or LET). This concept is relevant across all hierarchical levels. Obvious considerations are the age or maturity of the individual entity which gets irradiated,

the density of the energy deposition, the lifetime of the entity and its importance in the context of functionality of the higher hierarchical levels. Young entities are usually less stable and more vulnerable (or more adaptive?) than old entities because of their faster metabolic rate, higher rate of growth/cell division and at the ecosystem level, because of their less strongly developed interdependencies. There is also more capacity to absorb change in young entities, for example there are more available individuals, better reproductive rates and better viability from young parents , whether cells or organisms. The other aspect is that the delayed effects of radiation and bystander effects mean that radiation effects are not fixed in time or space to the energy deposition along ionizing track. The effects can persist and manifest at distant points in time and space. These concepts are also discussed elsewhere (Preston 2005, Baverstock and Rönkkö 2008).

3. The importance of mixed exposure analysis

Pollutants including radiation seldom occur in isolation. In fact most environmental radioactivity comes from radioisotopes which are chemical entities. This means that there is always a mixed exposure and that both the chemical and radioactive aspects need to be considered. Additive damage used to be an acceptable way to deal with mixed exposures (if any were used!). The new field of non-targeted effects with the consequent realization that emergent properties can exist, which were not predictable from the individual agent dose response data, makes this no longer acceptable. The complexities of mixed pollutant scenarios call for a re-think of fundamental approaches to both epidemiological causation after low dose exposures to anything. They also question the need regulators have to regulate to a number (dose unit/exposure unit). Some of the issues concerning the latter position include the following:

- How to ensure compliance if there is no "safe" or legal limit?
- How to deal with multiple stressors especially if the interactions are not known?
- How to correct for dose rate/ time of exposure? – DDREF values are clearly not effective.
- How to deal with mixed chronic and acute exposures?
- How to factor in possible hormetic, adaptive, or antagonistic effects?
- How to regulate in pristine versus dirty environments?

The issues of legal causation are highly relevant to the former point but outside the scope of this review. Discussion of these issues can be found elsewhere (Masse 2000, González 2005, Miller 2006). Ultimately, in order to resolve these issues, more data are needed for mixed exposure senarios using relevant species. Systems biology approaches involving close interaction between experimental biologists and modellers are also required.

Data concerning low dose effects of multiple stressors

There are very little data where low dose exposures to multiple stressors/mixed contaminants involving radiation and a chemical are investigated. The field was reviewed by Mothersill et al. (Mothersill et al. 2006). Recent interest in non-targeted effects probably means more attention will be paid to this area in future. Gowans et al. (Gowans et al. 2005) have data showing chemical induction of genomic instability. Data from the authors' own and other laboratories shows that heavy metals singly or in combination can cause genomic instability (Grygoryev et al. 2008, Bagwell et al. 2008, Mothersill et al. 1998, Dowling et al. 2005, Dowling and Mothersill 2001, Ní Shúilleabháin et al. 2006, Dowling and Mothersill 1999, Mothersill et al. 2001, Lyng et al. 2004, Glaviano et al. 2006, Glaviano et al. 2009, Coen et al. 2003, Coen et al. 2001). Delayed death and chromosome aberrations in human cells following nickel, titanium or cadmium exposure have been reported (Glaviano et al. 2006, Glaviano et al. 2009, Coen et al. 2003, Coen et al. 2001). Similar effects have been reported in fish cell lines [Dowling et al. 2005, Dowling and Mothersill 2001, Ní Shúilleabháin et al. 2006, Dowling and Mothersill 1999, Mothersill et al. 2001, Lyng et al. 2004], and more recently in live fish exposed to very low doses of gamma radiation 4-75mGy over 48hrs in the presence of heavy metals at levels just above background (Salbu et al. 2008, Mothersill et al. 2007).
Organic pesticides and detergents such as prochloras, nonoylphenol, nonoxynol and dichloroaniline have also been found to cause delayed lethal mutations in fish cells (Mothersill et al. 1998, Dowling et al. 2005, Dowling and Mothersill 1999).
Chromium and vanadium used in implants and dentures lead to a variety of genetic and reproductive delayed effects in vivo and to multiple endpoints associated with non-targeted effects in vitro (Glaviano et al. 2006, Glaviano et al. 2009, Coen et al. 2003, Coen et al. 2001).

What does this mean for environmental protection and human health?

While many of the studies cited above are concerned with fish rather than humans, the data show that non-targeted effects can be induced by low dose exposures to a number of environmental chemicals as well as ionizing radiation. This means that combined exposures to low doses of these agents cannot be regulated in isolation and that studies of potential mechanistic interactions are important. Radiation protection of humans could find use from the approaches which are being taken by the task groups within ICRP, IAEA and the US-DoE (see for example ICRP Publication 91, ICRP Publication 103 2009) who have to formulate policy to regulate exposure of non-human biota. Many of the issues involved such as dealing with non-cancer endpoints, mixed contaminants or chronic low dose exposure are real issues in human radiation protection.

Conclusions and summary

The challenge in the low dose exposure field is to tease out the "noise". Noise is the euphemistic term we use when the level of the disease which is un-attributable to our favoured causative agent, is too high to prove causation formally in any strict scientific or legal sense. Perhaps we should accept that we cannot assign causation and instead view ionizing radiation as one among many agents which *together* contribute to cause disease. Before we can do this it is vital to understand the key mechanisms and in particular to find areas of mechanistic commonality suggesting common causation. Biomarkers may be useful to identify possible common mechanisms and to validate their relevance across different hierarchical levels. If this is achieved it should be possible to model links between *effects* at one level e.g. cellular or individual leading to *harm and risk* at higher levels – in this example the individual or the population. Biomarker studies do need to be interpreted cautiously however because they are often used as surrogates for risk when in fact they may merely be pointing to change in the system. Without the back-up modeling and multi-level analysis of their relevance they may lead to false conclusions and confusion about the true risk of an inducing agent.

The problem of establishing causation following mixed exposures remains along with the issue of what constitutes "harm". In the non-human biota field, there is great concern about doing more harm than good, if action levels are enforced which might require "remediation" of a habitat – i.e. removal of contaminated

vegetation and soil. This could cause much more harm to the ecosystem than the original stressor. In the realm of human protection against low dose stressors, issues might include the ethics of genetic screening to identify sensitive sub-populations. If a sensitivity marker were available, who should be tested and when? Should diagnostic screening be forbidden to these individuals because of their possible sensitivity to low doses of radiation? There are also issues regarding lifestyle choices and risk benefit analysis at the biological level. Evolutionary adaptation leads to a fitter population (of cells, individuals) by eliminating the weak units but how is that population changed?

It would be nice to conclude this paper with a "way forward" but as we are still in the very early stages of accepting that radiation doses effects at low doses are non-linear, that multiple stressors impact the final outcome, and that what appears to be bad (or good) may be good (or bad)– it is perhaps best to recommend caution and consideration of these points rather than changing the regulatory framework!

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How reliable are the dose estimates of UNSCEAR for populations contaminated by Chernobyl fallout? A comparison of results by physical reconstruction and biological dosimetry.

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According to the United Nations Committee on the Scientific Effects of Atomic Radiation UNSCEAR which is adopted by the World Health Organisation WHO in evaluating the sequels of the Chernobyl accident the average dose of the population in the contaminated regions was very low – except for the thyroid in the nearby countries. The main contributions for the other tissues are thought to be generated – externally and internally – by the cesium isotopes 137 and 134. Relevant nuclides for the exposure as Sr-90 and Pu-239 are assumed to be negligible in distances greater than 100 km from the plant. Even for highly contaminated regions outside the evacuation zone where more than 37 kBq/m^2 of Cs-237 surface activity were measured the mean effective dose was estimated to only about 10 mSv. For the neigbouring country of Turkey und the Central European countries in greater distances the estimated exposures remain below 1.2 mSv (effective dose).

These results are in contradiction to findings by biological dosimetry. Several research groups investigated radiation-specific cytogenetic alterations in the lymphocytes of persons in the contaminated regions directly after the accident or some years later. The majority of studies revealed that the rate of unstable and stable chromosome aberrations is much higher – by up to about 1 to 2 orders of magnitude – as would be expected if the physically derived exposures were correct. A further finding was the occurrence of multiaberrant cells which indicate a relevant contribution of incorporated alpha activity. Emitted nuclear fuel and breeding products should therefore be considered in the physical dose calculations.

Introduction

Many observations about cancer and other radiation effects in the populations affected by Chernobyl fallout are denied by UNSCEAR and other international committees refering to the very low exposures which were derived by physical considerations. It is therefore important to realize that numerous reports in the literature show different results. The authors base their estimates either on own calculations or on EPR measurements in teeth or on cytogenetic studies which have been applied for the purpose of biological dosimetry.

We have compiled data about radiation-induced chromosome aberrations because they allow an assessment whether the physically derived value will grossly underestimate the true exposure. Some thousand persons have been investigated in the contaminated regions by cytogenetic methods who can be considered as random sample of the population living there. For such comparison, we prefer the results about dicentric chromosomes in the lymphocytes together with centric rings. These aberrations can be regarded as radiation-specific (Hoffmann and Schmitz-Feuerhake 1999).

Dicentric chromosomes are used as biological dosimeter since decades (Fig.1). They are instable, i.e., they leave the system with half-lives of about 1.5 years. The reason is that they fail to undergo a division in about 50 % of cases because of the two centromers. The advantage is, however, that the background rate remains low. Further, the background rate is almost constant over the world (only about 4 dicentric chromosomes in 10.000 metaphases of adults, 1 in 100.000 of children). Therefore, the method is very sensitive. The doubling dose is about 10 mSv for an acute and homogeneous whole body exposure. But even this method would show no significant elevation in a population if the average additional dose does not exceed a few mSv.

Centric rings (cr) are usually counted together with the dicentric chromosomes (dic). They are originated by the same primary mechanism. They undergo division without loss and thus they are stable, but they are generated less frequently (only 10% in comparison to dic). Sometimes, it is therefore possible to derive from the relation between cr and dic that the exposure occurred far back in the past.

The application of dose-effect relationships for chromosome aberrations demands an homogeneous whole body exposure which is usually not fulfilled in the case of incorporated radioactivity. The element cesium is, however, considered to distribute homogeneously in the body. Therefore, if the exposure is mainly generated by Cs

134 and Cs 137 – externally and internally – as claimed by UNSCEAR, the method can be used to decide whether the calculated dose values are realistic.

Another important information is given by the distribution of the aberrations among the cells. For low doses, a low LET radiation (gamma, x-rays) leads to a Poissonian distribution of the dic, i.e., there is usually only one dic per cell. If an overdispersion appears, i.e., a clustering of dic and/or multiple aberrations in a cell, it is an indication for densely ionizing radiation.

Fig.5.1 *Dicentric chromosomes (black arrows) in a human metaphase and associated acentric fragments after high dose exposure (from Fritz-Niggli 1997)*

We refer also to results of the studies about reciprocal translocations in lymphocytes (visualized by FISH) which are used to estimate the accumulated dose because these aberrations are also stable. The background rate is, however, highly variable and accumulating with age, therefore the sensitivity is not always sufficient to evaluate exposures by environmental radioactivity.

Chromosome aberration studies in evacuees

One day after the accident 45.000 inhabitants were evacuated from Prypiat, further 90.000 persons from the 30 km zone 7-9 days later (Imanaka and Koide 2000). The evacuation was finished 18 days after the accident. The evacuees were therefore exposed to very different degree. Among them acute radiation effects were registered by official report which means that whole body doses above 1 Sv have been reached.

A mean effective dose estimate for this population of 14 mSv is reported by UNSCEAR and WHO (UN 2005). The external dose alone was derived by Imanaka and Koide (2000) to 20-320 mSv. An estimate of Pröhl et al. (HP 2002) including the internal exposure lead to values for adults between 6 and 330 mSv and for the 1 year old child between 13 and 880 mSv.

Results of chromosome aberration studies in random samples of the evacuees are shown in table 5. 1. All investigations show significant elevations of the mean rate of dic+cr even when they were carried out several years after the main exposure. Elevation factors of 3 to 100 correspond to at least mean doses of 20 mSv to 1 Sv assuming homogeneous whole body exposure. Maznik and coworkers derive a mean dose of about 400 mSv for the evacuees from their chromosome studies which is higher by a factor 30 than the value given by UNSCEAR.

Chromosome studies in highly contaminated regions

Tables 5.2 and 5.3 show the results of chromosome studies in highly contaminated regions. They also exceed by far the physical dose estimates assumed by UNSCEAR. Remarkable is the appearance of overdispersion and multiaberrant cells which proves a significant contribution of incorporated alpha activity

Table 5.1 *Biological dosimetry in evacuees from the 30 km zone*

Dic dicentric chromosomes, cr centric rings

Region	Sample	Date of investiga-tion	Method	Results Mean elevation& specialities	Authors	Remarks
Evacuees from Prypiat and nearby	43 adults	1986	Dic	18-fold No overdispersion	Maznik et al. 1997	Result of the cited authors 430 mSv
Evacuated zone	60 children	1986	Dic+cr	15-fold No overdispersion	Mikhalevich et al. 2000	Result of the cited authors 400 mSv
Evacuees from Prypiat and nearby	102 adults 10 children	1987-2001	Dic+cr	Maximum 18-fold in 1987,then decline but staying sign. elevated	Maznik 2004	Result of the cited author 360 mSv
Evacuated zone	244 children	1991	Dic+cr	circ 100-fold*)	Sevan´kaev et al. 1993	Dose calculation IAEA (1991) 1-8 mSv
Evacuated from Pripyat	24 children	1991-1992	Dic	circ 3-fold*)	DeVita et al. 2000	
Evacuated zone	12 adults	1995	Dic+cr	7-10 fold *)	Pilinskaya et al. 1999	
Evacuation zone, residents	33 adults, not evacuated	1998-1999	Dic+cr	5.5-fold	Bezdrobnaia et al. 2002	

*) estimation by the writers

Table 5.2 *Biological dosimetry in inhabitants of Gomel and Gomel region*

Dic dicentric chromosomes, cr centric rings   Tralo translocations

Sample	Date of investiga- tion	Method	Results Mean elevation & specialities	Authors	Remarks
43 pregnant women 18 infants	1986-1987	Dic+cr	5-fold 40-fold	Feshenko et al. 2002	
8 persons	1988-1990	Dic+cr	circ 40-fold*)	Serezhenkov et al. 1992	Comparison with ESR
330 healthy adults	1988-1990	Dic+cr Tralo, FISH	15-fold 6.5-fold	Domracheva et al. 2000	
46 patients with hematol. malignancies	1988-1990	Dic+cr Tralo, FISH	(6-18)-fold (6.5-16)-fold	Domracheva et al. 2000	
35 adults	1990	Dic	circ 30-fold*) overdispersion; 2 multiaberrant cells	Verschaeve et al. 1993	
36 children	1994	Dic	(3.2-8)-fold	Barale et al. 1998	
20 children	1996	Tralo, FISH	3-fold significant	Scarpato et al. 1997	Controls from Pisa
70 children	1996	Dic+cr	18-fold	Gemignani et al. 1999	10 years after the accident !!

*) Estimation by the writers

Table 5. 3 *Biological dosimetry in highly contaminated regions > 37 kBq/m²*

Dic dicentric chromosomes, cr centric rings

Region	^{137}Cs kBq/m²	Sample	Date of investiga-tion	Method	Results Mean elevation & specialities	Authors	Remarks
Ukraine/Lugyny district Malahovka		130 children	1988-1990	Dic+cr	Increase to 6.6-fold in 1990	Eliseeva et al. 1994	Effect not explainable
Russia/Kaluga region Mladenik Ogor	140 43	17 adults 16 adults	1989	Dic+cr	circ 5-fold*) circ 2-fold*)	Bochkov et al. 1991	
Russia/Bryansk region Clynka Yordevka Klincy Russia/Kaluga region Uljanovo Chicdra	633 444 230 140 100	61 adults 432 adults 170 adults 666 adults 548 adults	1989-1998	Dic+cr	7-fold 1.5-fold 2-fold 4-fold 2.5-fold	Sevan´kaev 2000	2 multiaberrant cells 27 multiaberrant cells
Kaluga-Bryansk region Uljanova district	200	333 children	1989-1998	Dic+cr	3-fold	Sevan´kaev et	Physical estimates (to

		& juveniles				al. 2005	11.4 mSv and 6.7 mS
Chicdra district	100	407 children & juveniles	1990-2003		3.7-fold no decline		
Ukraine region	> 550	6 adults	1991	Dic	circ 5-fold*)	Ganina et al. 1994	
Bryansk and Bryansk region	> 550	1300	1992	unstable; stable	5 % > 400 mSv 1 % 1000 mSv	Vorob´ev et al. 1994	Physical estimate 17- multiaberrant cells
Bryansk region Mirnye	> 1100	100 adults	1993	cr	4-fold 6 multiaberrant cells	Salomaa et al. 1997	Controls from Krasny < 37 kBq/m^2 (Dics 0, multiaberrant cells 2)

*) Estimation by the writers

Biological dosimetry in western parts of Europe

In Austria and Germany, the Alps regions were predominantly affected by Chernobyl fallout which was washed out there by rain falls. Some chromosome studies were therefore also carried out in these regions. Pohl-Rüling et al. (1991) studied 16 adults of Salzburg city, Austria, in 1987 (June-August). The results for dic+cr are given in Table 5.4. The physical dose estimate was derived by the authors using UNSCEAR modeling. Two of the citizens had been studied already in 1984/1985, i.e., before the accident. They were followed up also in 1988 and 1990 (Fig. 2).

Stephan and Oestreicher (1993) studied 29 persons in Berchtesgaden, Germany, which is only 20 km away from Salzburg. Two areas with low contamination in southern Germany, Baden-Baden and Tirschenreuth (near to the Czech frontier), were selected for control (Table 4). The physical dose estimates were taken by the authors from German authorities. The elevation factors given for the dic+cr rate in table 5.4 were derived by us using the former published labor control of the authors 0.9 10^{-3} (Stephan and Oestreicher 1989).

Both studies in the Alps region lead to elevations of dic+cr which are far above the equivalent calculated excess exposures. While the Salzburg investigators found a correlation between aberration rate and measured Chernobyl deposition, the German investigators doubted the causation by radiation because of the high aberration rates in their controls. In contrast to this they found a significant decrease with time in a subgroup of the Berchtesgaden sample (Table 4). Further there were several cells showing an overdispersion of aberrations and therefore an incorporation of alpha radioactivity.

Norway was contaminated in spots up to 600 kBq/m^2 of Cs 137. Brogger et al. (1996) carried out chromosome studies in three such regions and found a 10-fold elevation of dic+cr still 5 years after the accident. The doses were calculated based on whole body counter measurement of Cs 134 and Cs 137 using dose conversion factors of the ICRP. The authors interpret the enormous discrepancy to the aberration findings as due to a biphasic dose-response. Salbu et al. (2004) reported that radioactive particles from Chernobyl were released predominantly by the fire after the explosion which contributed significantly to the population exposure even in Norway. They contained fission products but also heavy fuel and breeding products as U and Pu.

Table 5. 4 *Biological dosimetry in persons living in West European regions contaminated by Chernobyl releases*

Region	Sample	Date of study	Results dic+cr	overdispersion	Physical excess dose estimate
Austria Salzburg	16 adults	1987	6-fold		0.1-0.5 mSv
Germany Berchtesgaden	27 adults and 2 children	1987-1991	3-2 fold	6 cells with 2 dic	≤1.6 mSv
Baden-Baden	20 adults	"	3-fold		
Tirschenreuth	11 adults	"	2-fold	In 1 person 3 cells with 2 dic	<0.14 mSv
Berchtesgaden Subgroup "	5 "	87/88 90/91	3-fold 1.6-fold	1 multiaberrant cell	<0.14 mSv
Norway, selected regions	44 reindeer sames and 12 sheep farmers	1991	10-fold		5.5 mSv
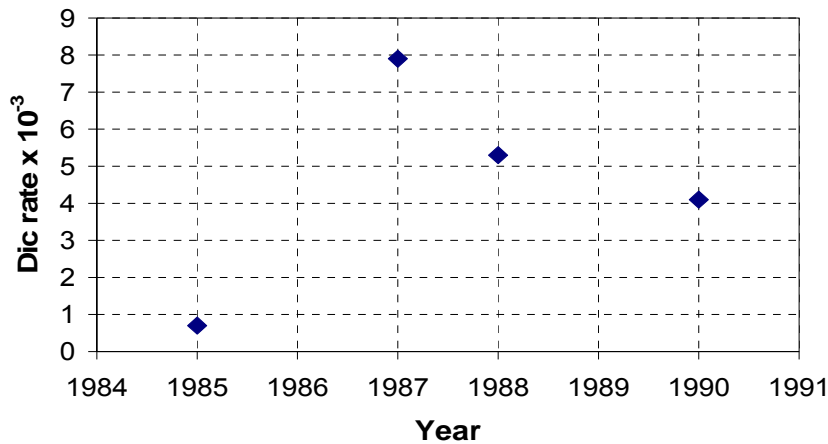
Fig.5. 2 *Mean rate of dic+cr in 2 citizens of Salzburg*

(Pohl-Rüling et al. 1991)

Discussion

Some of the cited authors used control cohorts from so-called uncontaminated regions, e.g. from Kyiv or Minsk. Persons living there show, however, significant elevations compared to background rates in really non-exposed individuals even after several years. This can be explained by the consumption of contaminated food.

To evaluate the real mean exposure of the population such investigations in the regions of low surface contamination by Cs-137 would be most informative. They are also to find in the literature. It must be mentioned that this present compilation of data is preliminary and incomplete.

Conclusions

Cytogenetic studies which are suitable to evaluate the dose estimates in regions contaminated by Chernobyl fallout were done in some thousand persons. The following conclusions can be drawn:

1. Assuming predominant exposure by external and internal Cs-137 the rate of dic+cr allows to estimate a minimum accumulated dose and using FISH to estimate the accumulated dose in the highly contaminated regions.

Physically estimated dose values can therefore be falsified if being much lower.

2. Clustering of the aberrations in the cells and/or multiaberrant cells are a reliable indicator of incorporated alpha activity. This was observed in several studies outside the distance of 100 km from the source and means that the assumption of UNSCEAR that fuel and breeding products are abroad negligible is wrong.

3. If the rate of the instable dic does not or not adequately decline over years, which is shown in some of the studies, the exposure can also not be generated by predominant Cs-137 contribution because of the short biological half-life of Cs (circ 100 days), otherwise one had to assume a still increasing Cs-contamination in the food.

4. The dose assumptions of UNSCEAR have to be revised. The physical estimates of other authors and the numerous EPR-measurements should be also taken into account.

5. Statements that an observed effect can not be radiation-induced because there is no dose-effect relationship should be checked regarding the assumptions for dose calculation. A lacking correlation with the ground contamination by Cs-137 dose not justify such a conclusion.

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6

Cancer risks of low dose ionising radiation

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I will start by discussing the characteristics of the Life Span Study Cohort (LSS) in Japan. Survivors with dose estimates in excess of 1Gy comprise less than 3% of the cohort. Of the 105,000 members of the LSS included in the current analysis, about 35,000 received doses between 5 and 200 mGy. In fact, they comprise about 75% of the cohort members with dose above 5 mGy (Preston et al 2007)

The mean dose in the LSS cohort was 200mSv (Preston et al 2003).
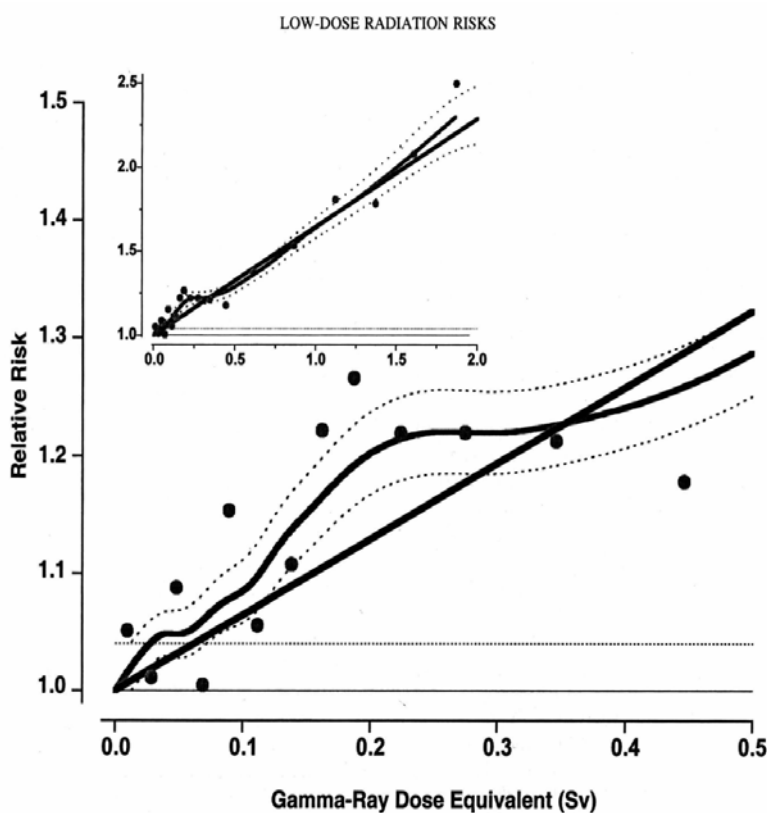
Figure 6.1 – Radiation related cancer risks at low doses among atomic bomb survivors

In Fig 6.1 we can see age-specific cancer rates over the 1958–1994 follow-up period relative to those for an unexposed person, averaged over the follow-up and over sex, and for age at exposure 30. The dashed curves represent ±1 standard error for the smoothed curve. The straight line is the linear risk estimate computed from the range 0–2 Sv. Because of an apparent distinction between distal and proximal zero-dose cancer rates, the unity baseline corresponds to zero-dose survivors within 3 km of the bombs. The horizontal dotted line represents the alternative baseline if the distal survivors were not omitted. The inset shows the same information for the fuller dose range (Pierce and Preston 2000)

Analyses of these data sets based on more than 40 years of cancer incidence data for the members of the LSS were made. Thirty four percent of the cancers included in the current analyses were diagnosed during 1988-1998. There is a statistically significant dose response when analyses were limited to cohort members with doses of 0.15 Gy or less (Preston et al 2007)

Region	Collective dose for children and adolescents (0—18 at the time of the accident), person-Gy	Collective dose for adults (19 years and older at the time of the accident), person-Gy	Total collective doses of Belarusian population, person-Gy
Brest	21129	24042	45171
Vitebsk	1164	1560	2724
Gomel city	36998	38236	75234
Gomel	112812	171939	284751
Grodno	3329	4453	7782
Minsk city	15063	19244	34307
Minsk	6404	8121	14525
Mogilev	22328	27694	50022

Figure 6.2 – Collective thyroid doses for two age groups in Belarus: [20 Years after the Chernobyl Catastrophe: the consequences in the Republic of Belarus and their overcoming. (National Report, 2006)]
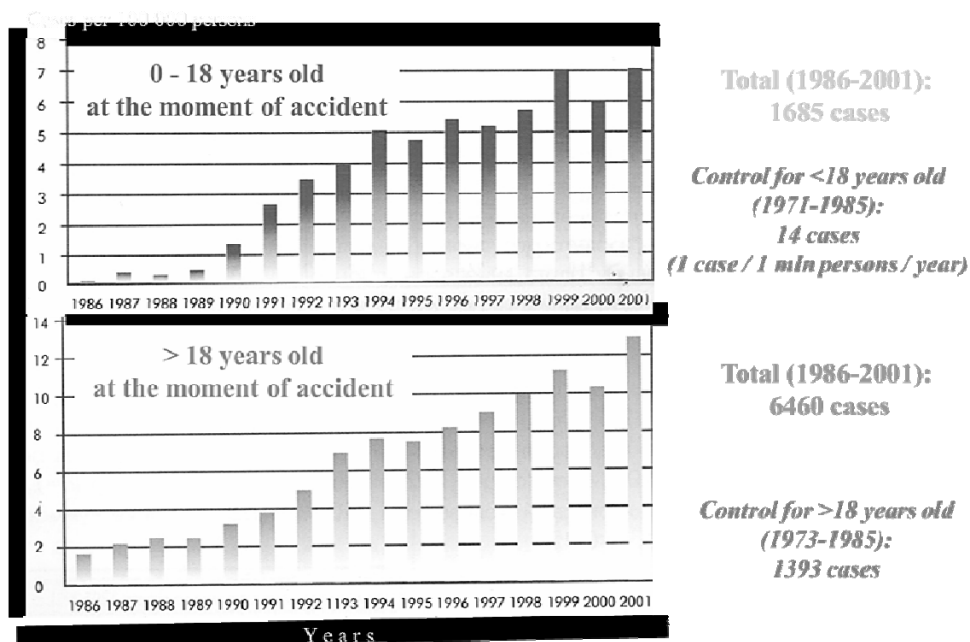
Figure 6.3 *– In cases per hundred persons, the time course of thyroid cancer incidence in Belarus (National Report, 2003)*

Time period	Collective effective dose, person-Sv		
	external	internal	cumulative
1986—1995	9636	5504	15140
1986—2005	11900	6800	18700

Figure 6.4 - *Collective cumulative effective doses (excluding thyroid doses) for two time periods for territories of Belarus with density of cesium-137 contamination over 37 kBq/m2[20 Years after the Chernobyl Catastrophe: the consequences in the Republic of Belarus and their overcoming. National Report, 2006]*

Tumor site	ICD X code	Male		Female	
		GPR 5	Control	GPR 5	Control
Total	*C00-97*	*542.95**	*487.21*	*359.12**	*301.89*
Stomach	C16	69.55	65.75	29.33	28.22
Colon	C18	23.31*	17.94	16.41	15.43
Lungs	C34	115.91	121.16	8.56	8.81
Skin	C44	57.56*	39.82	47.27*	32.96
Breast	C50			72.29*	59.25
Kidney	C64-65	19.9	20.71	9.26	9.37
Bladder	C67	26.38	24.61	3.37*	2.69
Thyroid gland	C73	6.54*	2.58	22.08*	16.63

Figure 6.5 - Standardized incidence rate of malignant tumors among the population living on the territories of Belarus with 37-555 kBq/m^2 and in the control group for the period of 1993-2003 (per 100 000 populations) [Okeanov A.E.//Zum int. Kongress "20 Jahre Leben mit Tschernobyl, 2006]

Tumor site	ICD X code	1993-1996		1997-2003	
		RR	95% CI	RR	95% CI
Total	C00-97	1.09	1.07 – 1.12	1.15	1.13 – 1.17
Stomach	C16	1.03	0.97 – 1.09	1.03	0.96 – 1.07
Colon	C18	1.01	0.91 – 1.12	1.23	1.15 – 1.32
Lungs	C34	0.91	0.86 – 0.97	0.93	0.89 – 0.98
Skin	C44	1.26	1.18 – 1.35	1.48	1.42 – 1.54
Breast	C50	1.16	1.08 – 1.26	1.25	1.18 – 1.32
Kidney	C64-65	1.04	0.91 – 1.18	0.94	0.86 – 1.02
Bladder	C67	1.05	0.93 – 1.19	1.05	0.97 – 1.15
Thyroid gland	C73	1.45	1.23 – 1.71	1.46	1.33 – 1.59

Figure 6.6 - Relative risk of malignant tumors incidence among the population living on the territories of Belarus with 37-555 kBq/m^2 [Okeanov A.E.//Zum int. Kongress "20 Jahre Leben mit Tschernobyl, 2006]
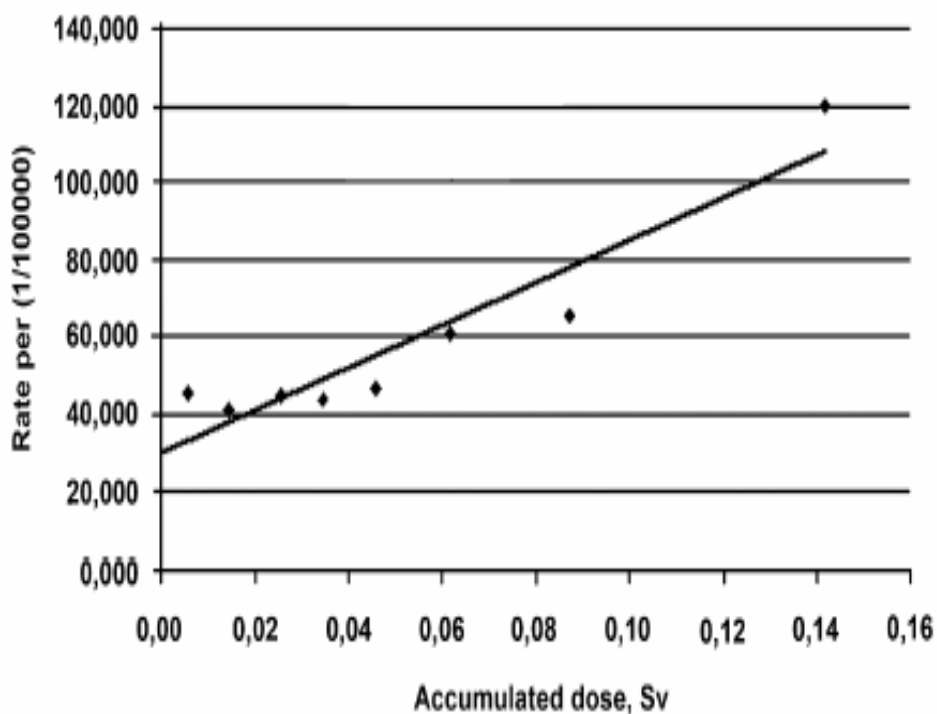
Figure 6.7 - *Dose dependence of breast cancer incidence in women of Gomel region, Belarus [20 Years after the Chernobyl Catastrophe: the consequences in the Republic of Belarus and their overcoming. National Report, 2006]*

Now if we recall *Figure 6. 8*, the radiation-related cancer risks at low doses among atomic bomb survivors we can compare the populations.

Dose category	ERR	ERR per Sv
0.005–0.02	0.03	2.6 ± 2.1
0.02–0.05	0.05	1.6 ± 0.90
0.05–0.10	0.04	0.60 ± 0.40
0.10–0.20	0.06	0.43 ± 0.25
0.20–0.50	0.12	0.38 ± 0.13

Figure 6.8 - *Studies of the mortality of atomic bomb survivors. Report 12, Part I. Cancer: 1950–1990 [D.A. Pierce, Y. Shimizu, D.L. Preston, M. Vaeth, K. Mabuchi // Radiation Research, 1996]*

Inverse dose-rate effects
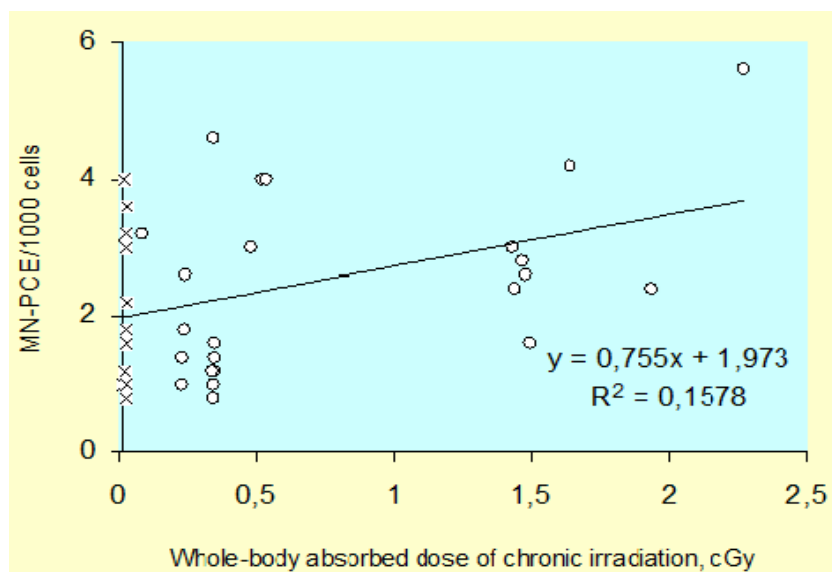
Figure 6.9 –*Relationship between the MN-PCE frequency in bone marrow and lifetime whole-body absorbed dose in bank voles at site 2 (×) and site 4 (○)*
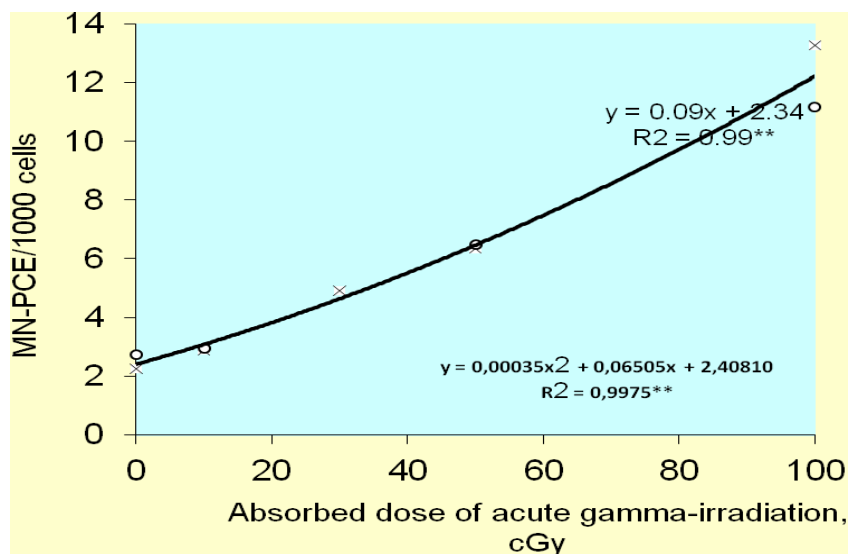
Figure 6.10 - *Relationship between the MN-PCE frequency in bone marrow and absorbed dose of acute gamma-irradiation in animals at site 2 (×) and site 4 (○)*

Employer/site	Dose range, mSv				Total no. of workers	Collective dose, person Sv	Mean dose, mSv
	<10.0	10.0–50.0	50.0–100.0	100.0+			
Atomic Weapons Establishment	10.778	1.053	174	139	12.144	76	6.2
British Nuclear Fuels plc	12.057	8.621	3.334	5.233	29.245	1.936	66.2
Industrial[a]	1.931	603	120	76	2.730	48	17.6
Ministry of Defence	26.282	5.169	1.102	931	33.484	418	12.5
Nuclear Electric and Magnox Generation	5.718	4.153	954	586	11.411	275	24.0
Nycomed Amersham	2.096	594	171	285	3.146	118	37.4
Research[b]	1.944	696	100	46	2.836	36	12.7
Scottish Nuclear	1.374	693	327	189	2.583	71	27.8
United Kingdom Atomic Energy Authority	16.271	6.824	1.974	2.095	27.164	832	30.7
Total	78.501	28.406	8.256	9.580	124.743	3.810	30.5

[a] Industrial: Rolls-Royce and Associates, plus non-destructive testing firms.
[b] Research: Council for the Central Laboratory of the Research Councils, MRC Radiobiology Unit and NRPB.

Figure 6.11 - *Study population for the second analysis of the National Registry for Radiation Workers (NRRW) by lifetime dose and first employer [Muirhead C.R., O'Hagan J.A., Kendall G.M. // Radiat Biol. Radioecol, 2008]*

Analysis	Leukaemia excluding CLL	All malignant neo-plasms excluding leukaemia	All malignant neo-plasms excl. leu-kaemia and lung cancer
2nd NRRW analysis (Muirhead et al., 1999)	2.55 (−0.03, 7.16)	0.09 (−0.28, 0.52)	0.17 (−0.26, 0.70)
1st NRRW analysis (Kendall et al., 1992)	4.28 (0.40, 13.6)	0.41 (−0.17, 1.15)	0.56 (−0.14, 1.48)
IARC International Study (Cardis et al., 2005, 2007)	1.93 (<0, 7.14)	0.97 (0.27, 1.80)	0.59 (−0.16, 1.51)
Japanese A-bomb survivors (Pierce et al., 1996)	2.15 (0.43, 4.68)	0.24 (0.12, 0.37)	0.19 (0.07, 0.33)

Figure 6.12 - *Estimates of excess relative risk (ERR) per Sv (and 90% CI) in the NRRW, the IARC study and the Japanese A-bomb survivors [Muirhead C.R., O'Hagan J.A., Kendall G.M. // Radiat Biol. Radioecol, 2008]*

Conclusions

Doses of the whole body irradiation of affected populations of the Republic of Belarus, Ukraine and contaminated regions of the Russian Federation are in the dose range of 0–0.15 Gy, i. e. within the range of doses that caused statistically reliable increase in cancer incidence in atomic bomb survivors. Thyroid cancer incidence increases steadily among adult population of Belarus (National report, 2006).

A statistically significant increase of the breast cancer incidence among women of Gomel region in comparison with appropriate value among women living in the less contaminated areas was observed in the period 1990-2003. Dose dependence between accumulated radiation dose and realized relative risk of breast cancer was shown (National report, 2006). According data of A. Okeanov population living in regions with contamination levels of 37–555 kBq/m2 demonstrated considerable growth of the incidence in cancers in 1997-2003 in comparison with the previous period 1993-1996. We suppose that an increased thyroid cancer incidence in children born by irradiated parents chronically exposed due to the Chernobyl accident can be resulted from a induced genomic instability (Goncharova, 2005). There is an increasing set of data showing that radiation risks of chronic irradiation of populations at low doses and low dose rates are higher than radiation risks of atomic bomb survivors. The 15-country collaborative study of cancer risk among radiation workers of the nuclear industry give evidence that excess relative risks (ERR) of all malignant neoplasm excluding leukaemia and lung cancer is approximately 3 times higher than radiation risk of atomic bomb survivors. This means that using of radiation risks established for atomic bomb survivors and Dose and Dose Rate Effectiveness Factor (DDREF) higher than 1 in case of chronically irradiated populations will underestimate numbers of radiation-induced cancers. Thus any declarations about an absence of radiation-induced increases in the incidence of solid cancers excluding thyroid cancer simply mean an ignoring of data established in Belarus. It is clear that conclusions of the UN Chernobyl Forum report have no scientific base and are therefore misleading.

7

Nanoparticles and Radiation

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(These results were originally given as a poster: Elsaesser A, Busby C, McKerr G and Howard CV (2007) Nanoparticles and radiation. EMBO Conference: Nanoparticles. October 2007 Madrid and also: Elsaesser A, Howard C. V., & Busby C. (2009) The biological implications of radiation induced photoelectron production, as a function of particle size and composition. *International Conference; Royal Society for Chemistry NanoParticles Liverpool 2009)*

Interaction of Radiation and Matter

Electromagnetic radiation and matter interact predominantly by three different mechanisms: Compton scattering, the photoelectric effect and pair production. Compton scattering basically describes the loss of incident photon energy by the scattering of shell electrons. Pair production is the simultaneous production of an electron and a positron and occurs at energies above 1.022MeV, which is equivalent to the invariant mass of an electron plus positron. With the photoelectric effect electrons absorb the incident photon energy and are either emitted or lose energy in secondary processes. For energies below 1MeV the photoelectric effect is the predominant one. The cross section σ for the photoelectric effect is proportional to Z (atomic number) to the power 5 and roughly proportional to the incident photon energy to the power -7/2.

$$\sigma = Z^5 \, E_\gamma^{-7/2}$$

Most of the photoelectrons produced in an absorbing material lose their energy though electron-electron scattering and Bremsstrahlung (breaking radiation). Therefore the escape depth of photoelectrons generated in solids is usually a few nanometers [1].

Hence, irradiated particles with diameters in the range of a few nanometres will emit most of the generated photoelectrons without internal absorption. Therefore nanoparticles are likely to emit the largest quantity or secondary electrons in proportion to their mass. Furthermore, secondary electron emission of high Z

materials could provide a partial explanation of the toxicity of various heavy metals. Due to their size, nanoparticles can penetrate into the human body and some are able to reach the cell nucleus. This may be crucial; in explaining the toxicity of incorporated nanoparticles of materials with a high atomic number [2,3].
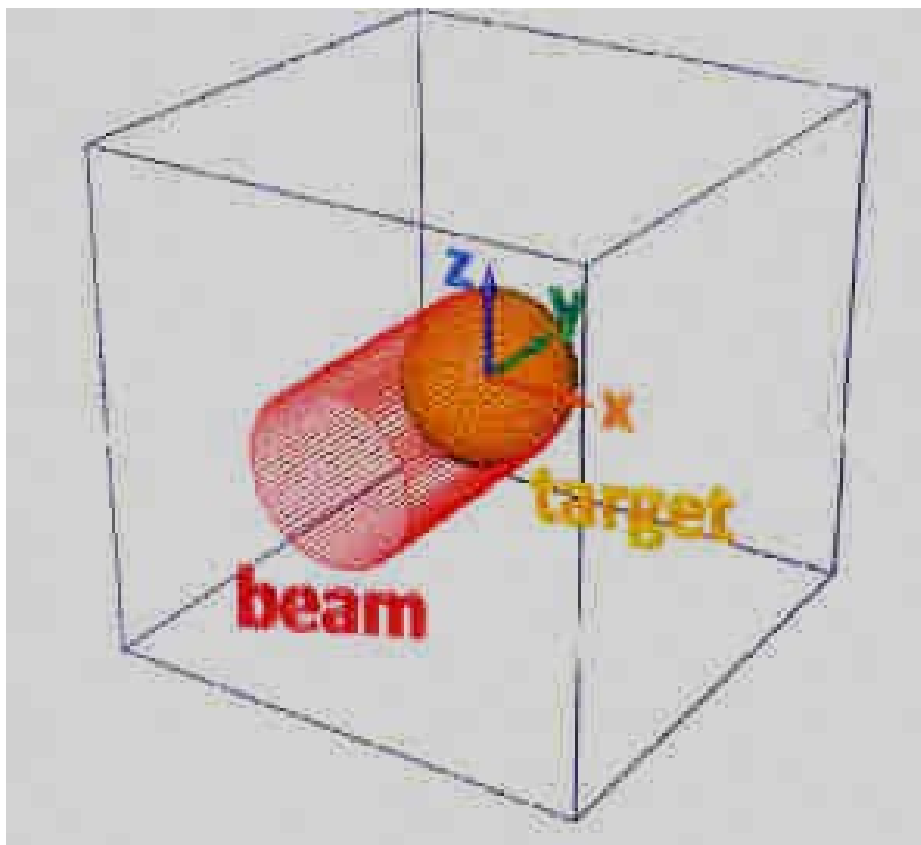
Fig 7.1 *Beam and target geometry*
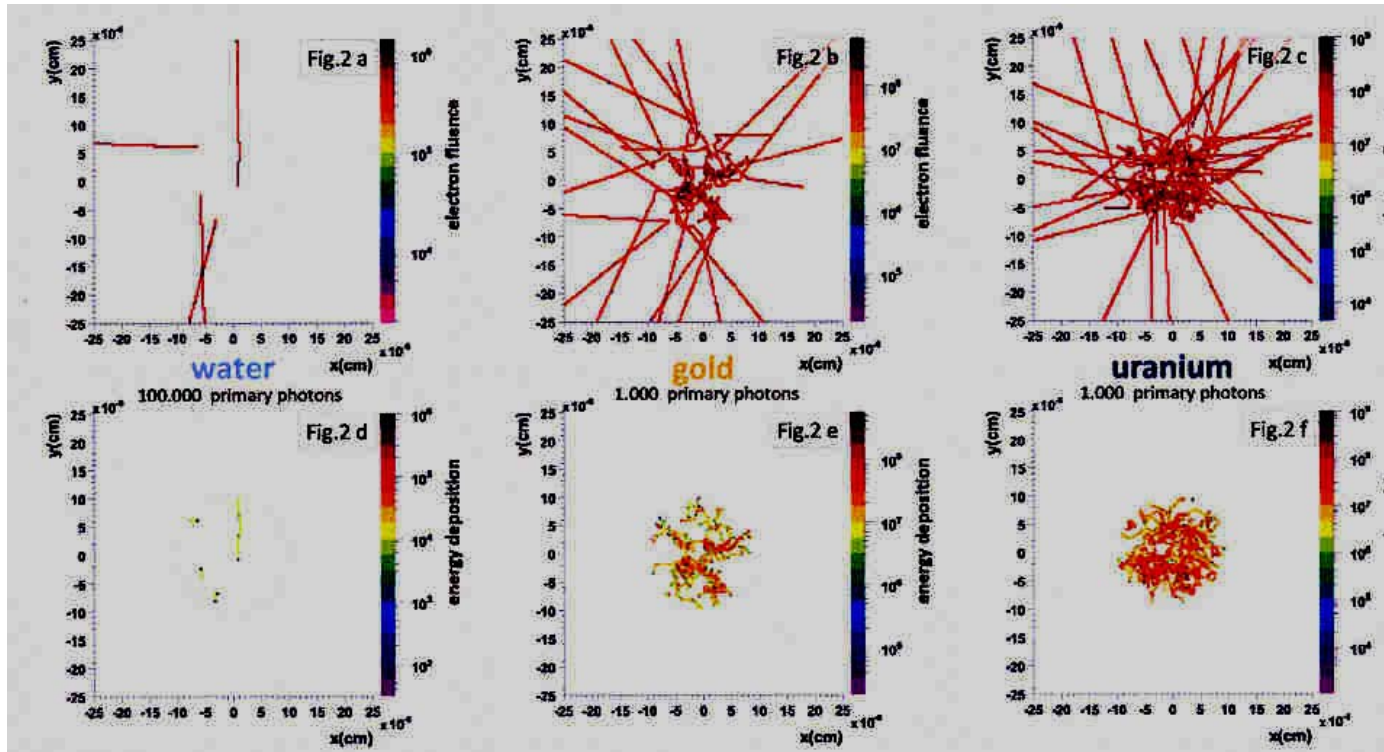
Fig 7.2 *Secondary electron production by 100keV primary photons within the target and escaping electrons overlayed by the target geometry for water (a), gold (b) and Uranium (c). Fig 2 d-f (lower) shows the corresponding energy deposition. Note that these are projections in two dimensions: tracks out of the plane of the paper are not shown. For water the scale is 100 times greater i.e. 100,000 photons produce the 4 tracks compared with 1000 photons producing the tracks shown in the Uranium and Gold case.*

Monte Carlo Simulations

Monte Carlo simulations are widely used in computational and statistical physics, physical chemistry and high energy physics to model particle transport and particle matter interactions. We employed FLUKA [4,5] a Monte Carlo code to simulate the interaction and propagation or photons and photoelectrons in matter composed of different particles. FLUKA is capable of simulating particle interactions from 1keV to TeV for different hadrons, leptons and bosons with high accuracy. We modelled photon absorption and secondary electron production of particles from 1cm to a Angstrom for incident photon energies in the keV region. Target materials we used were water (Z eff = 7.5), Gold (Z=79) and Uranium (Z=92). Fig 1 shows the arrangement of photon beam and target. Fig 2 shows secondary electron production and energy deposition. Fig 3 illustrates the ratio of secondary electromn production to primary incident photons and Fig 4 shows the same ratio but weighted with the beam projection area and the target volume.
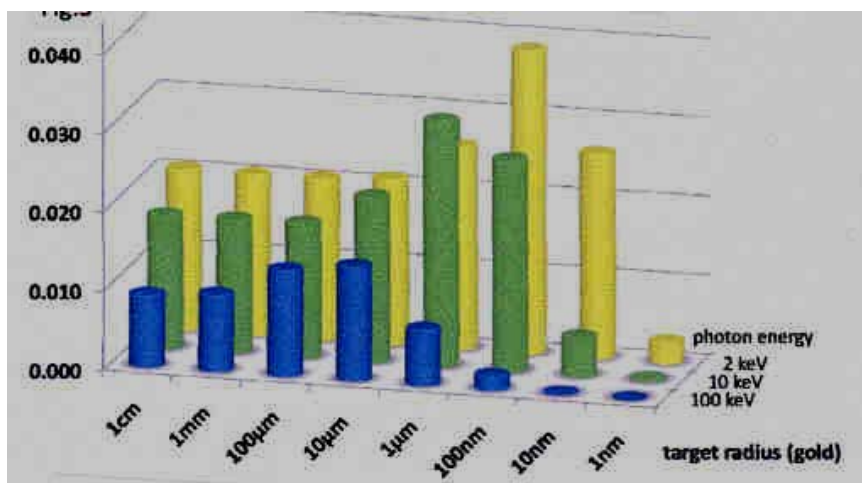
Fig 7.3 *Ratio of electrons leaving the target material (gold) to incident primary photons (100kev, 10keV and 2 keV)*

Conclusion

Secondary electron emission from 1nm nanoparticles is about 25000 times higher than from the equivalent particle of 1cm radius. At target sizes of about 10nm the emission reaches a plateau with no further increase for smaller targets. This is probably due to the negligible internal absorption within the target material and hence the increases yield of secondary electrons leaving the nanoparticle. This *size effect* shows an energy dependent maximum for the ratio of generated electrons to incident primary photons which shifts for lower photon energies to smaller target diameters. The simulations also show an increase in secondary electrons and energy deposition within high Z target materials compared to a water phantom. It also confirms the energy dependence of secondary electron production as expected by the photoelectric cross section.
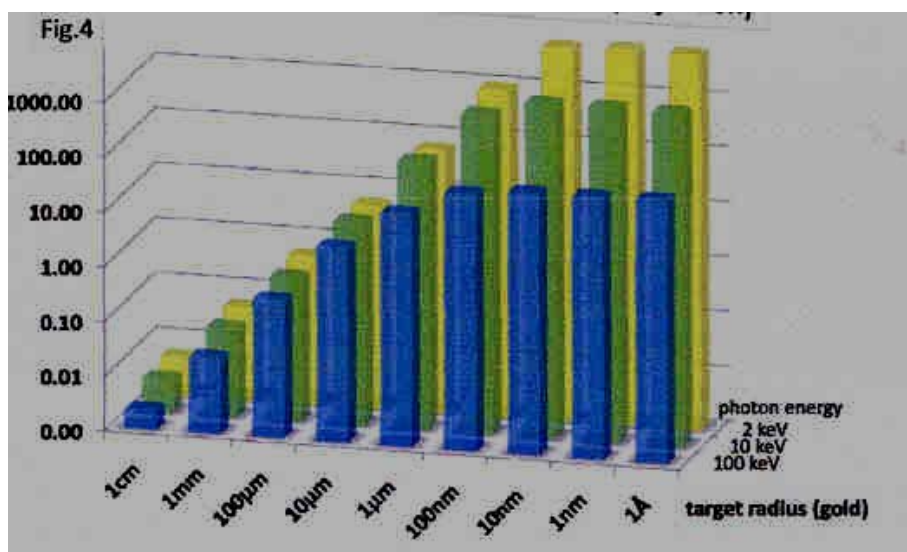
Fig 4. *Same ratio as Fig 3 but weighted with the perpendicular beam projection area and the target volume.*

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4. Fasso A, Ferrari A., Ranft J, Sala PR (2205) FLUKA: a multi particle rtransport code, CERN 2005-19 INFN/TC_05/11, SLAC-R-773

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8

Childhood cancer near German nuclear power plants: The KiKK study

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The KiKK study is an epidemiologic study of childhood cancers near German nuclear power plants. It was commissioned by the Federal Office for Radiation Protection (*Bundesamt für Strahlenschutz*), and conducted by German Childhood Cancer Registry (GCCR) between April 2003 and December 2007. It comprised an external advisory expert commission of 12 people, and after the results were published in an American scientific journal in 1999, the wide media coverage forced the German Federal Office of Radiation Protection to take action. In 2001 it commissioned a new study which was meant to investigate the causes for possible increased cancer rates near NPPs. The study design differed from a purely ecological study – the distance from the plant was included as a proxy of the radiation exposure[1].

The design of the study follows:

- Case-control study (3 controls per case, matched by age, sex and reactor site)
- All cancers, sub group: leukaemias
- All German commercial NPPs
- Children below age < 5
- Longest possible study period (1980-2003)
- One-tailed statistical test
- Proxy of radiation exposure:
  Inverse distance of place of residence at diagnosis
- Main question:
  Increase of cancer rates with decreasing distance from NPP?
- Additional test:
  Cancer rate greater for r < 5 km than for r > 5 km?
  Cancer rate greater for r < 10 km than for r > 10 km?
- Linear logistic regression model:

- $ln(odds) = ß0+ß1/r$
  where
  odds = cases / controls
  $r = distance\ from\ NPP;\ x = 1/r$
  ß0, ß1: parameters (ß1: trend parameter)
- Negative distance trend if parameter $ß1>0\ (H0 <= 0)$
- The relative risk is the ratio of two odds:
  $RR = odds(x)/odds(x=0) = exp(ß0+ß1*x)/exp(ß0) = exp(ß1*x)$
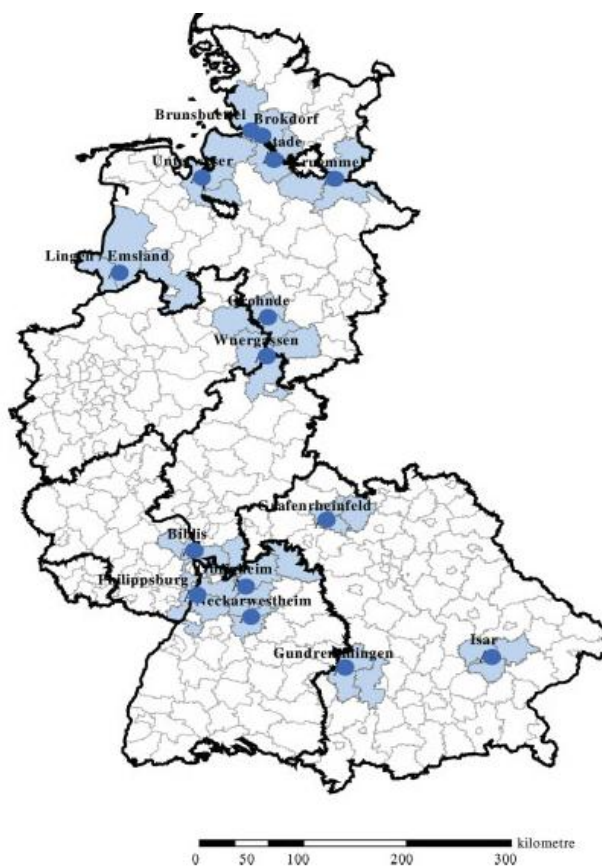
Figure 8.1 *– Study region: countries (3) next to reactor sites (16) – collectively 41 counties*

Diagnosis	$\beta_1 \pm SE$	90% CI	P value	cases	controls
cancer	1.18 ±0.44	0.46, 1.90	0.0034	1592	4735
leukaemia	1.75 ±0.67	0.65, 2.85	0.0044	593	1766

Figure 8. 2 *– Results of the study*

We discovered the following:

- Significant negative distance trend for all cancers (p=0.0034) as well as for leukaemia (p=0.0044)

- Relative risk for r < 5 km vs. r > 5 km is
  RR=1.61 for all cancers and *RR=2.19 for leukaemia*

- Relative risk for r < 10 km vs. r > 10 km is
  RR=1.18 for all cancers and *RR=1.33 for leukaemia*

- Significant excess in the *5-km zone*:
  29 excess cancer cases, *20 excess leukaemia cases*

- Negative distance trend also significant when NPP Krümmel - with known leukaemia cluster - is excluded
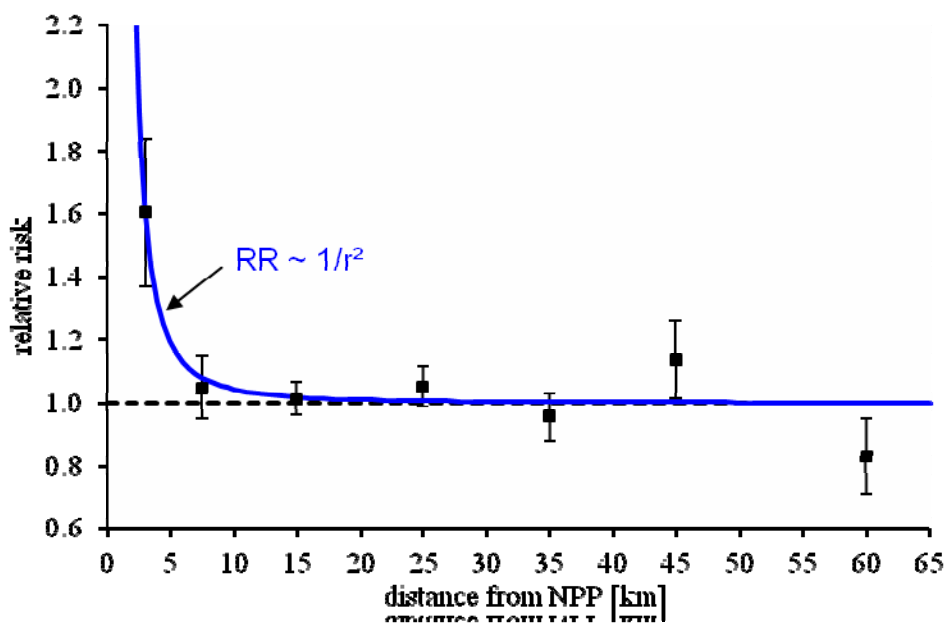
Figure 8.3 – Cancer risk (study region)
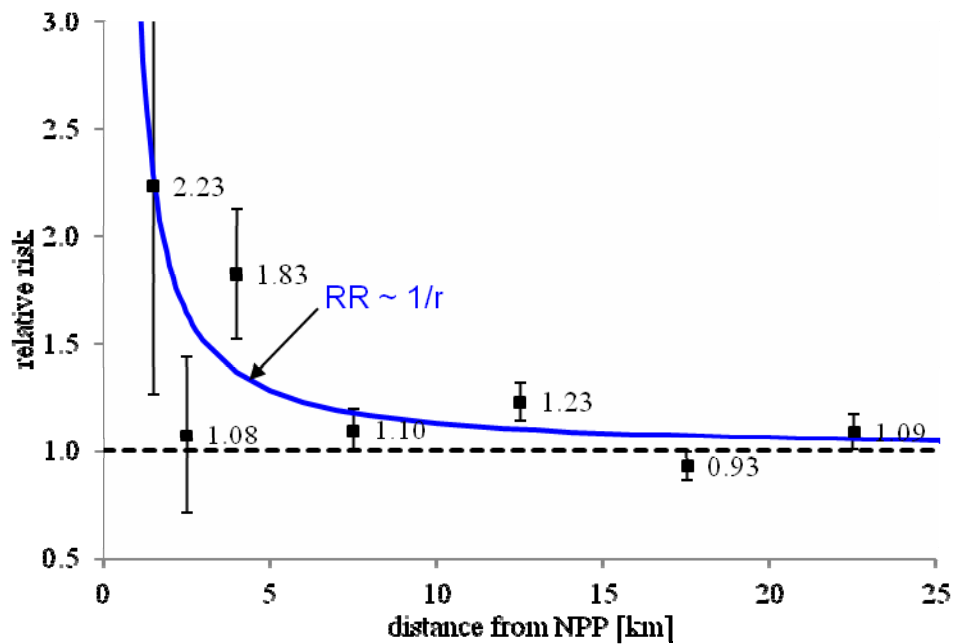
Figure 8.4 – Cancer risk (r < 25km)
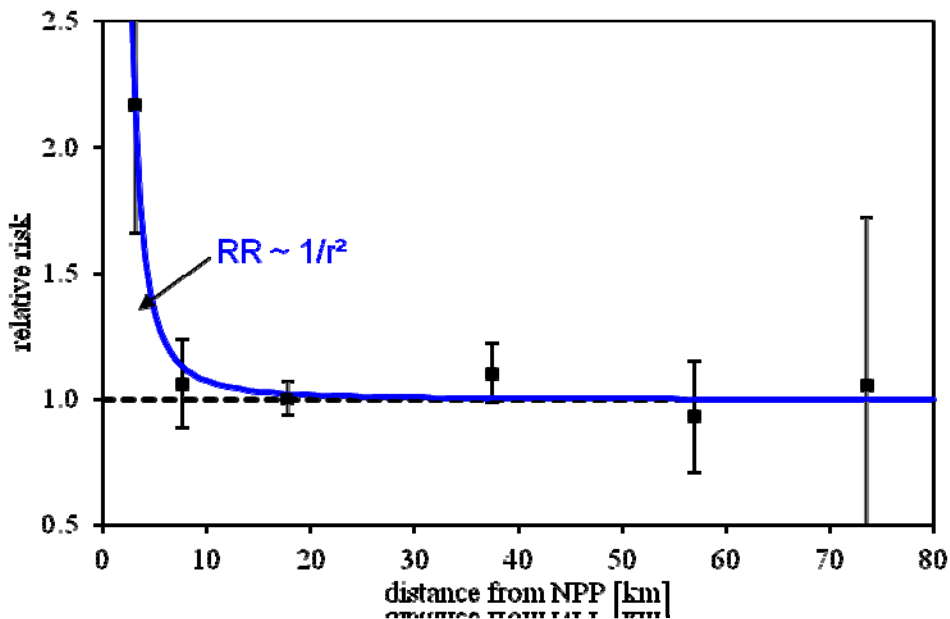
Figure 8.5 – *Leukaemia risk (Study region)*

The second part of the study comprised a questionnaire. A sub-group (360 cases, 696 controls) with selected diagnoses (leukaemia, lymphoma, and ZNS tumours) were interviewed with regard to the presence of known risk factors for leukaemia between 1993 and 2003. None of the risk factors (confounders) had an appreciable influence on the distance trend, ie the main result – a negative distance trend – could not be explained by confounders. However, we must recognise the low power of the study due to the small sample size.

KiKK Conclusions

The KiKK study indicated a ignificantly increased cancer risk, mainly for leukaemia, when living in the proximity (r < 5 km) of German NPPs. The results were crucially not consistent with most international studies, and 'unexpected' given the level of radiation exposure.

The conclusions made were that the causes were unknown, but that radiation could be ruled out on principle. Thus the findings are this unexplained. Could there be Confounding? Could it be a chance result?

Inconsistencies

A meta-analysis by Baker et al. (2007), explored a pooled analysis of 37 studies from 9 countries (136 nuclear facilities). It yielded a demonstrably significant increase of leukaemia in children below age 10. New findings of the effects of radiation at very low doses point to higher risks from internal emitters (eg genomic instability, bystander effect).
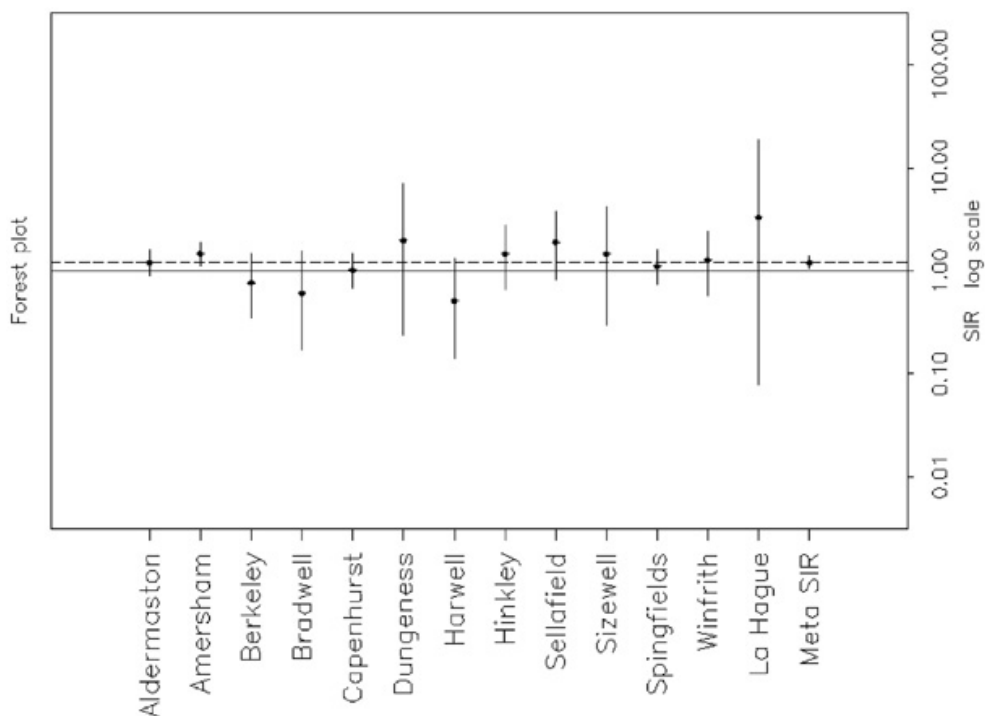
Figure 8. 6 *– Baker et al. 2007 results*

The inconsistency is more clear if we compare-

- ***Baker and Hoel 2007***

   Increase of leukaemia incidence in the 15-km-radius:
   children and young adults   < 26 y: 11%

   children   < 10 y: 23%

- ***KiKK***
   in the 10 km radius:
   children   < 5 y: 33%

KiKK found that leukaemia risks were ~doubled (RR=2.19) in children below age 5 near NNPs. Doubling the dose for childhood leukaemia is a few mSv after in utero exposure (from OSCC data). Official German dose estimates for 1 year old children are a few µSv per year (see:

http://dip21.bundestag.de/dip21/btd/16/068/1606835.pdf). The difference is clear - by a factor of 1000!

Figure 8.7 – Releases of I-131 and particulates from German nuclear plants in 2006 (Bq).

Abbildung II.1-2

Ableitung radioaktiver Stoffe mit der Fortluft aus Kernkraftwerken im Jahr 2006
$^{14}CO_2$, Tritium und Edelgase
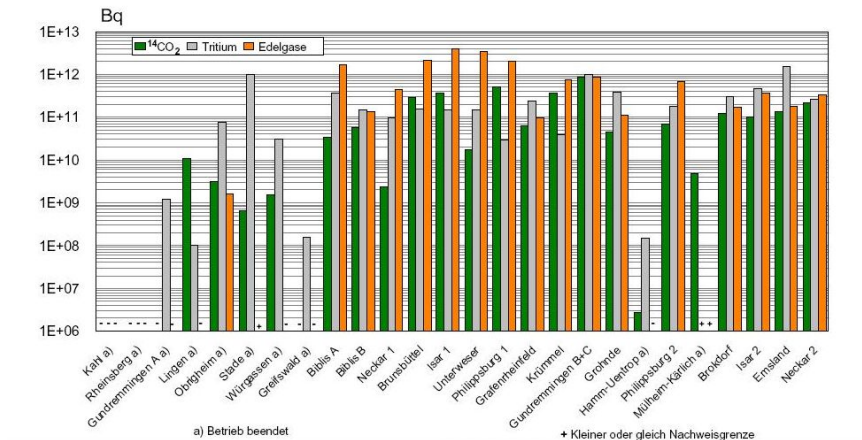
Figure 8.8 – Releases of Tritium, C-14 and radioactive Noble Gases from German nuclear plants in 2006 (Bq).

Deutscher Bundestag - 16. Wahlperiode   - 17 -   **Drucksache** 16/6835

Abbildung II.1-7

Strahlenexposition im Jahr 2006 in der Umgebung von Kernkraftwerken durch die Ableitung radioaktiver Stoffe mit der Fortluft
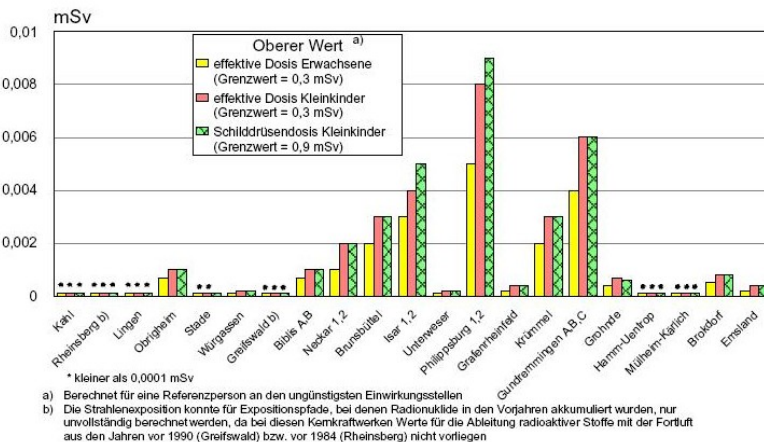
Figure 8.9 – Radiation doses from German nuclear plants to adults, small children and infants in 2006 (ICRP model calculation).

The official dose estimates seem questionable – a number of solutions are presented. Firstly, there could be a possible incomplete registration and measurement of radionuclides emitted by NPP. Official dose calculations use simple propagation models:a two dimensional Gauss model might be in error up to factor 10. The ICRP model for internal emitters might underestimate doses, especially for alfa and low energy beta emitters, eg H-3 (See UK Government CERRIE report (2004) on dose uncertainties). Therefore official dose estimates might be low by a factor of between ten and a hundred. However, we need to explain a factor of 1000.

It is an implicit assumption that excess leukaemia risk is proportional to dose, but this is only justified if the dose-response relationship is linear. Firstly, residents near NPPs are exposed to widely fluctuating dose rates over the year, and not to a constant low dose rate. Secondly, the shape of the dose-response curve might be curvilinear.

Vergleich der vom Betreiber und dem BfS ermittelten Kohlenstoff-14-Aktivitätskonzentrationen in der Fortluft am Beispiel eines süddeutschen Druckwasserreaktors (KKW Neckarwestheim 2)
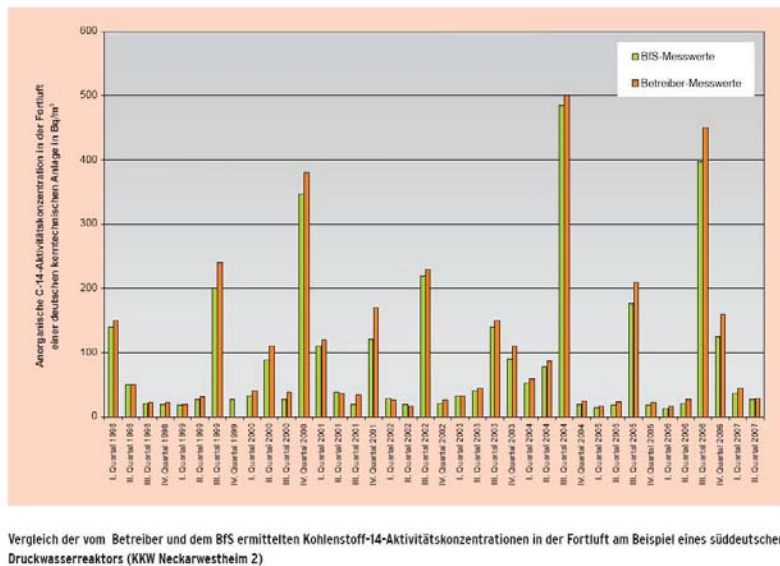
Figure 8.10 – *Concentration of Carbon-14 CO2 in air Bq/m3 in the area of south German reactors*

Teratogenic risk
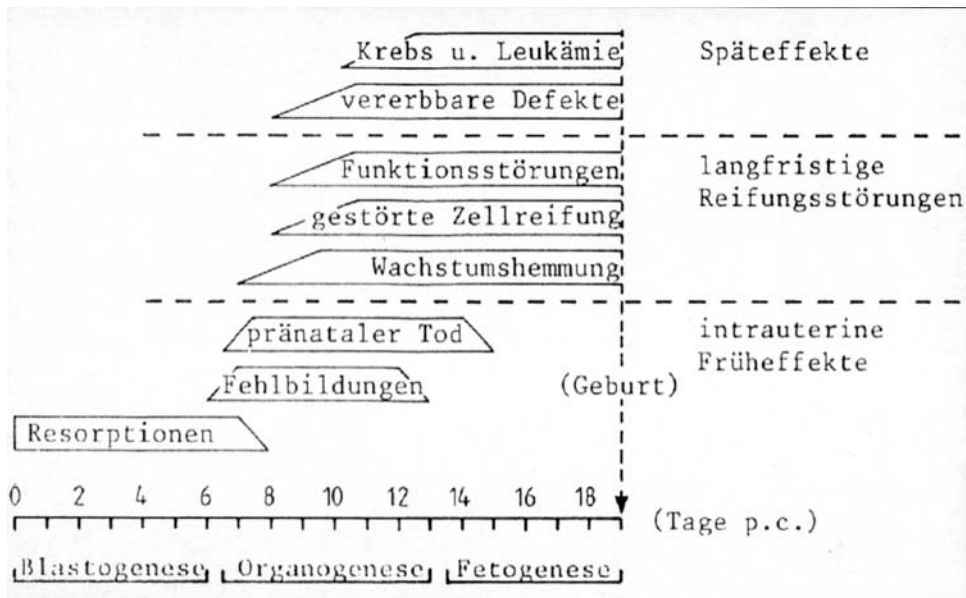
Figure 8.11 – Teratogenic risk: Prenatal induction of radiation damage in the mouse

In Fig 11 we see the development of different end points as dose increases. Early effects in the 0-6 week period of foetal development results in resorption. In the organogenesis period of 6 to12 weeks there can be malformation induction with intrauterine deaths. These are the early effects of intrauterine exposure. Late effects, including cancer and leukemia result from exposures after 8 weeks but also during the 14+ week period.

The studies' assumptions are as follows:

1. annual background dose (excluding radon) ~1 mSv/a

2. additional dose from NPP: ~0.1 mSv per year
    (ie ~10-100 times larger than official estimates)

3. leukaemia 100% radiation induced

4. prenatal origin of leukaemia in children under age 5

5. discontinuous emissions from NPPs

6. non-linear dose response

Following the Chernobyl accident, a significant association of perinatal mortality with the caesium burden of pregnant women in Germany was found. The dose response is curvilinear with a best estimate of 3.5 for the power of dose (95% CI: 1.5-7.5) [3]. Significant association between stillbirth rates and caesium ground deposition in Bavaria. A 3rd degree polynomial yields the best fit to the data (*Körblein, unpublished*). Significant association of stillbirth rates in Cardiff, GB, with the tritium emissions of Amersham pharmaceutical plant. A linear- quadratic model best describes the dose response relationship (*Körblein, unpublished).*
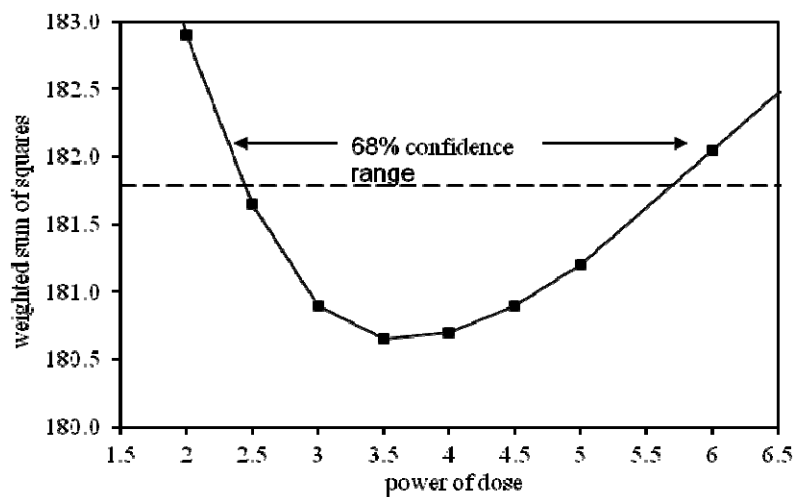
Figure 8.12 – *Power of dose in West German mortality data*
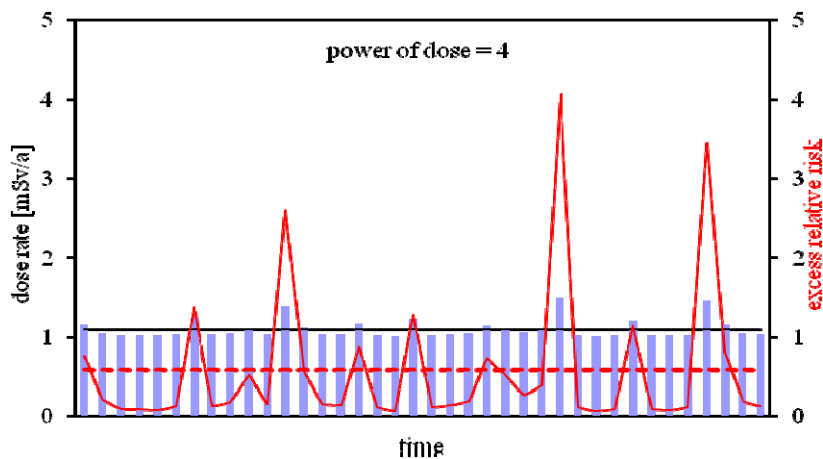
Figure 8.13 *– Dose-effect relationship*
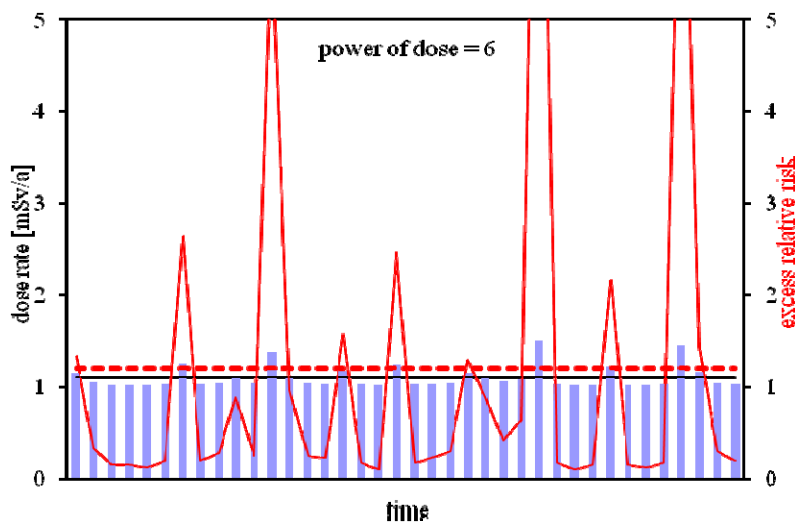
Figure 8.14 *– Dose-effect relationship*

The discovered excess relative risk (ERR) depends on the power of dose n. For n = 2.5, 4, and 6, the results for ERR are 0.3, 0.6, 1.2. The KiKK study found ERR=0.6 for all cancers and ERR=1.2 for leukaemias.
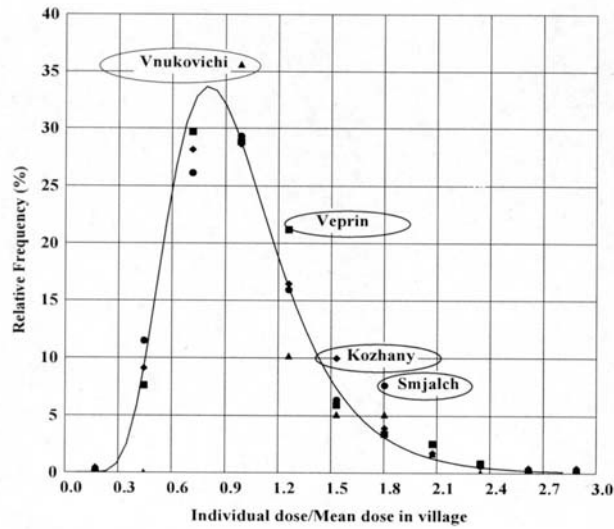
FIG. 4.11. Frequency distributions of monthly effective external doses of individual persons as measured in summer 1993 with TL dosimeters in four villages of the Bryansk Oblast (points) and calculated by the stochastic model (curve). Doses are normalized to the arithmetic mean of the individual doses determined for each of the villages. From Golikov et al. (2002).

Figure 8.15 – *Frequency distribution of doses*

From these results, we can attempt to derive a dose-response curve.
We assume:

- Random distribution of doses in a cohort:
  lognormal distribution with median dose $x=\mu$ and standard deviation σ:
  density function $f(x) = 1/(x*\sigma*(2\pi)^{1/2})*exp(-(ln(x)-\mu)^2/2\sigma^2)$
- Random distribution of radiation sensitivities:
  cumulative lognormal distribution function $g(x)$
- Effect in dose interval $(x,x+dx)$ is $\sim f(x)*g(x)*dx$
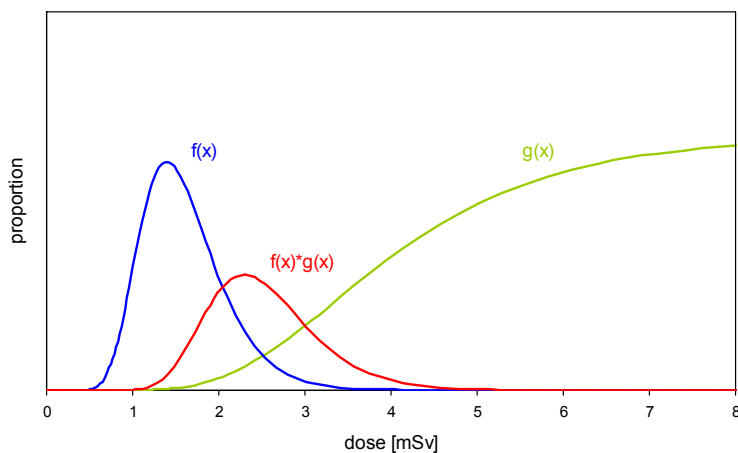
Figure 8.16 *– Distribution curves*
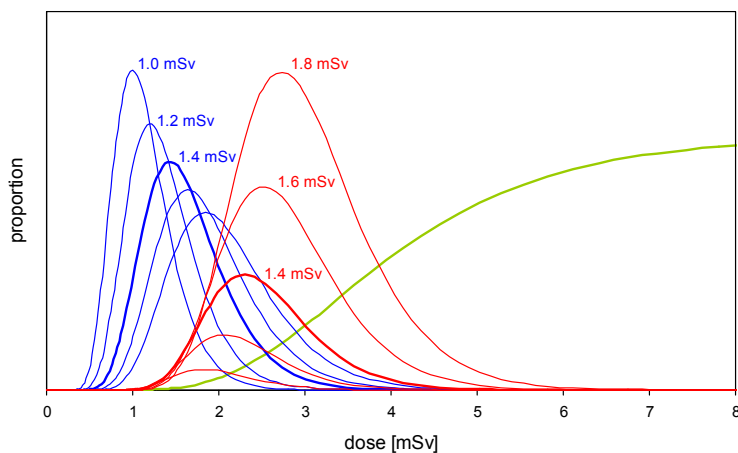
Figure 8.17 *– Numerical calculation of dose effects*

The sum effect is the integral effect of radiation exposure of a population to median dose x is proportional to the area under the red curve. In the following graphs, the results for median doses of 1.0, 1.2, 1.4, 1.6, and 1.8 mSv and σ=0.3 are plotted as a function of dose.
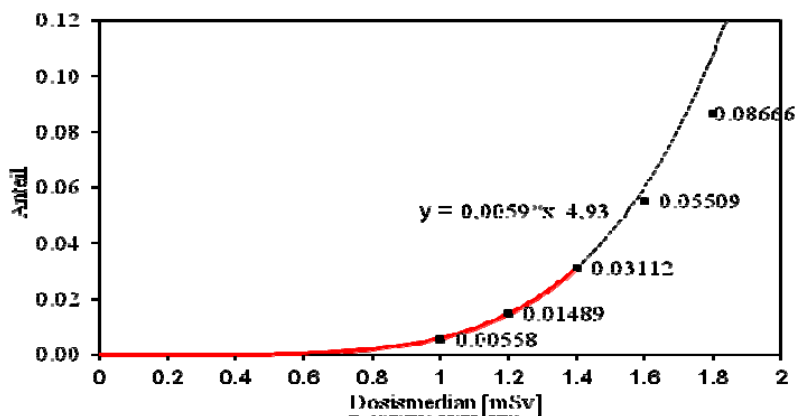
Figure 8.18 - Dose response relationship: Box-Tidwell model: y=x^n (dose to the n-th power)
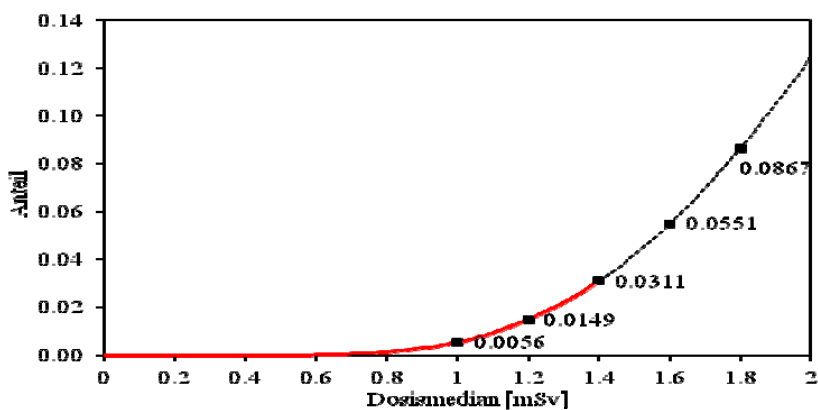
Figure 8.19 - Dose response relationship (Regression model: lognormal distribution function)

	estimate	SE	z-value	p-value
(Intercept)	-1.0600	0.1310	-8.0916	0.0000
ß1	-2.1110	2.7950	-0.7553	0.4501
ß2	13.0610	8.1320	1.6061	0.1082
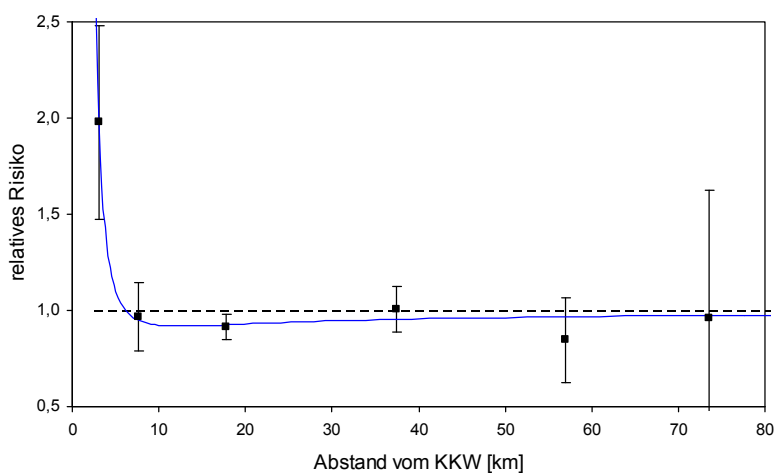
Figure 8.20 - *Linear-quadratic regression model (RR=exp(β1/r+β2/r²))*
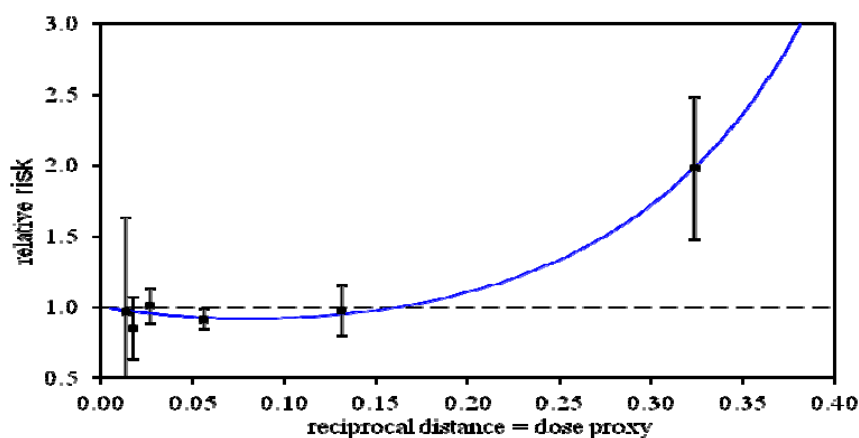
Figure 8.21 - *Linear-quadratic regression model (non linear dose response)*

The mathematical form of the dose-response relationship is a cumulative lognormal distribution function. The only assumption for the calculation is that both the doses and the radiosensitivities are randomly distributed in a population. The present model, together with revised dose estimates, has the potential to explain the size of the increased childhood leukaemia observed near German NPPs.

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Estimation of Residual Radiation Effects on Survivors of the Hiroshima Atomic Bombing, from Incidence of the Acute Radiation Disease

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Abstract : *The effects of exposure due to radioactive fallout on the survivors of the Hiroshima atomic bomb are estimated by analyzing the incidence rates of acute radiation diseases, depilation, purpura and diarrhea, among the survivors. It is found that the effects of radiation exposure due to the fallout exceeds, on the average, the primary radiation effects in people who were beyond about* 1.2 km *from the hypocenter of the Hiroshima bomb. The average effects of radiation exposure from the fallout increases with distance from the hypocenter, reaches a peak at around* 1.2 km*, and then decreases gradually for farther distances but remains even at about 6 km. The peak value of estimated effective exposure from fallout are comparable with that of acute external exposure of gamma ray doses around* 1Gy*. The fact that the effects of residual radiation estimated from the incidence rate of acute diseases are significantly larger than physically measured residual radiation doses suggests that the main effects resulting from residual radiation were caused through internal exposure, especially intake of radioactive small particles among fallout by ingestion and inhalation.*
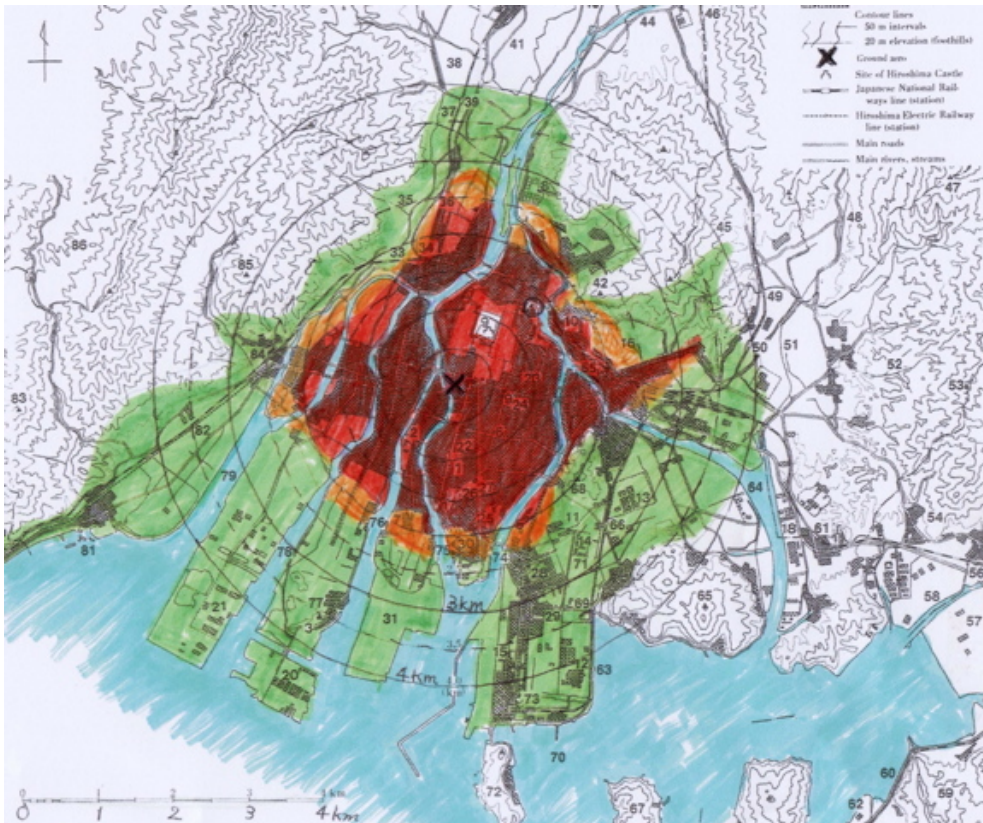
§1 Introduction

Doses of the primary radiation emitted within one minute after from the atomic bombs exploded on Hiroshima and Nagasaki cities are well estimated by the Dosimetry System 2002(DS02) [1] in the regions within 1.2 km from the hypocenter, estimates which are supported by experimental measurements on irradiated materials. On the other hand the residual radiations which were emitted one minute later or more from the bomb explosion have been not clarified well compared to the primary radiation. There are two origins of the residual radiations. One is from the fallout and the other from neutron induced radioactive substances. Estimates of fallout radiation dose that have been made so far are based on measurements of radiation emitted from radioactive matter resulting from radioactive fallout in rain which had been absorbed into soil and retained. However, these measurements had been carried out after a big fire involving the whole of Hiroshima city and also following major typhoon events . It follows that these measurement detected only a

small fraction of the radioactive matter which remained without having been washed away.   Furthermore, unlike the nuclear atmospheric tests, in Hiroshima and Nagasaki radioactive fine particles existed in the fallout, filled the air, were not measured and were carried away by the wind.   In addition, effects of residual radiation resulted from both external and internal exposure through intake of radioactive microscopic particles by inhalation and ingestion.   In general, physical measurements of these exposure effects were not done and quantification through measurement is now difficult.   These facts imply that there are severe limitations for the estimation of the residual radiation doses delivered by the Hiroshima atomic bomb by physical methods.

There have been many investigations related to acute radiation diseases among atomic bomb survivors, both from immediately after the bombing and later on, and all results of these investigations show that acute diseases such as depilation, purpura and diarrhea, etc. appeared even in regions 2 km or more distant from the hypocenter.   The fact that the diseases occurred among survivors who were present in the regions where the primary radiations scarcely reached suggests that they should be explained in terms of fallout radiation.   In order to grasp residual radiation effects comprehensively it is possible to investigate the results of such examinations of acute diseases as well as risks of chronic diseases, frequency of chromosomal aberration, i.e. biological effects caused by radiation exposure among survivors.

If initially the relation between exposed doses and incidence rates of a specific acute disease condition can be determined then it is possible to obtain the effective dose of exposed radiation necessary to cause that condition.   Then by subtracting the primary prompt radiation dose from this resulting effective dose we will obtain the mean effective dose for the condition of interest due to exposure from fallout radiation alone.   This biological dosimetry method will be useful to examine combined effects from both residual external and internal exposure to the survivors.

In this paper, in order to clarify the effects of residual radiation from fallout, the incidence rates of acute radiation diseases among survivors of the Hiroshima atomic bomb are analyzed.   The fact that the calculated effects of residual radiation estimated from the incidence rate of acute diseases are significantly larger than physically measured residual radiation doses suggests that the main effects resulting from residual radiation were caused through internal exposure, especially the intake of radioactive small particles among fallout by ingestion and inhalation as well as external exposure from radioactive particles clinging on skin or clothes. The results of the effects of residual radiation obtained here from the incidence rates

are consistent with studies of frequency of chromosomal aberration and mortality and incidence rates of chronic diseases.

§2   Relation between Incidence Rate of Depilation and Exposed Dose

In this section a relation will be derived between the exposure dose and the incidence rates of depilation, a typical acute radiation disease. Stram and Mizuno[2] first derived a relation between the exposure dose of the atomic bomb primary radiation and the incidence rates of depilation. They employed the results of the Life-Span-Study (LSS) group of the Atomic Bomb Casualty Commission (ABCC, the predecessor of Radiation Effect Research Foundation, RERF) obtained around 1950 for the heavy depilation (above 67 %) which appeared within 60 days after the detonation of the bomb. In Fig. 1 their results are shown by small black circles where the horizontal axis is scaled by the primary radiation dose estimated by the Dosimetry System 1986 (DS86) [3]. As shown in Fig. 1 the incidence rate increases slowly up to 0.85 Gy of the primary radiation dose, then rapidly increases above 1 Gy and exceeds 50 % at around 2.4 Gy. However, beyond 3 Gy the rates do not increase and even *decrease* as dose approaches 6 Gy. This unnatural behavior of the incidence rates in the high dose region can be explained by the fact that the LSS group contains only survivors who could survived though they had exposed near or more of a half-death-dose about 4 Gy as pointed up by Stewart et. al. [4]
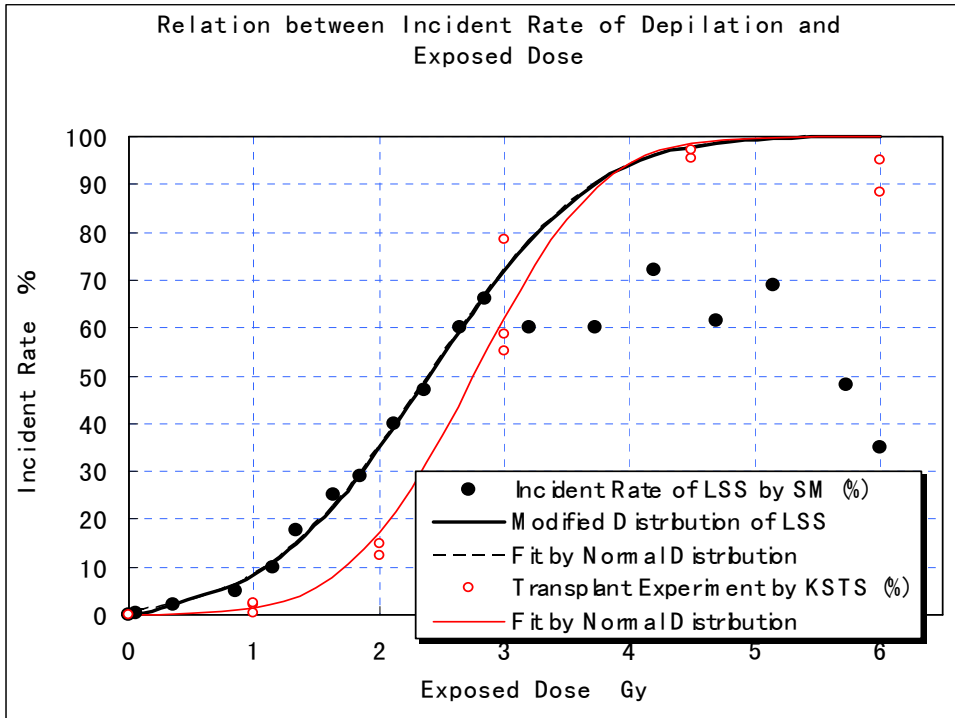
Fig. 9.1 *Relation between incidence rates of depilation and exposure dose. Closed circles are incidence rates of depilation among LSS-Hiroshima group against primary exposure dose obtained by Stram and Mizuno. Full line is the fitted curve of the modified normal distribution to the closed circles below 3 Gy region. Open red circles are incidence rates from the transplant experiment by Kyoizumi et al. The red full line is the normal distribution fitted curve.*

  Incidence rates of depilation shown by open circles in Fig. 1 are those obtained by Kyoizumi et al. [5] by means of radiation exposure to transplantated human head skin onto mice. As seen in Fig. 1 the incidence rates increase very slowly in the low exposure region compared to those given by Stram and Mizuno and increase to 95.5 % and 97 %, almost 100 % at exposure of 4.5 Gy. From experimental studies with animals it is known that most of dose dependence of incidence rates or death rates are represented by a Normal (Gaussian) distribution. The incidence rates given by Kyoizumi et. al. over the whole range of the exposure region can be fitted well by the Normal Distribution with an expectation value of 2.751 Gy and Standard Deviation 0.794 Gy, i.e. N(2.751 Gy, 0.794 Gy), and shown by a solid curve in Fig. 1. The Normal Distribution N(2.751 Gy, 0.794 Gy) will be referred to as the KSTS

relation and adopted as the relation between incidence rates of depilation and exposed dose in the following analysis.

The incidence rates of depilation below the 3 Gy exposure region given by Stram and Mizuno can be fitted by a Normal Distribution N(2,404 Gy, 1,026 Gy) except for the region near zero dose. This Normal Distribution, however, can not reproduce the increase of the incidence rates in the region near zero dose represented by black circles which are rapid in comparison with the KSTS relation. The broken line shown in Fig.1 is generated by the modified normal distribution which is obtained by multiplying another normal distribution function N(0.165 Gy, 0.1155 Gy) to the original normal distribution function N(2,404 Gy, 1,026 Gy). This different behavior of the incidence rates found by Stram and Mizuno from that of Kyoizumi will be explained later by taking account of fallout exposure.

In the following the incidence rates of acute diseases of the region below 1 km from the Hiroshima hypocenter are excluded from analysis because most of people bombed within 1 km were killed and the reported rates are statistically unreliable. Furthermore, the total sums of gamma ray and neutron dose at 1 km are 4.48 Gy from the estimation by DS02, by which the calculated incidence rate attained almost 100 % on the basis of the assumed normal distribution of the KSTS relation.

§3 Estimation of Fallout Exposure from Incidence Rate of Depilation among LSS Group

In this section the radiation exposure effects from the fallout of the Hiroshima bombing are estimated on the basis of incidence rates of depilation among the LSS-Hiroshima group. Preston et al.,[6] reported separately the incidence rates of depilation of Hiroshima and Nagasaki survivors among the LSS group. In Fig. 2. the dependence of the incidence rates of depilation of 58,500 Hiroshima survivors among the LSS on distance from the hypocenter is shown by squares. The incidence rate of 100% at 0.75 km is scaled out of the frame. The black circles and a dashed line in Fig. 2 for the primary radiation dose dependence are translated into distance dependence by use of the DS86 estimation neglecting shielding effects and are plotted by black diamonds and a broken line. If the shielding effects are taken into account the diamonds shown in Fig. 1 will move to left toward hypocenter and the difference between the squares will increase. In the following it is assumed that the systematic difference between squares and diamonds shown in Fig. 2 represents exposed effects from fallout radiation.

In the analysis of the incidence rate of depilation it is assumed that the total exposed dose $D(r)$ at distance r km from hypocenter is given by a sum of the primary radiation exposure $cP(r)$ with shielding effects represented by a parameter c and exposure $F(r)$ from fallout radiation as

$$D(r) = cP(r) + F(r). \qquad\qquad (1)$$

The formula for exposure from fallout radiation $F(r)$ is assumed as

$$F(r) = a\, r \exp(-r^2 / b^2) + d \qquad\qquad (2)$$

where parameters a, b, and d represent magnitude, extension and distance independent component of fallout exposure effects, respectively. Theoretical incidence rates are calculated from the exposure dose $D(r)$ given in (1) by use of the KSTS relation between incidence rate and exposed dose. A set of four parameters in (1) and (2) is determined so that the χ^2 value takes minimum which represents fitness of the calculated incidence rates to those of LSS group and obtained as $c = 0.522$, $a = 0.808$ Gy/km, $b = 2.062$ km, and $d = 0.786$ Gy. The resulting fitted incidence rates are shown by a bold line in Fig. 2.
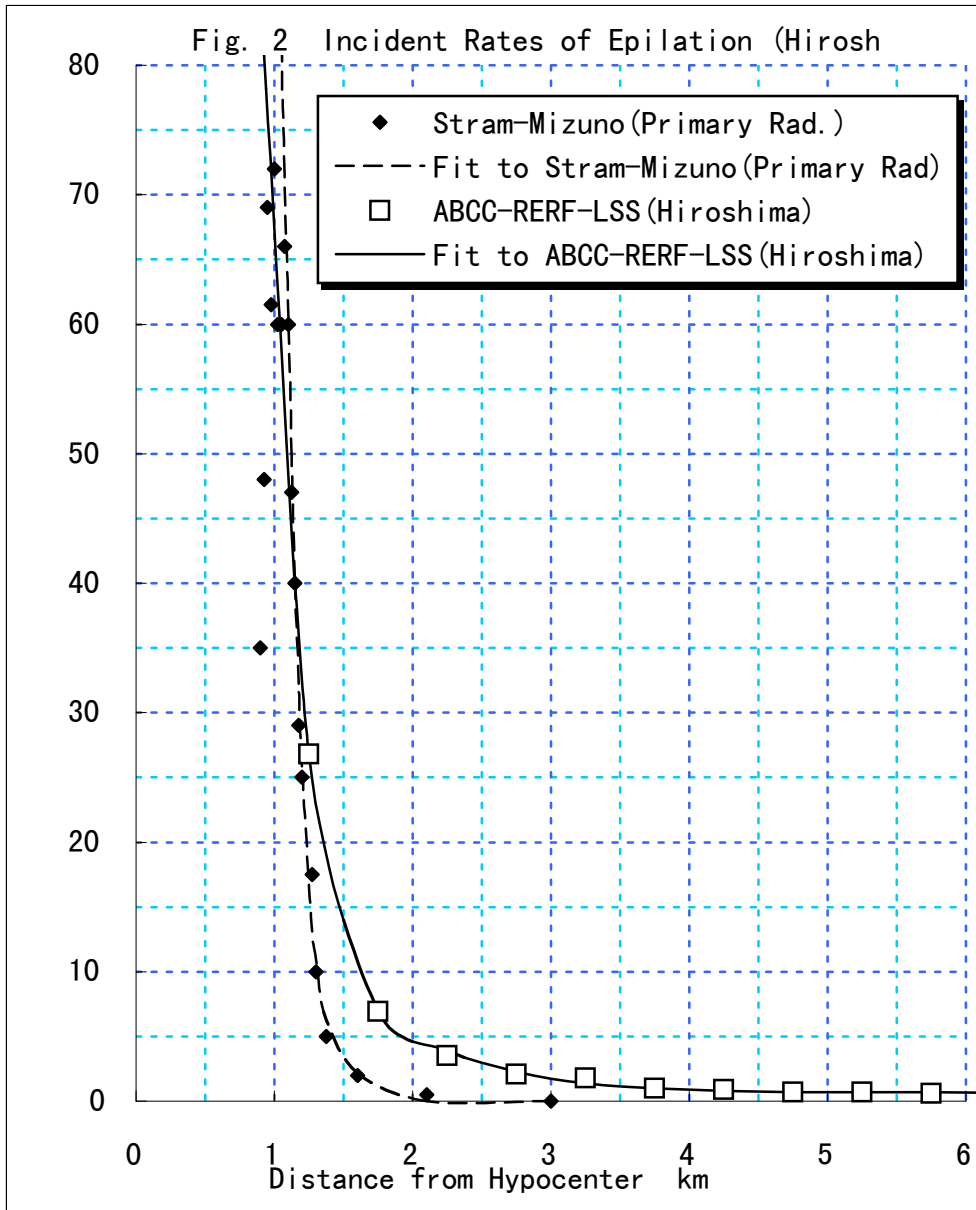
Fig9.2. *Incidence Rates of Depilation of LSS Hiroshima. Squares indicate the incidence rates of depilation among Hiroshima survivors of the LSS. Full line shows the curve fitted by formula (1) and (2) with the minimum value of χ^2 of about 10 which is below 14.1, the lower limit of 5% of rejection area of χ^2 distribution of freedom degree (FD) 7. Black diamonds shows the approximate incidence rates corresponding to the primary radiation.*

The doses of total, primary and fallout exposure, $D(r)$, $cP(r)$ and $F(r)$, with the obtained parameter set are shown by a bold dashed curve, a thin dashed curve and a bold solid curve, respectively and the primary doses estimated by DS02 are also shown by a thin solid line in Fig. 3. As seen in Fig. 3, the effects of fallout exposure increases with distance from hypocenter up to 1 km, but this has large ambiguity because the incidence rates in the region below 1 km were not employed in the present analysis. Exposure from the primary radiation rapidly decreased with distance from the hypocenter and at about 1.2 km the fallout effects cross over that of primary radiation. The estimated exposure from fallout radiation reaches about 1.5 Gy at around 1.45 km then decreases slowly. Beyond 4 km the exposure effect of fallout takes an almost constant value of 0.79 Gy. This result from the incidence rates of depilationm, one of the actual accepted and universally agreed conditions of the bombed survivors, indicates overwhelming effects of fallout beyond about 1.5 km from the hypocenter of Hiroshima. For example at 2.25 km and 2.75 km from hypocenter the dose estimation of the primary radiation by DS02 are 0.0302 Gy and 0.0053 Gy while the incidence rates of depilation among the LSS-Hiroshima at these distances are 3.5 % and 2.1 %. The estimated fallout exposure effects from these incidence rates is 1.34 Gy and 1.16 Gy, about 44 and 219 times of the DS02 primary radiation.

   The maximum cumulative exposure from fallout of the Hiroshima bomb has been considered hitherto between 0.006 and 0.02 Gy in the Koi-Takasu region mentioned in the DS86 report and which are shown by cross marks in Fig.3. These absorbed doses were obtained from measurement of radiation from fallout matter retained in the soil of these regions which are located between 2 and 4 km to the west of the hypocenter where light radioactive fallout rain fell but heavy rain caused by the big whole city fire did not. As seen in Fig.3 exposure from fallout estimated from depilation incidence rates in 2 to 4 km region are 1.4 Gy to 0.85 Gy which are 40 to 230 times of physically obtained values. This large discrepancy suggests that the physically measured values are only measurements of a part of fallout and that large effects of internal exposure should be taken into account which can be deduced only by the biological methods.
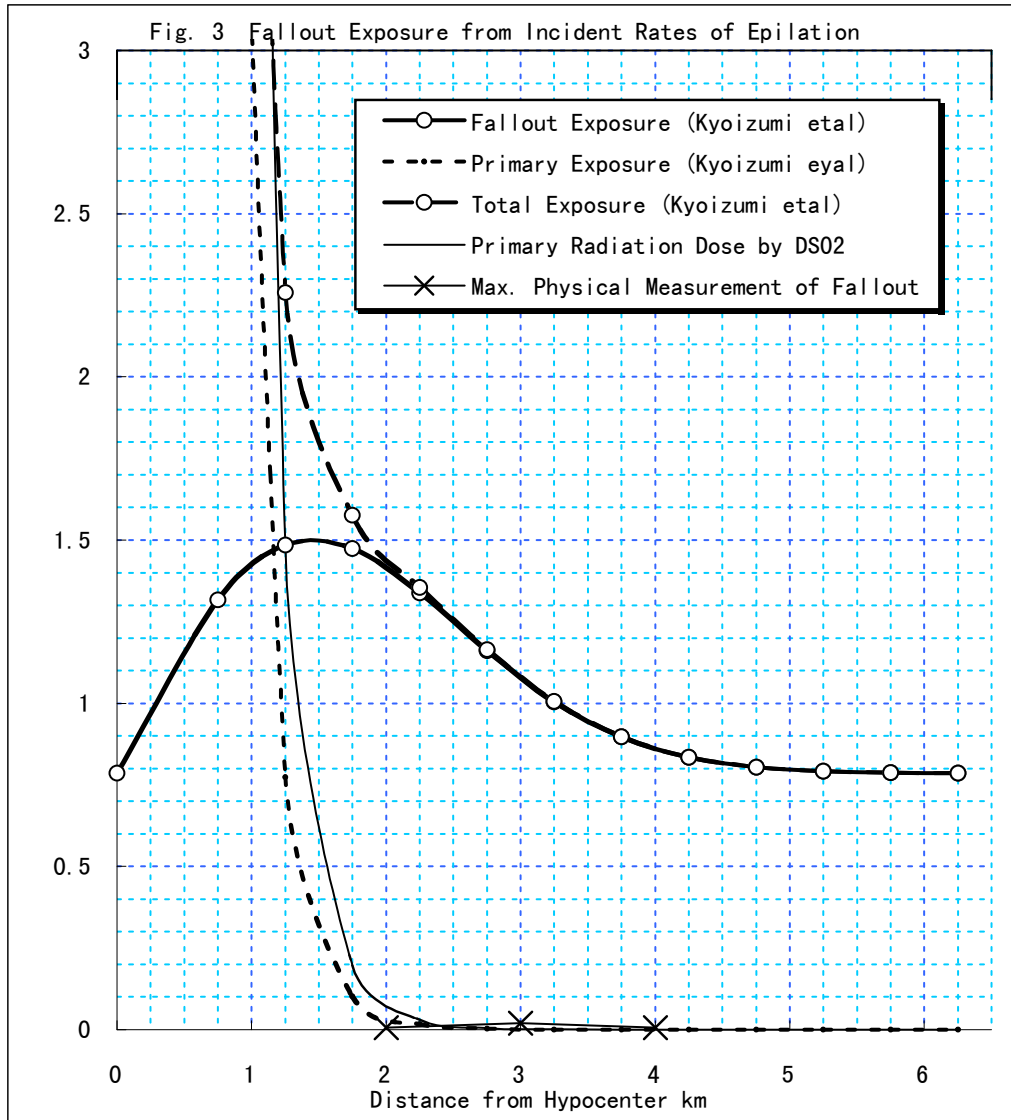
Fig.9. 3 *Exposure doses(Gy) estimated from the incidence rates of depilation among the LSS Hiroshima group. Total, primary and fallout exposures are given by bold dashed, bold full and thin dashed lines, respectively. The primary radiation absorption dose is estimated by DS02 and is shown by thin full line. Physically measured maximum exposures from fallout at Koi-Takasu region are shown by cross marks.*

The values obtained here are average exposures in the same distant regions from the hypocenter irrespective to directions. It is supposed that the fallout fine particles

were moved toward northwest direction by wind. To clarify these effects it is necessary to carry out a direction dependent analysis.

§5   Estimation of Fallout Exposure from Incidence Rates of Depilation Other Examinations than LSS

 In Fig. 4 incidence rates of depilation examined by the Joint Commission for the Investigation of the Atomic Bomb[7] and Tokyo Imperial University[8] in 1945 and investigated by O-ho[9] in 1957 are shown together with those of LSS-Hiroshima. In investigation by O-ho, all survivors were classified into four types according to whether they were exposed indoors or outdoors and did or did not enter within 3 months into the central region within 1 km from the Hiroshima hypocenter. The O-ho examination of the No Entrance case is very important because the exposures from the induced radioactive matter in the central region were not included.

   Except for two incidence rates at 2 km and 4 km*[1] by O-ho all the examined incidence rates of depilation among the Hiroshima survivors almost coincide with each other indicating the reliability of all these investigations. That the rates of the LSS-Hiroshima between 1.75 km and 2.75 km are slightly lower systematically than the others may be explained by the fact that in the LSS examination depilation is defined as only heavy depilation with 67% loss of hair within 60 days from atomic bombing.

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*[1] These data at 2 km and 4 km given by O-ho are omitted in the χ^2 fitting.

Fig. 4.   Incident Rates of Epilation (Hiros
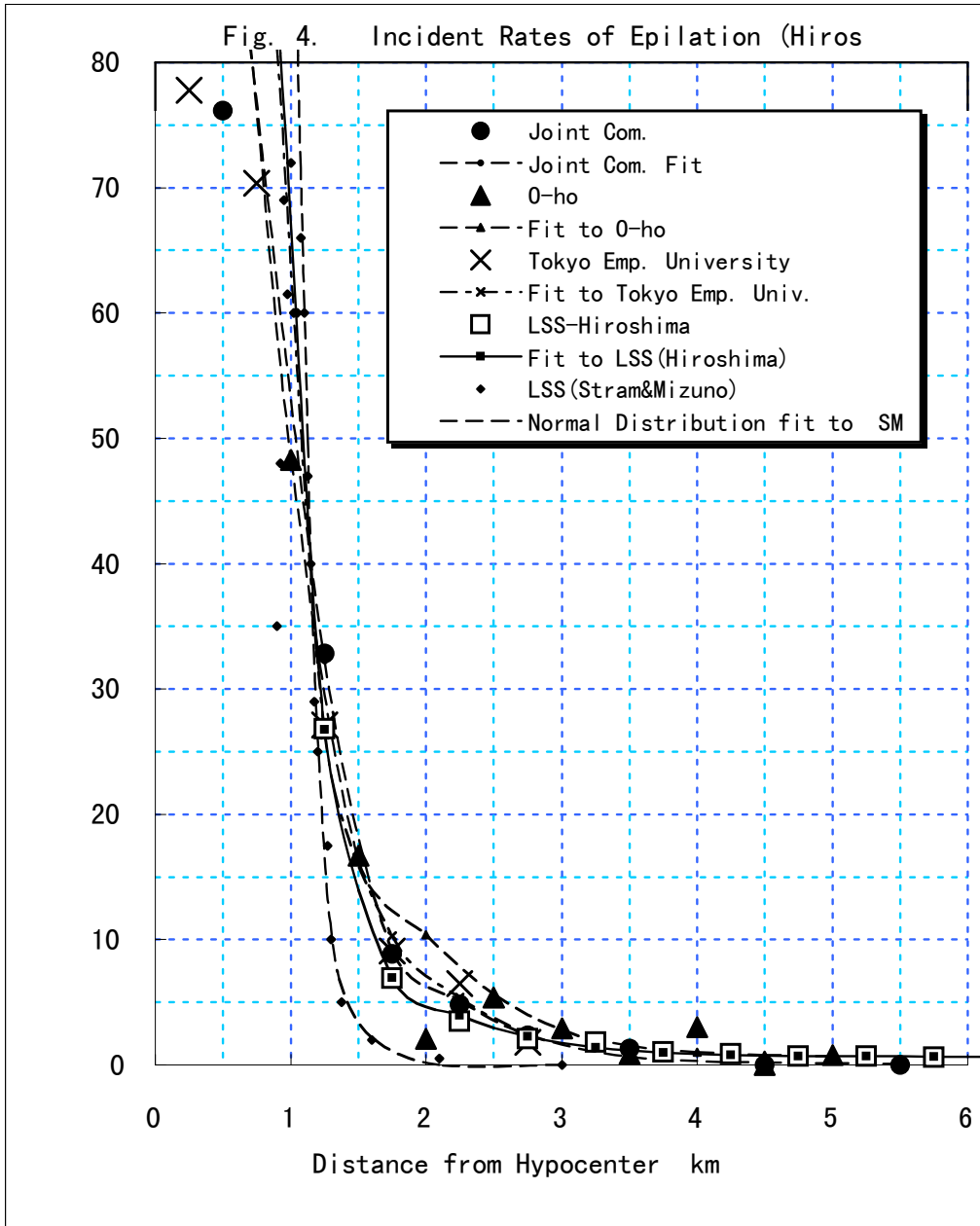
Fig.9. 4 *Incidence Rates of Depilation among Hiroshima Survivors.   The marks □, ●, × and ▲ are incidence rates examined by ABCC, the Joint Commission, the Tokyo Imperial University and O-ho, respectively. The χ^2 values fitted to Joint Com. and Tokyo Imp. Univ. examinations are 4.2 and 5.6, respectively, compared to 6.6, the lower limit value of 1% risk region of χ^2 distribution of DF 1 and fitted to O-ho case is 3.3 compared to 9.2, the lower limit of 1% risk region of of χ^2 distribution of DF 2.*

The same fitting method used in the LSS group is applied for these incidence rates of depilation. The resulting sets of parameters from application of formulae (1) and (2) are given in Table I. The fitted incidence rates curves are shown by thin dashed lines in Fig. 4. The calculated doses of total, primary and fallout exposure, $D(r)$, $cP(r)$ and $F(r)$, obtained by fitting to the reported incidence rate curves of depilation are shown by a bold dashed curve, a thin dashed curve and a bold solid curve, respectively in Fig. 5.

Table 9. I   Parameters in formulae (1) and (2) of exposed doses from incidence rates of depilation examined ABCC, Joint Commission, Tokyo Imperial University and O-ho.

	primary rad. exposure $cP(r)$	fallout radiation exposure $F(r)$		
	c shielding effect	a (Gy/km) magnitude	b (km) extension	d (Gy) constant part
ABCC LSS-Hiroshima (heavy depilation)	0.522	0.808	2.06	0.786
Joint Commission (outdoors or Japanese house)	0.600	1.272	2.34	0.300
Tokyo Imperial University (outdoors and indoors)	0.390	1.330	2.11	0.501
O-ho (indoors, no entrance into central region)	0.226	1.166	2.06	0.751

Fig. 9.5 *Estimation of exposures from incidence rates of depilation among the Hiroshima survivors. Total, primary and fallout exposures are shown by bold dashed lines, thin dashed lines and bold full lines, respectively. Marks ○, , and □ indicate examined by ABCC, Joint Commission, Tokyo Imperial University and O-ho.*

The peak values of exposure by fallout are found to lie between 1.58 Gy and 1.78 Gy slightly higher than that of the LSS as expected from the small difference among incidence rates. In the region beyond 3 km from the hypocenter the fallout exposure estimation from O-ho's incidence rates is almost similar to those from the LSS. A rapid decrease of fallout exposure dose is seen beyond 3 km in the case of the examination by the Joint Commission, where incidence rates of depilation in the region 4·5 km and beyond 5 km are zero based on very few survivor examination compared with LSS.

§6 Comparison of Fallout Exposure Estimated from Incidence Rates of Three Different Acute Diseases

In the following it will be examined whether the incidence rates of three different acute diseases, depilation, purpura and diarrhea can be explained by the same exposure dose or not. The incidence rates of depilation, purpura and diarrhea among Hiroshima survivors who were exposed indoors and did not enter the central region examined by O-ho[9] are shown in Fig. 6. As is seen in Fig. 6 incidence rates of purpura shown by closed circles are of similar behavior to those of depilation shown by squares. Then for the incidence rate-exposure relation of purpura the same normal distribution of depilation is used. Incidence rates of diarrhea shown by triangles are very large compared to depilation or purpura in the distant regions beyond 1.5 km where the fallout exposure gave significant effects. The incidence rates of diarrhea were rather small in the short distance regions where the primary radiation exposure dominated. Therefore in the case of diarrhea, a larger expectation value for the normal distribution than those of depilation and purpura is required for external exposure from the primary radiation and smaller expectation value is required for the fallout exposure. The adapted expectation values and standard deviations are listed in Table II and were obtained by multiplying the ratios shown there. By use of the normal distributions with expectation values and standard deviation given in Table II the incidence rates of depilation, purpura and diarrhea in Fig. 6 are fitted and the resulting incidence rates are displayed by thin dashed, solid and chain curves for depilation, purpura and diarrhea, respectively whose parameters of formulae (1) and (2) are listed in Table III.

Table 9. II Normal distributions of incidence rate-exposure dose relations of acute radiation diseases

acute disease		ratio	expectation value (Gy)	standard deviation (Gy)
depilation		1	2.751	0.794
purpura		1	2.751	0.794
diarrhea	primary radiation	1.1	3.026	0.873
	fallout exposure	0.72	1.981	0.572

Table 9.III Parameters in formulae (1) and (2) of exposed doses from incidence rates of depilation, purpura and diarrhea

	primary rad. exposure $cP(r)$ c shielding effect	fallout radiation exposure $F(r)$		
		a (Gy/km) magnitude	b (km) extension	d (Gy) constant part
Depilation(1,0.52)	0.5 (fix)	0.984	2.07	0.855
Purpura (3, 3.2)	0.5 (fix)	0.995	2.36	0.713
Diarrhea (5,12.7)	0.511	0.959	2.37	0.743
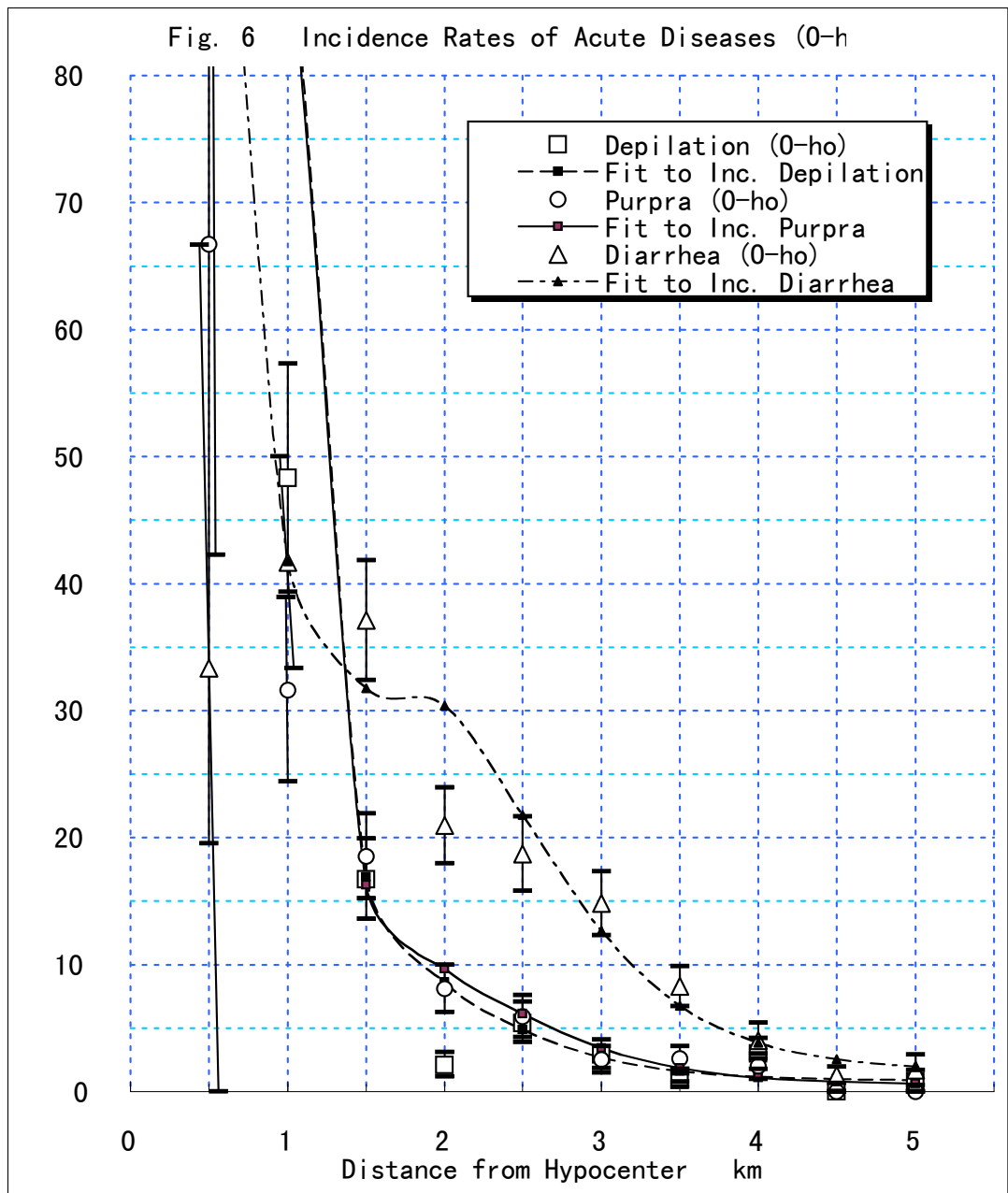
Fig. 9.6 *Incidence rates of acute diseases among survivors who were exposed indoors and did not enter into the central region within 1 km from the hypocenter within 3 months. Marks □, ○ and indicate incidence rates of depilation, purpura and diarrhea, respectively. Full line, dashed line and chain line are fitted curves to the incidence rates of depilation, purpura and diarrhea with χ^2 values 0.52, 3.2 and 13.3 compared to 9.5, 12.6 and 16.9, the lower limit of 5% rejection area of χ^2 distribution of FD of 4, 6 and 9, respectively.*

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In this analysis of depilation and purpura the shielding effect parameter c is fixed to 0.5 and the data of incidence rates of these diseases at 1 km are omitted because if these data of depilation and purpura are used, unnaturally small values of c, 0.22 and 0.23 are obtained. These unnatural small values at 1 km may be explained by a similar reason appeared in the incidence rates of depilation among the LSS in the large exposed region given by Stram and Mizuno i.e. many died.

The results of exposure doses calculated from the calculated parameters listed in Table III are shown in Fig. 7. As seen in Fig. 7 incidence rates of three entirely different acute diseases are reproduced with high accuracy by almost similar exposure doses. This fact tell us that depilation and diarrhea as well as purpura occurred in the regions where the primary radiation could scarcely reach and were caused by fallout radiation not by mental shock nor by poor sanitary conditions.

The fact that the expectation value of the normal distribution of diarrhea incidence is small for fallout exposure while large for the primary exposure can be explained by means of difference between external and internal exposures as follows. In the case of fallout exposure radioactive fine particles and radionuclides with specific affinity for biological materials and tissues among fallout were taken into body, reached directly to intestinal wall and were retained there for a period of time. Then the emitted radiation of weak penetration power gave dense ionizations and caused heavy damages in the thin membrane and diarrhea followed. The exposure was chronic as the particulate and chemical radioisotopic material (e.g. Sr-90, Cs-137) was retained for some time. On the other hand in the instantaneous acute primary radiation exposure case only strong penetrative radiation such as gamma ray could reach from outside of body to intestinal wall but passed away through thin membrane leaving scarcely any damage.

Fig. 7 Exposed Doses from Acute Diseases (O-ho)
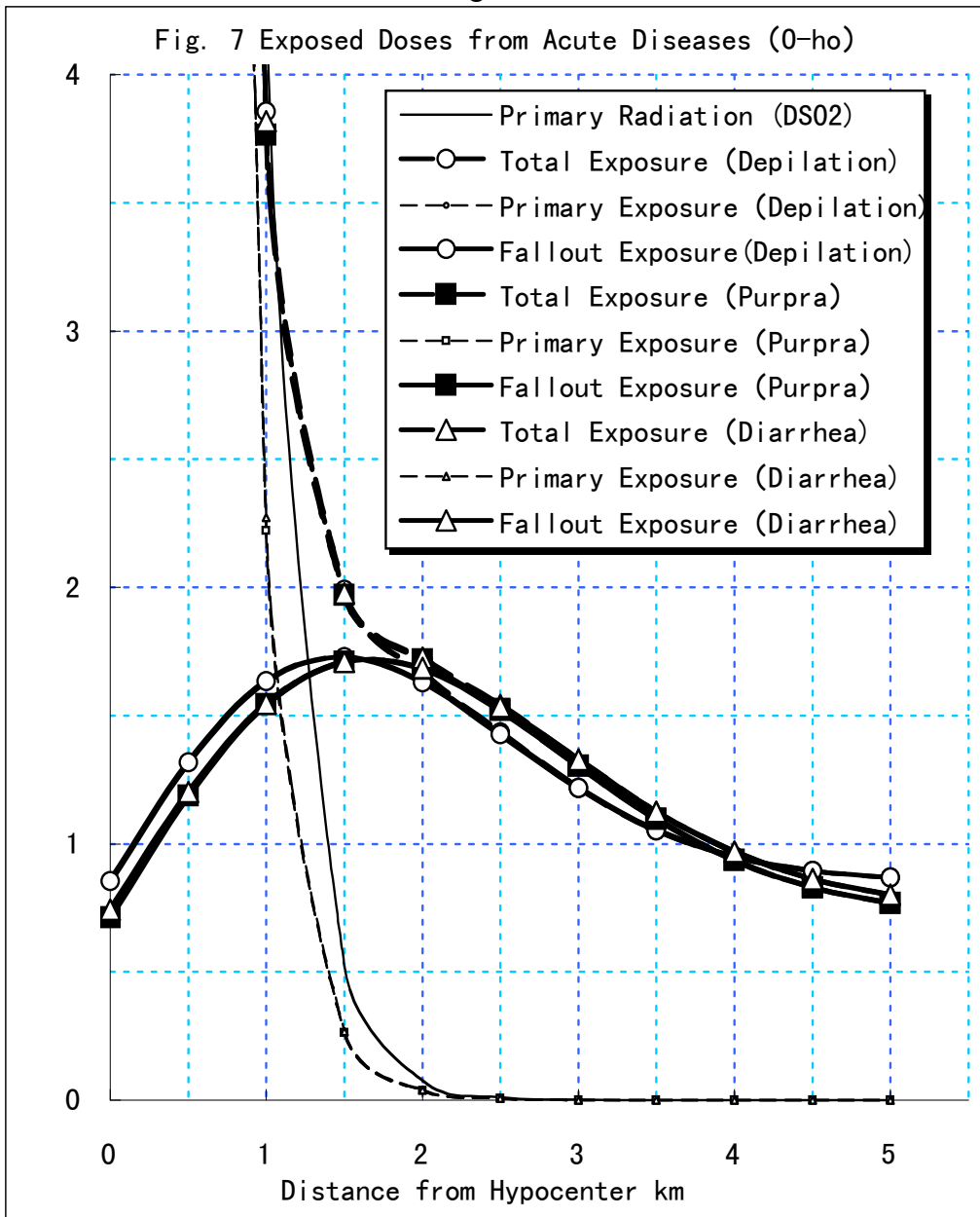
Fig. 9.7 Exposed doses from acute diseases. Attached marks ○, ■ and indicate estimations from incidence rates of depilation, purpura and diarrhea. Total, primary and fallout exposure are specified by bold dashed, thin dashed and bold full lines, respectively. The primary radiation dose given by DS02 is represented by thin full line.

§7 Summary and Discussion

As described in the foregoing sections the exposure effects of fallout of Hiroshima atomic bombing estimated from incidence rates of acute diseases among survivors are very large and extended to a wide area. Exposure effects of fallout radiation were greater than the effects of primary prompt radiation beyond about 1.2 km from the hypocenter and decreased slowly with distance remaining about 0.7・0.8 Gy even at 6 km. The maximum exposure effects from fallout 0.02 Gy at Takasu, the special region located at 3 km west from the Hiroshima hypocenter were obtained from physical measurement of radiation emitted from radioactive nuclei brought by fallout rain and retained in the soil. Fallout exposure effects estimated from acute diseases lie between 1.1 Gy and 1.3 Gy at 3 km distant from the hypocenter irrespective of direction from the hypocenter. This large difference between physical measurement and biological estimations of fallout exposure imply that the main exposure effects were either caused by fallout fine particles widely distributed resulting in internal exposure due to their intake or to a error in the currently accepted radiobiological effectiveness of certain ingested or inhaled isotopic components of the fallout.

Since the various examinations of incidence rates of acute radiation induced diseases analyzed here give almost the same results on fallout exposure then the greatest ambiguity of exposure doses obtained will arise out of an ambiguity of the relations between the incidence rates and exposure dose used here, that is, ambiguity of the expectation values and values of the standard deviation of the generated normal distributions. However, if the fallout radiation exposure of 1.0 to 1.5 Gy obtained here is added to the primary prompt radiation exposures in the region between 1 Gy and 3 Gy corresponding to exposure distances between 1.0 km and 1.2 km and added to incidence rates of depilation of about 10 %, which corresponds to the difference between the solid line and the broken line in the region between 1km and 1.2 km in Fig. 2, then the broken line in Fig. 1 shifts to the higher dose direction and higher incidence rate direction and almost overlaps with the full line obtained by Kyoizumi et al. The unnaturally rapid increase of incidence rate of depilation in near zero dose region of the Stram-Mizuno relation shown in Fig. 1 can be correlated to the decreases of incidence rates in the region between 1.5 km and 3 km distant from the hypocenter where the primary radiation exposures were between 0 to 1 Gy. This fact supports the conclusion that the relation between the incidence

rates and exposure dose among survivors is not much different from those used here on the basis of the relation given by Kyoizumi et al.

The results obtained here do not contradict results of investigations of chromosomal aberration among survivors. The frequency of chromosome aberrations in circulating lymphocytes of survivors of the Hiroshima bombing was compared with 11 non-irradiated healthy controls visiting the Japan Red Cross Central Hospital in Tokyo between April 1967 and March 1968 by Miyata and Sasaki[10]. It was found that more than 1.6 km from the hypocenter, the effects of exposure from fallout estimated from frequency of chromosomal aberration exceeded that of primary irradiation. If we note that the estimated dose based on the frequency of chromosomal aberrations in circulating lymphocytes represents the effects averaged over the whole body and that local effects from insoluble radioactive particles or other internal isotopic exposures which are considered in the incidence rates of acute diseases, are not included, then the present results from acute diseases do not contradict to that obtained from chromosomal aberration.

Present results from incidence rates of acute diseases also do not contradict to the similar results of investigation obtained from chronic after effects in the LSS of RERF. Schmitz-Feuerhake[11] had obtained the standard relative risks, mortality ratios, and incidence rates of various diseases in the LSS control groups, who were exposed to less than 0.09 Gy according to the 1965 tentative dosimetry system(T65D), compared with all Japanese. The standard risks for mortality from all causes and all diseases are less than unity (this was in the early 1980's results of survivors but are now almost unity or slightly larger than unity) indicating that control cohort of LSS were healthier than the Japanese average. However, the high relative risk of death from leukemia and cancer of the respiratory system and the incidence of thyroid and female breast cancer in the control group show that they had been affected by fallout radiation. Recent study by Watanabe et al. [12] on the mortality of the LSS Hiroshima group from all diseases and various cancers compared with those of all inhabitants of Hiroshima prefecture and with those of all Okayama prefecture, a neighbor prefecture of Hiroshima, indicates comparable effects of fallout exposure with the present estimation among extremely low exposure groups (exposed from primary radiation less than 0.005 Sv) and low exposure groups (exposed from primary radiation between 0.005 Sv and 0.1 Sv) of the LSS.

By the use of the same method employed here similar effects from the residual radiation exposure can be estimated for the survivors of Nagasaki as well as for the

'entrant survivors' who were entered into regions about 1 km from the hypocenter after the explosion of atomic bomb and who were exposed to residual radiation emitted by induced radioactive matter. The estimated results from these cases will be reported elsewhere.

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11) I. Schmitz-Feuerhake, I., Health Phys. 44, 693-695 (1983); Schmitz-Feuerhake, I., & Carbonell, P., Publication SM-266-23. Vienna:IAEA, 45-53 (1983).

12) T. Watanabe, M. Miyao, R. Honda and Y. Yamada; Environ Health Prev Med., Vol. 13, No.5(2008).

Editor's note:

Prof Sawada also spoke at the conference about Nagasaki and gave some slides.

These are reproduced below:

Nagasaki effects

大村湾　大村湾

時津田　諫早市

.1

.5

東長崎地区　2.0

飯盛町

爆心地　西山地区

18　20Bq　10Bq　5Bq　2Bq

日見地区

長崎湾

茂木地区　橘湾

1.2
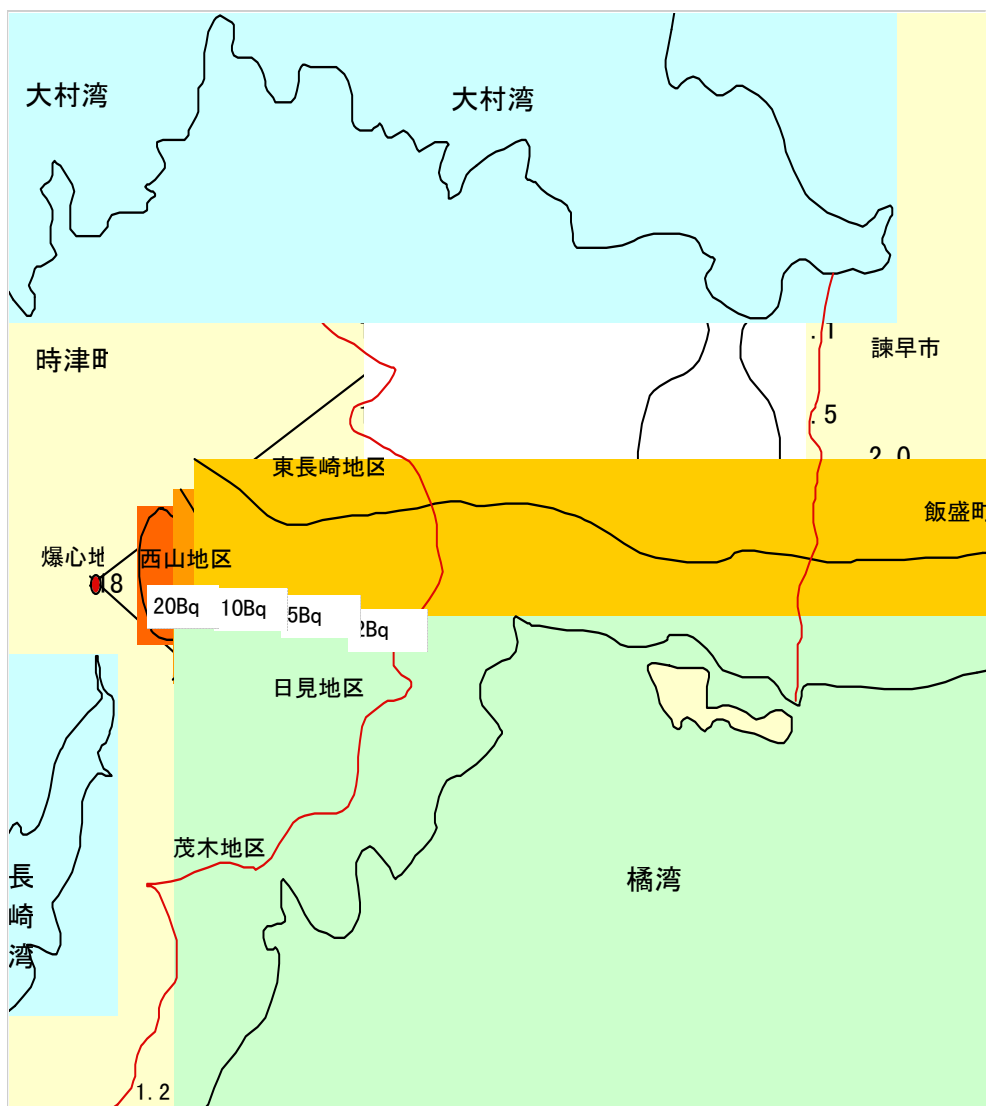
Figure 9.8 - *Measurement of Pu239 in soil brought by fallout rain of Nagasaki bomb (Bq/kg soil)*

In Nagasaki, as opposed to in the contamination after Hiroshima, the fire rain was much less powerful. As a result, the radioactive fallout matter did not wash out*.*
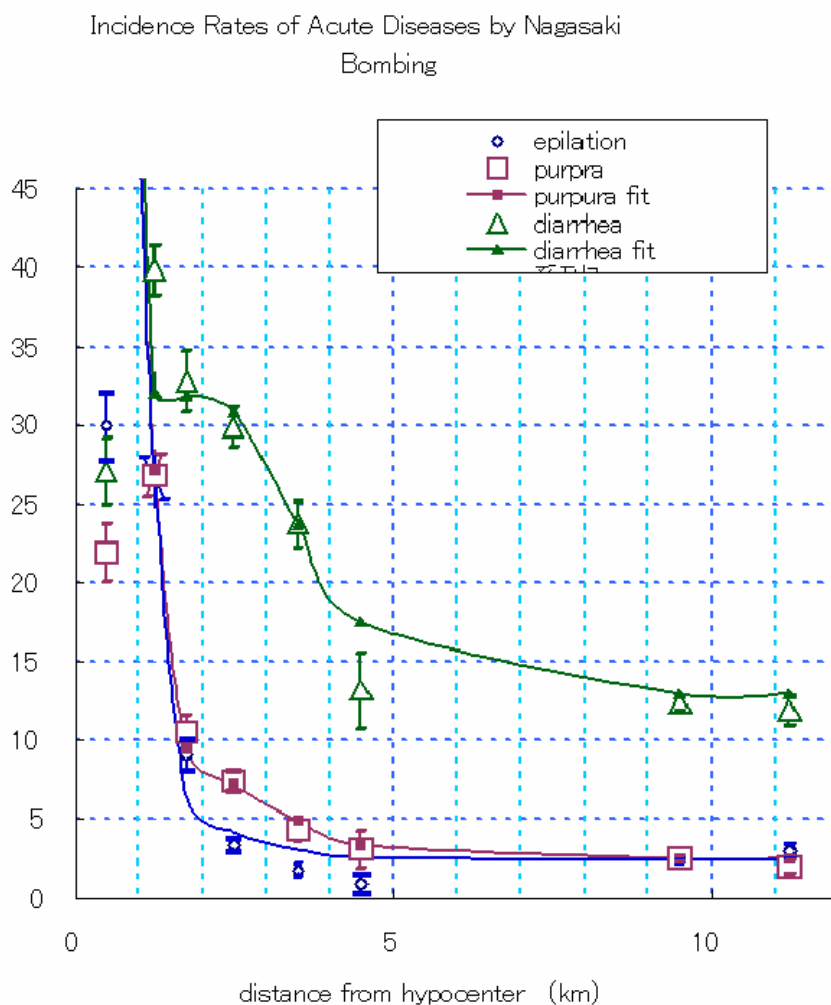
Figure 9.9 - *Estimation of Exposure due to the Fallout of Nagasaki Bomb in terms of Incident Rate of Acute Radiation Disease*

Combined Analysis of Examination of Acute Diseases for Nagasaki City (<4.5 km) by Nagasaki Medical College 194. For Enlargement of Designated Region of A-Bombing. Peripheral of Nagasaki City (Av. 9.5 km) by Government of Nagasaki City. Surroundings of Nagasaki City (Av. 11.3 km) Local Gov. Town & Village)

In Figure 9, the closed circles, squares and triangles show incident rates of epilation, purpura and diarrhea, respectively as the acute diseases among survivors of Nagasaki city (< 4.5 km from the hypocenter) examined in 1945 by the Nagasaki Medical College and those incident rates examined by the local government of

Nagasaki City (average distance is 9.5 km from the hypocenter) and surrounding towns and villages of Nagasaki (average distance is 11.2 km from the hypocenter) which were published in 2000.
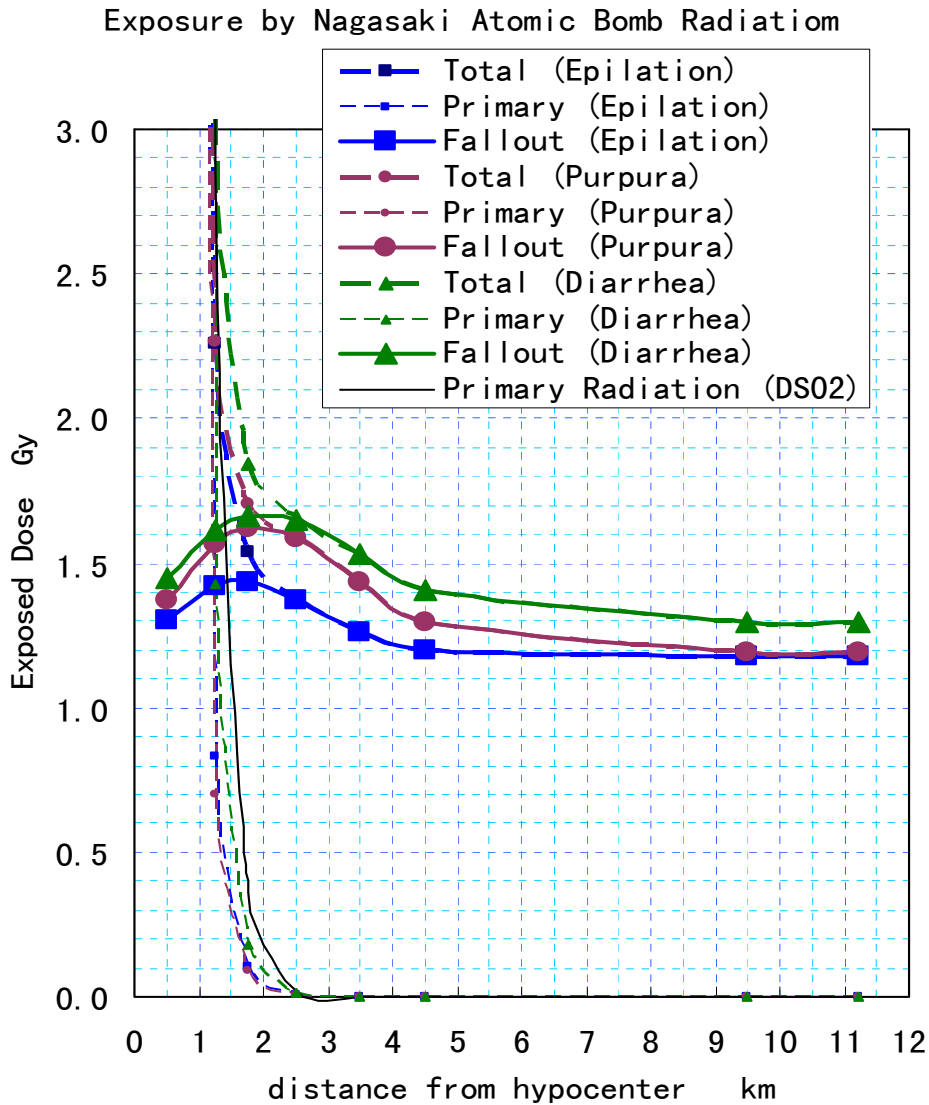
Figure 9.10 – Exposure to the Nagasaki bomb radiation

The peak values of fallout radiation dose is, about 1.4 Gy at 1.7 km for epilation 1.6 〜1.7Gy at 2.0 km for purpura and diarrhea, respectively. It should be noticed here that the fallout exposed dose decrease until about 5 km from the ground zero but

then become flat with constant values about 1.2～1.3 Gy which continue toward examined distance about 12 km.

On the basis of the dose-incident rate relations given, I analyze the combined data of incidence rates of acute diseases and obtained the results summarized in Figure 12. The full lines with closed circles, open squares and triangles are corresponded to the estimated doses from the incident rate of epilation, purpura and diarrhea, respectively. As shown the obtained exposure dose F(r) from fallout exceed those of from the primary radiation cP(r) in the region more distant 1.2 km from the hypocenter. The peak values of fallout radiation dose F(r) about 0.8 Gy at 1.3 km, 0.95 Gy at 1.7 km and 0.8 Gy at 2.0 km for epilation, purpura and diarrhea, respectively. It should be noticed here that the F(r) decrease until about 5 km from the hypocenter but then become flat with constant values about 0.5 Gy which continue toward examined distance about 12 km.
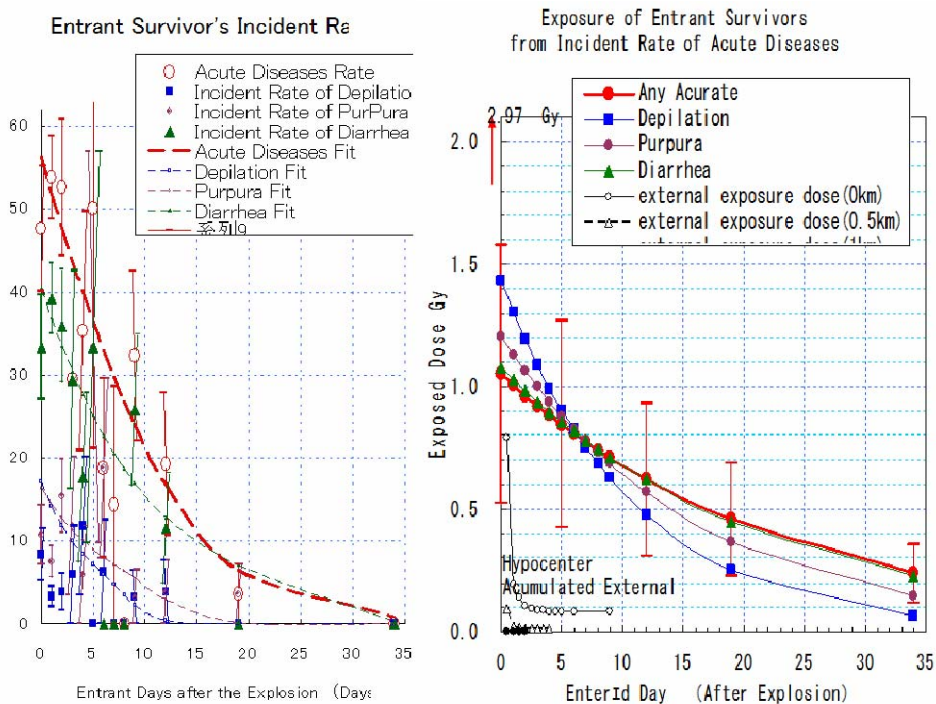
Figure 9.11 – Entrant survivor exposures

10

Risk assessment of radiation-induced stomach cancer in the population of Belarus

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Abstract

Results of analysis of the incidence in stomach cancers in the Belarusian population are described in the present report. They were established by using a modified ecological method based on the analysis of temporal patterns of the crude incidence in stomach cancers in different regions of Belarus in 1970-2006. It was found that approximately 2047 additional stomach cancers appeared in Belarus in 1991-2001 (95% CI from 1,472 to 2,630 cases). The number of stomach cancers registered in Belarus in this period is about 42,587 cases (40,540 expected cases).

The performed analysis shows that the numbers of additional stomach cancers manifested in different regions of Belarus are proportional to collective equivalent doses of the whole body irradiation delivered as a result of the Chernobyl accident and the relative risk, RR, is a linear function of the population dose of the whole body irradiation caused by this accident. These findings indicate that additional stomach cancers manifested in regions of Belarus after the accident at the Chernobyl NPP .were caused by radiation.

Assuming radiation origin of additional stomach cancers time-averaged radiation risks were assessed for the period 1991-2001 in the report. According to assessment the relative risk, RR, estimated for the entire Belarusian population is 1.050 (95% CI from 1.036 to 1.065). The excessive absolute risk of stomach cancers, EAR, averaged for this period is assessed as 85 cases per 10^4 PYSv (95% CI from 60 cases to 110 cases per 10^4 PYSv). The averaged excessive relative risk, ERR, is estimated equal to 2.4% per 1 mSv (95% CI from 1.7 to 3.1% per 1 mSv) and the averaged attributive risk, AR, is assessed equal to 5.0% (95% CI from 3.6 to 6.5%).

Introduction.

The accident at the Chernobyl NPP caused a quasi-acute irradiation of the thyroid gland and a long-term irradiation of the whole body of affected populations.

According to assessment [1] the collective equivalent dose of the thyroid gland irradiation delivered as a result of the Chernobyl accident to the Belarusian population could reach 1.3 Million PGy. This gives the population dose of the thyroid gland irradiation of the entire Belarusian population equal to 130 mGy. This is comparable with arithmetic mean dose of the thyroid gland irradiation of atomic bomb survivors [2]. Individual thyroid doses of the Belarusian children exceeded in some cases 60 Gy [3]. Doses of the whole body irradiation of the Belarusian population are much less than doses of the thyroid gland irradiation. For comparison, the highest dose of the whole body irradiation in Belarus is not higher than 1,500 mSv [4]. This is by factor 40 less than the maximal dose of the thyroid gland irradiation in Belarus. The same relation exists between the collective equivalent doses of the thyroid gland and the whole body irradiation in Belarus as well as in other affected countries including Ukraine and Russia.

High doses of the thyroid gland irradiation caused in Belarus manifestation of radiation-induced thyroid cancers already some years after the Chernobyl accident [5-7].

Reliable data found by Russian, Belarusian and Ukrainian specialists for liquidators and people living in areas with high level of contamination demonstrate also manifestation of medical effects other than radiation-induced thyroid cancers among populations affected as a result of the Chernobyl accident.

In case of Belarusian liquidators a statistical reliable manifestation of radiation-induced thyroid, urinary bladder, lung and stomach cancers has been established [8]. The similar findings were also established for Russian and Ukrainian liquidators [9-13].

Manifestation of radiation-induced malignant neoplasms among Belarusian, Russian and Ukrainian liquidators can be considered as some indirect evidence of manifestation of radiation-induced cancers also among inhabitants of contaminated regions of Belarus, Russia and Ukraine because radiation risk of this category of affected people has to be even higher than radiation risk of liquidators. It is well known that only healthy young people that had no some chronic diseases were employed at the mitigation of the Chernobyl accident consequences [10]. Their mean age was approximately 30 years at the moment of involving in mitigation of Chernobyl consequences. Practically all liquidators were males (approximately 97%). This specific of liquidators indicates that their radiation risk can be different from radiation risk of general population that is heterogeneous in respect of carcinogenic impact of ionizing radiation, has different age distribution and has not only external irradiation but a comparable internal irradiation as a result of consumption of contaminated food staffs and drinking water.

The mentioned assumption about the possibility of radiation-induced cancers among affected populations other than liquidators of the Chernobyl accident

is in full agreement with data established after this accident. Practically the same or even higher increase in the incidence of different malignant neoplasms was registered in high contamination regions of Belarus. In accordance with data established by author [14] relative risk of stomach, rectum, lung and urinary bladder of inhabitants of Mogilev oblast living in areas with the mean level of contamination with the isotope 137Cs from 555 to 1480 kBq/m^2 exceeded factor 2.

Data of the report [14] are in a good agreement with results of studies [15-19].

To the most outstanding features of radiation cancers caused in affected population as a result of the Chernobyl accident belong very high coefficients of radiation risk. They are by many factors higher than coefficients of radiation risk established for atomic bomb survivors [15-19]. For example, the excessive relative risk of the incidence in stomach cancers in Belarus according to data of the report [16] is equal to 13.9/Sv. This value is approximately 40 times higher than the excessive relative risk of stomach cancers by atomic bomb survivors irradiated at the age 30 years [20]. Such significant disagreement contradicts with main principles of the radiation paradigm based on the assumption that radiation risk of long-term irradiation at low dose rates is by some factors less than radiation risk of acute irradiation. The main task of the present report is an assessment of radiation risk of stomach cancers by using empirical data established in longer follow up period than it was done in reports [14-16] in order to examine the correctness of conclusions made in these report about very significant disagreement in radiation risk of normal population and atomic bomb survivors.

Materials and methods.

Published data of the Belarusian Cancer Registry on the standardized and crude incidences of stomach cancers in mixed populations of regions of Belarus established for the period 1970-2006 were used in the present work [21-32].

Registration of malignant neoplasms in Belarus is obligatory and exists from 1953 [32]. Information about the incidence as well as about the mortality from malignant neoplasms is collected and assessed in 10 oncological dispensaries and 2 oncological centres of Belarus: Oncological Department of Grodno Regional Hospital and N.N.Alexandrov Research Institute for Oncology and Medical Radiology of the Ministry of Healtn Care of the Republic of Belarus (Minsk). The last centre is situated in Minsk and is responsible for collecting of the necessary information in the Minsk oblast (region).

The system of data on malignant neoplasms collecting in Belarus improved significantly beginning from 1953 richening the modern level allowing correct assessment of malignant neoplasms. It is fully computerized and automatized. This

allows direct flowing of information from oncological dispensaries and oncological centres to the Belarusian Cancer Registry that is responsible for a critical evaluation of registered information preparing annual collections about malignant neoplasms in Belarus. These collections are published annually from 1994. They consist information for the entire Belarus and for separate regions of the country including the capital of the country, the city Minsk.

Belarus is the unitary state. In administrative respect it is divided into 6 oblasts (regions). They are: Brest, Gomel, Grodno, Minsk, Mogilev and Vitebsk oblasts (regions).They are similar in size and in the number of inhabitants (from 1,2 up to 1.5 Millions of people). The city Minsk is the capital of the country and at the same time it is a centre of the Minsk region.

Each administrative of Belarus unit has at least one oncological dispensary and this allows covering the entire territory of Belarus.

All solid cancers (carcinoma and sarcoma) as well as malignant neoplasms of hematopoietic and lymphatic tissues (leukaemia, lymphoma, multiple myeloma and mucosis fungoides [32] are registered and evaluated in Belarus including rare cancers. However the information about rare cancers is not included in annual collections of the Belarusian Cancer Registry.

The indices on the morphological verification of cancer diagnoses are improving steadily in Belarus and as it is known this is the main criterion of its realibity. According the updated data, on the average, 92.5% of all cancer cases were morphologically verified in 2004 and 94.9 in 2006 [32]. In case of many significant primary sites such as stomach, rectum, female breast, cervix and corpus uteri, prostate gland, thyroid gland the morphological verification is almost 100%. Comparison of data on standardized incidences in different cancers shows that data established in Belarus are similar to data found in developed countries having cancer registries [21]. This is an indication of a high quality of data of the Belarusian Cancer Registry.

The crude incidence rates of stomach cancers published by the Belarusian Cancer Registry were used in the present report for an assessment of observed and expected numbers of stomach cancers manifested after the accident at the Chernobyl NPP. The method of "window" was used for this purpose. This method is based on approximation of observed crude rates of the incidence in stomach cancers by excluding data registered in some defined period of time. The established approximation is used later for an assessment of expected incidences and expected numbers of stomach cancers in this period of time. Using expected numbers of stomach cancers estimated on a way allows assessing relative risk in the "window" period. The period from January1 1991 to December 31 of 2001 was chosen as the "window" period because analysis of observed incidences in stomach cancers give

an indication of manifestation of additional stomach cancers in regions of Belarus affected at the Chernobyl accident in this period.

The time-averaged relative risk of the incidence in stomach cancers in the "window" period was assessed by formula:

$$RR_w = \frac{O_w}{E_w},$$ (1)

where O_w and E_w are numbers of observed and expected stomach cancers in this period.

The expression (1) was used for an assessment of relative risk of the crude incidence in stomach cancers for all regions of Belarus as well as for the city Minsk.

Excessive absolute and relative risks, EAR and ERR, as well as attributive risk, AR, were also assessed in the report.

The excess absolute risk was assessed on the basis of the following expression:

$$EAR_w = \frac{O_w - E_w}{N_{PYSv}^w}.$$ (2)

Here EAR_w - excessive absolute risk in the "window" period,

N_{PYSv}^w - number of person-years-sievert accumulated in this period.

The value of N_{PYSv}^w in the last expression is determined as:

$$N_{PYSv}^w = \sum_{i=1}^{n} H_{i,w}^{Coll}.$$ (3)

Here $H_{i,w}^{Coll}$ - collective equivalent dose of the whole body irradiation in *ith* year of the "window" period and *n* number of years included in this period.

The excess relative risk was assessed by using the formula:

$$ERR_w = \frac{(O_w / E_w) - 1}{N_{PYSv}^{w} / N_{PY}^{w}}.$$ (4)

The value of N_{PY}^{w} is estimated by using the following formula:

$$N_{PY}^{w} = \sum_{i=n}^{n} N_i$$ (5)

Here N_i is a number of persons in *ith* year of the "window" period.

The attributive risk, AR_w, was assessed on the basis of the expression:

$$AR_w = 100\% \cdot \frac{(O_w - E_w)}{E_w}$$ (6)

Confidence intervals of time-averaged values of RR_w, EAR_w, ERR_w and AR_w were also assessed in the present report. Method of assessment is described in appendix of the present report.

Time-averaged collective and population doses of the whole body irradiation used for an assessment of radiation risks were taken from the report [33]. They are given in Tables 1 and 2.

Table 10.1. *Collective and population doses of the whole body irradiation of populations of Belarus in 1986-2007 as a result of the Chernobyl [33].*

Region, city	Collective doses, person-sievert			Population doses, mSv		
	Mixed	Males	Females	Mixed	Males	Females
Brest	1,873	988	885	1.27	1.43	1.13
Gomel	9,702	5,711	3,991	6.48	8.11	5.03
Grodno	901	515	386	0.77	0.93	0.62
Minsk	3,694	2,474	1,220	2.36	3.37	1.47
Mogilev	2,529	1,502	1,028	2.05	2.59	1.57
Vitebsk	646	421	225	0.46	0.64	0.31
city Minsk	1,705	1,125	580	1.03	1.44	0.66
Combined	21,050	12,736	8,314	2.11	2.71	1.57

By assessment of data given in Table 1 all possible pathway of the whole body irradiation of the Belarusian population were considered. Data presented in Table 2 show contribution of these pathways to total doses.

Table 10.2.*Collective doses of the whole body irradiation of populations of the Belarusian regions in 1986-2007 as a result of the Chernobyl [33].*

Region, city	H_{DD}^{Coll}	H_{ME}^{Coll}	H_{MI}^{Coll}	H_{Ev}^{Coll}	H_{Re}^{Coll}	H_{Lq}^{Coll}	H_{Σ}^{Coll}
Person-sievert							
Brest	1,250	-55	96	0	378	204	1,873
Gomel	6,030	-350	-500	640	1,711	2,171	9,702
Grodno	293.5	-13	62.5	0	384	174	901
Minsk	303	-14	174	0	1,837	1,394	3,694
Mogilev	942	-103	-196	0	1,296	590	2,529
Vitebsk	6.5	0	124.5	0	295	220	646
city Minsk	200	-20	239	0	676	610	1,705
Combined	9025	-555	0	640	6,577	5,363	21,050

Here H_{DD}^{Coll} - collective dose as a result of the whole body irradiation from deposited

radionuclides (sum of external and internal irradiation doses;

H_{ME}^{Coll} - collective dose of the whole body irradiation related to migration of people to

countries of the world;

H_{MI}^{Coll} - collective dose of the whole body irradiation related to migration from one

oblast of Belarus to other;

H_{Ev}^{Coll} - collective dose of the whole body irradiation of people evacuated in 1986 from

so-called 30-km zones of the Chernobyl NPP;

H_{Re}^{Coll} - collective dose of the whole body irradiation of people related to resettlements of

inhabitants of contaminated areas of Belarus ;

H_{Lq}^{Coll} - collective dose of the whole body irradiation of liquidators;

H_{Σ}^{Coll} - combined collective dose of the whole body irradiation.

As can be seen from data shown in Tables 1 and 2 the population of Vitebsk oblast accumulated lowest collective and population doses of the whole body irradiation caused by the Chernobyl accident.

Results and discussions.

The crude and standardized incidence rates in stomach cancers of the Belarusian population are the highest in Europe (excluding Russia and Ukraine). Tables 3-6 present comparison of crude and standardized incidence rates of stomach cancers in 1983-2008 observed in Belarus and in some countries of the North, Central, South and West Europe demonstrating this peculiarity of the Belarusian population. It can be considered as some indirect evidence that there was no underestimation of the incidence at least in stomach cancer in Belarus before the accident at the Chernobyl NPP.

Data given in Tables 3-6 show that the crude and standardized incidence rates of stomach cancers in the Belarusian men and women were approximately 3-5 times higher in this period than in the Danish men and women. This difference was not so high in case of the former socialist countries (Slovakia, Slovenia) and the former European Soviet republics (Latvia). The reason of high incidence in stomach cancers of the Belarusian population is not known. Possibly this is a result of different diets in Belarus and other countries of Europe.

Table 10.3. *Crude incidence rates of stomach cancers in men in 1983-2008 [34-38]*

Country	Time period				
	1983-1987	1988-1992	1993-1997	1998-2002	2008
Belarus	47.8	50.9	47.8	45.1	44.9
UK (England and Wales)	27.8	27.0[a]	-	-	-
Denmark	20.6	15.0	13.6	11.9	14.3
Finland	25,7[b]	22.6[c]	18.8	16.6	14.0
France (Doubs)	18.9	13.8	13.7	14.9	-
Italy (Biella Province)	-	-	35.3[d]	33.5	31.5
Latvia	39.6	37.5	36.2	33.5	33.1
Slovakia	36.3	31.7	27.8	23.5	20.8
Slovenia	32.1[e]	31.4	30.9	30.2	29.6

Notice: a -1988-1990, b – 1982-1986, c – 1987-1992, d – 1995-1997, e – 1982-1987

Table 10.4. *Standardized incidence rates in stomach cancers in men in 1983-2008 [34-38]*

Country	Time period				
	1983-1987	1988-1992	1993-1997	1998-2002	2008
Belarus	46.7	46.8	40.5	35.7	34.2
UK (England and Wales)	16.9	16.1[a]	-	-	-
Denmark	12.5	9.0	8.2	7.1	7.8
Finland	20.3[b]	16.6[c]	12.6	10.2	7.3
France (Doubs)	15.1	10.7	9.5	9.3	-
Italy (Biella Province)	-	-	15.9[d]	14.5	14.8
Latvia	34.1	31.1	28.2	24.0	21.7
Slovakia	31.7	27.1	23.5	19.2	15.3
Slovenia	27.9[e]	27.0	23.8	20.9	17.2

Notice: a -1988-1990, b – 1982-1986, c – 1987-1992, d – 1995-1997, e – 1982-1987

Table 10.5. Crude incidence rates of stomach cancers in women 1983-2008 [34-38]

Country	Time period				
	1983-1987	1988-1992	1993-1997	1998-2002	2008
Belarus	31.1	32.8	30.0	28.6	29.1
UK (England and Wales)	17.0	16.1[a]	-	-	-
Denmark	13.2	10.3	7.9	6.9	7.7
Finland	22.4[b]	19.3[c]	15.6	13.1	10.7
France (Doubs)	10.3	7.9	8.0	7.6	-
Italy (Biella Province)	-	-	26.4[d]	22.7	20.8
Latvia	27.6	25.0	24.4	25.5	21.4
Slovakia	18.5	16.2	14.9	13.8	13.8
Slovenia	22.0[e]	19.4	19.7	18.3	18.4

Notice: a -1988-1990, b – 1982-1986, c – 1987-1992, d – 1995-1997, e – 1982-1987

Table10. 6. Standardized incidence rates in stomach cancers in women in 1983-2008 [34-38]

Country	Time period				
	1983-1987	1988-1992	1993-1997	1998-2002	2008
Belarus	20.1	20.1	17.4	15.3	15
UK (England and Wales)	6.8	6.3[a]	-	-	-
Denmark	5,7	4.7	3.6	3.2	3.6
Finland	11.2[b]	9.2[c]	7.0	5.6	4.4
France (Doubs)	5.5	3.7	3.7	3.4	-
Italy (Biella Province)	-	-	8.1[d]	7.1	7.7
Latvia	15,5	13.0	11.6	14.1	9.3
Slovakia	12.2	10.3	9.0	7.8	7.1
Slovenia	12.8[e]	10.6	10.4	8.8	7.5

Notice: a -1988-1990, b – 1982-1986, c – 1987-1992, d – 1995-1997, e – 1982-1987

In qualitative respect the crude and standardized incidences of stomach cancers in men and women of Belarus are similar to crude and standardized incidences of this cancer in other European countries. At first it is to see from Tables 3-6 that crude and standardized incidences in stomach cancers in the Belarusian men is approximately 1.5 times higher than in the Belarusian women as in case of other European countries. Secondly, it is to see that at least in the period 1983-2008 a permanent decrease of the crude and standardized incidences in stomach cancers occurred in Belarus as well in other European countries.

Figure - 1 demonstrates crude incidence rates in stomach cancers in different regions (oblasts) of Belarus in 1970-2006 in comparison with the crude incidence registered in this period in Vitebsk oblast. The collective and population doses of the whole body irradiation of this oblast are much lower than respective values estimated for other regions of Belarus. This means that the possible manifestation of radiation-induced malignant neoplasms has to cause minimal influence on the spontaneous incidence in population of Vitebsk region. Therefore comparison of the incidence in stomach cancers observed in Vitebsk region and other regions of Belarus can demonstrate the possible impact of irradiation caused as a result of the Chernobyl accident.

As can be seen from data shown in Figure -1 the incidence in stomach cancer in Vitebsk region was the highest in Belarus in the entire period 1970-2006. Only in case of Mogilev region crude incidence rates of stomach cancers are similar to crude incidence rates of this cancer in the Vitebsk population.

The difference between incidence rates in stomach cancers in Vitebsk and other regions of Belarus was especially very high in the period before the accident at the Chernobyl NPP. For example, the time-averaged crude incidence rate of the incidence in stomach cancers in the city Minsk in 1970-1986 was by1.7 times less than the time-averaged crude incidence rate of the incidence in stomach cancers in Vitebsk region estimated for the same period. In case of Brest oblast the time-averaged crude incidence rate of the incidence in stomach cancers in 1970-1986 was by 1.4 times less than in Vitebsk region.
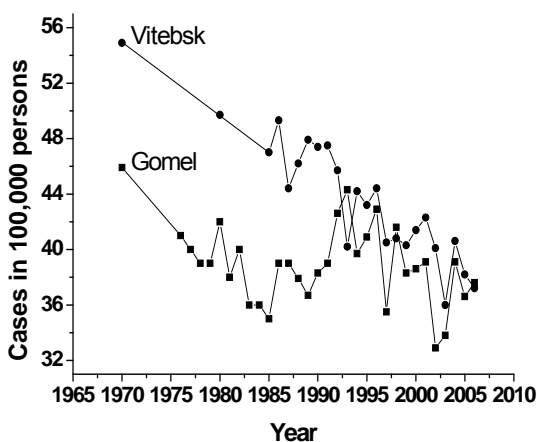
The difference in the crude incidence rates of stomach cancers of the Belarusian regions is a result of the difference in age specific coefficient of the incidence in stomach cancers and the difference in age distribution of populations of different regions. This is demonstrated by data shown in Figure -2 and Figure -3.

Figure -2 gives standardized incidence rates of stomach cancers in different regions of Belarus in 1970-2006 and Figure -3 shows fractions of people older than 60 years in different regions of Belarus.

As in case of crude incidence rates standardized incidence rates of the incidence in stomach cancers as well as fractions of people older than 60 years are

given for different regions of Belarus in comparison with respective values estimated for population of Vitebsk region.

Comparison of data presented in Figure -2 with data given in Figure -1 shows similarity of temporal patterns of standardized rates and crude ra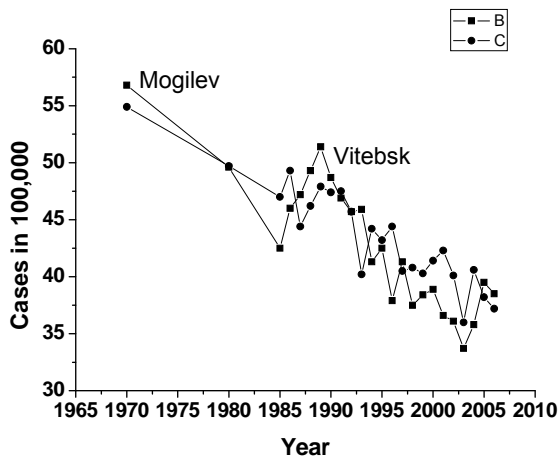tes of the incidence in stomach cancers for all regions of Belarus. This means that difference in age-specific coefficients of the incidence in stomach cancers in different regions before the accident at the Chernobyl NPP is a main reason of the difference in the observed crude incidence rates of stomach cancers in case of Brest, Gomel, Grodno and Minsk oblasts.
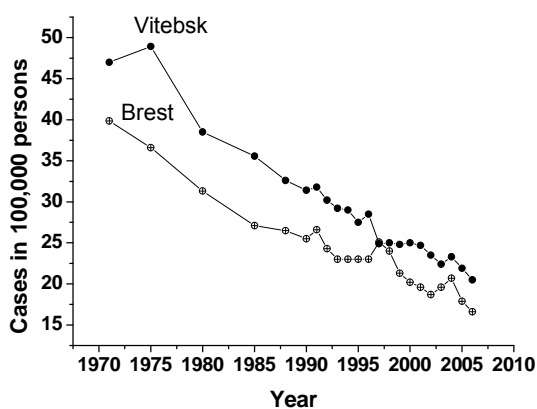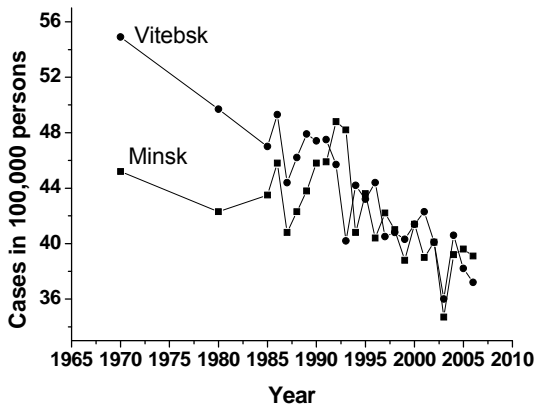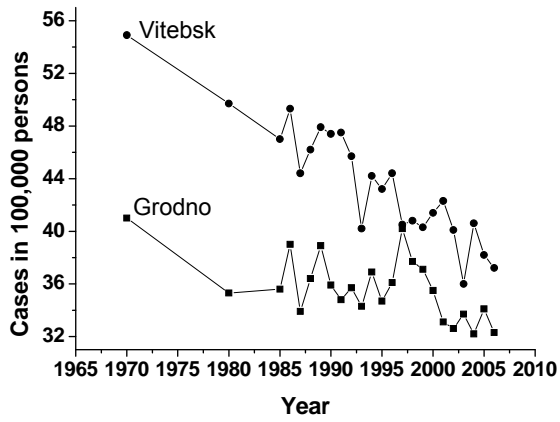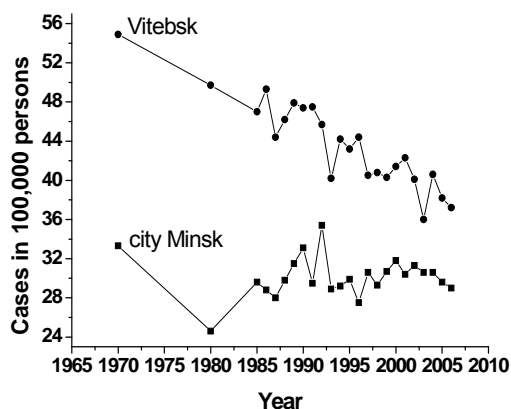
Figure 10.1 *- Crude incidence rates of stomach cancers in mixed populations of different regions of Belarus in 1970-2006.*

Data given in Figure -2 demonstrate that standardized incidence rates in stomach cancers in populations of Vitebsk oblast, Mogilev oblasts and the city Minsk practically the same in the entire period 1970-2006. This is an indication that age-specific coefficients of the incidence in stomach caners in these regions of Belarus are practically equal in the entire period 1970-2010. Lower crude incidence rates in Mogilev oblast and the city Minsk in comparison with crude incidence rates of Vitebsk oblast are mostly result of difference in age distribution. Data shown in Figure -3 demonstrate that fractions of people at the age 60 years and older in Mogilev region and the city Minsk ale smaller than respective fractions of the Vitebsk population.
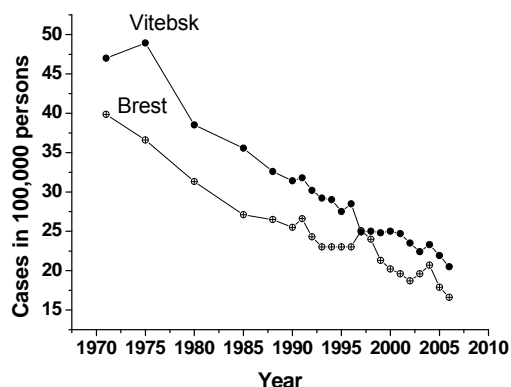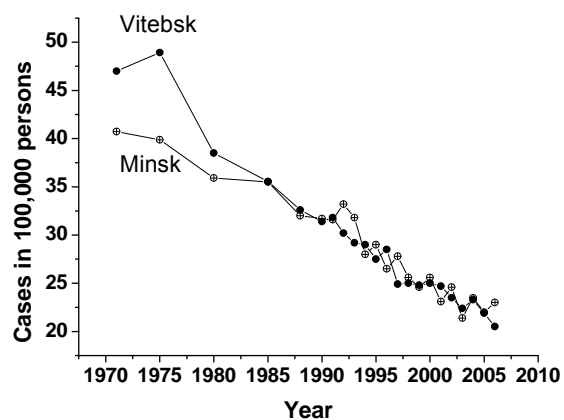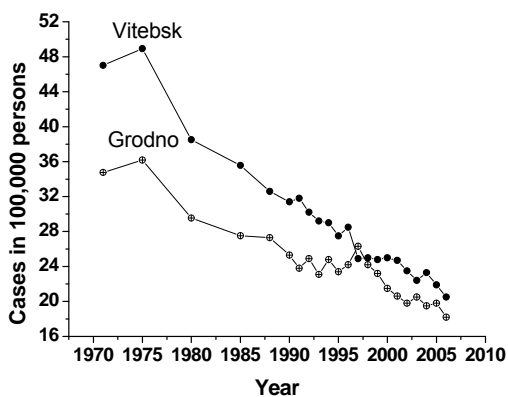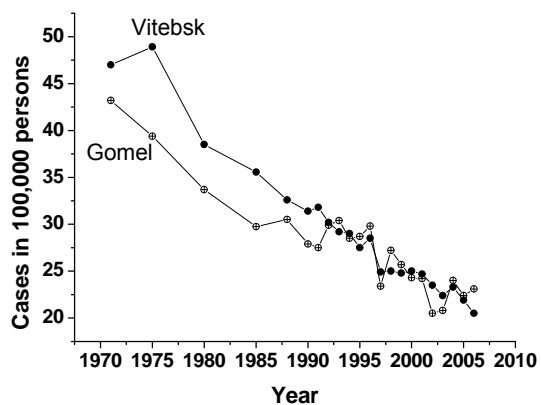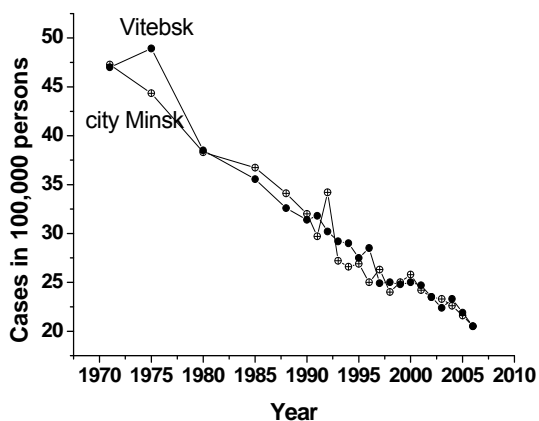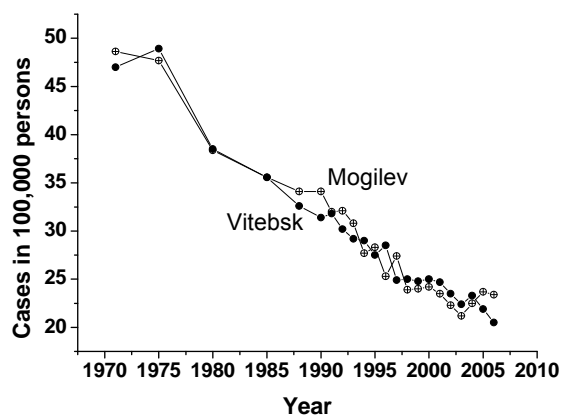
Figure 10.2 - *Standardized incidence rates of the incidence in stomach cancers in regions of Belarus.*

It is known that age is one of many factors of carcinogenic risk. Smaller values of fractions of people at the age 60 years and older at similar age-specific coefficients result in the lesser crude incidence rates of stomach cancers in Mogilev oblast and the city Minsk in comparison with Vitebsk oblast.
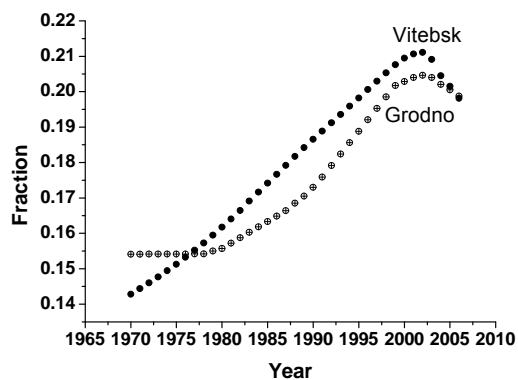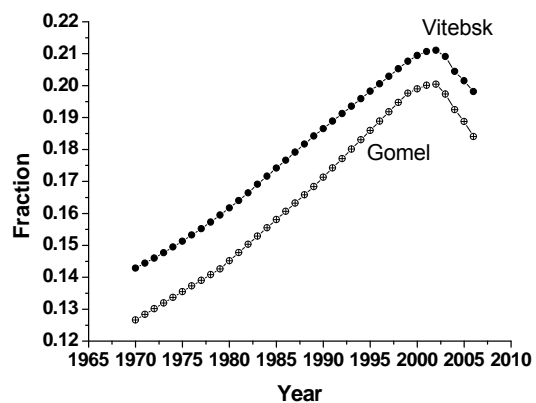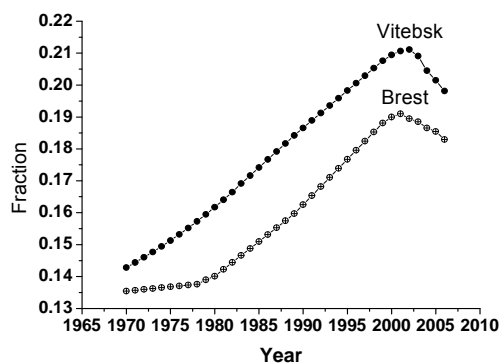
In case of the city Minsk the low fractions of people at the age 60 years and older are main reasons for very significant difference in crude incidence rates of

stomach cancers in comparison with Vitebsk region. Lower fractions of people at the age 60 years and older in Brest, Gomel? Grodno and Minsk regions contribute to lower values of crude incidence rates of stomach cancers in these regions of Belarus.

Data presented in Figure -1 and 2 show that discussed difference in crude and standardized incidences in stomach cancers in regions of Belarus decreases after the accident at the Chernobyl NPP. This is especially clear in the case of Gomel oblast. In case of this region an increase in crude and standardized incidences in stomach cancers began approximately from 1990 with reaching some maximal values in 1990-1995 and beginning of decrease after 1995 . These changes of temporal patterns of crude and standardized incidences in stomach cancers occurred in Gomel region practically in the period 1991-2001. Similar change of temporal patterns of crude and standardized incidences in stomach cancers occurred in other regions of Belarus though they were not so strongly pronounced as in case of Gomel region.

No such change occurred in Vitebsk oblast that has the lowest collective and population doses. In case of Vitebsk region one can see practically linear decrease of crude and standardized incidences in stomach cancers in the entire period 1970-2006.

Two different reasons can be responsible for mentioned change of temporal patterns of crude and standardized incidences in stomach cancers in Belarus. At first, this can reflect improved screening in stomach cancers after the accident. At second, this can reflect manifestation of additional or radiation-induced stomach cancers in regions of Belarus affected as a result of the Chernobyl accident.

The difference in age-specific coefficients of the incidence in stomach cancers as well as difference in age study of possible reasons of discussed change in temporal patterns of the incidence in stomach cancers in regions of Belarus. This problem can be solved by using the method of "window" that is based on a study of temporal patterns of the crude incidence in stomach cancers in each separate region of Belarus. The period 1991-2001 was chosen in the present report as the "window". Table 7 shows approximations of the crude incidence in stomach cancers in all regions of Belarus developed by using of squire quadrat method by excluding incidence rates observed in the period 1991-2001.

Table 10.7. *Approximation equation for assessment of expected incidence rates of the incidence in stomach cancers*

Region	Equation	R^2	p
Brest	$Y = 0.0086730184 \cdot x^2 - 34.79018 \cdot x +$ $+$ 34919.004		$p < 0.0001$
Gomel	$Y = 0.0070268989 \cdot x^2 - 28.236662 \cdot x +$ $+$ 28399.869	0.71492	$p < 0.0001$
Grodno	$Y = -0.199306 \cdot x + 423.4566$	0.64386	$p < 0.0010$
Minsk	$Y = -0.214101 \cdot x + 468.1799$	0.55324	$p = 0.0036$
Mogilev	$Y = 0.0069764645 \cdot x^2 - 28.290633 \cdot x +$ $+$ 28713.827	0.872422	$p < 0.0001$
Vitebsk	$Y = -0.486444 \cdot x + 1013.4898$	0.91493	$p < 0.0001$
city Minsk	$Y = 0.006603 \cdot x + 16.831372$	0.00107	$p = 0.9156$
Belarus	$Y = 0.0093634034 \cdot x^2 - 37.582179 \cdot x +$ $+$ 37746.0774	0.91892	$p < 0.0001$
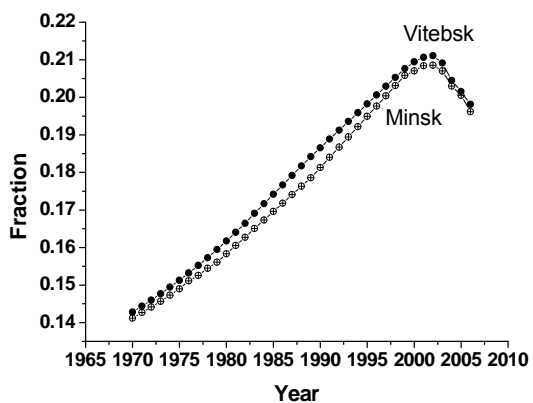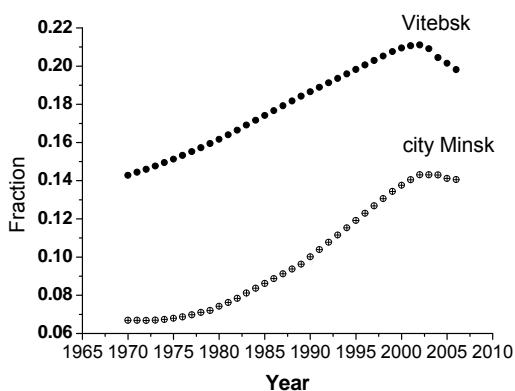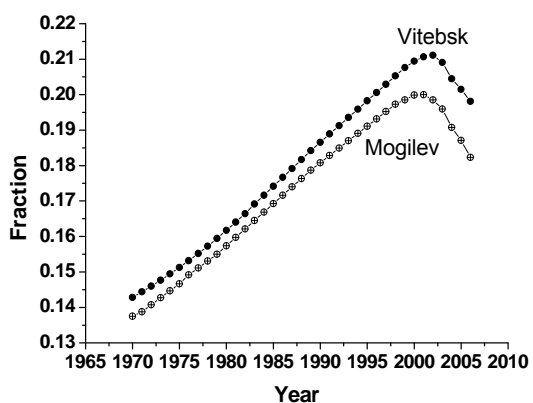
Figure 10.3 - *Fractions of persons at the age 60 years and older in regions of Belarus in 1970-2006.*

Figure 4 demonstrates crude incidence rates in stomach cancers in different regions of Belarus estimated by using approximations shown in Table 7 (expected incidence rates) as well as observed incidence rates in the period 1970-2006
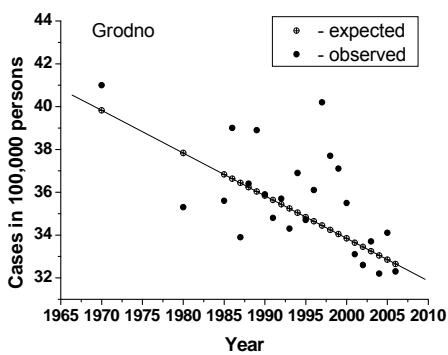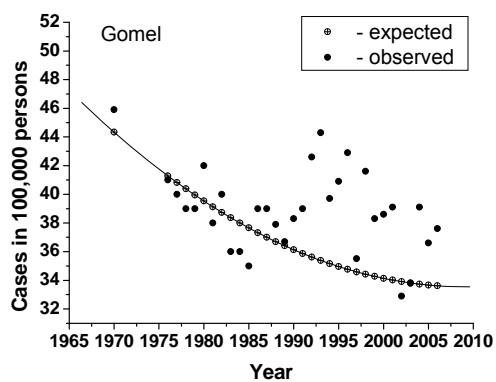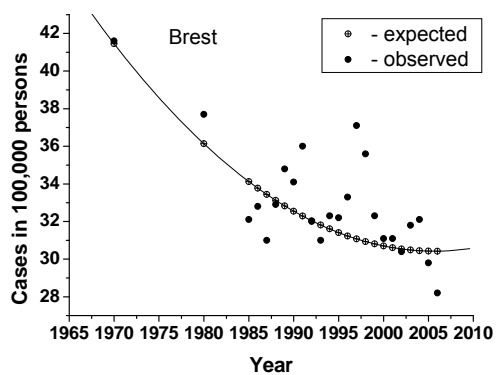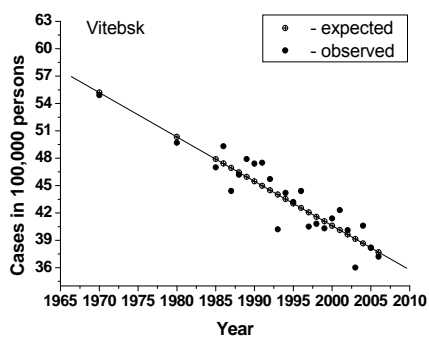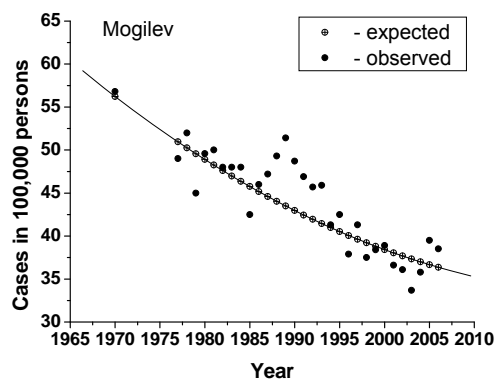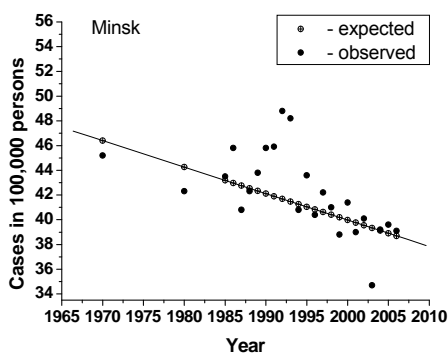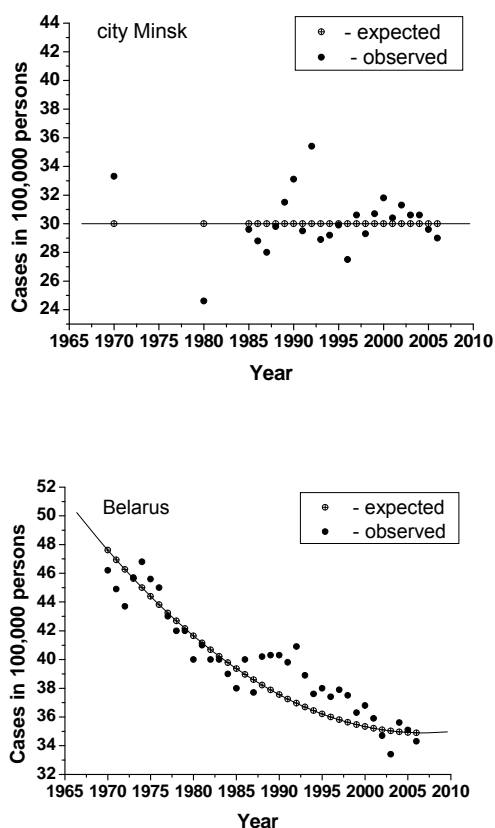
Figure 10.5 - *Expected and observed incidence rates of stomach cancers in regions of Belarus in 1970-2006.*

Table 8 gives expected and registered numbers of stomach cancers estimated for different regions of Belarus for the "window" period or for the period 1991-2001. The third row from below in this table presents data estimated by summing of respective data assessed for separate regions of Belarus. The last row of the Table 8 gives data estimated for Belarus by using expected and observed incidence rates established for the entire country as an independent unit.

Comparison shows a very good agreement of observed and expected stomach cancers estimated for the entire Belarus by using these two methods. For example, the deviation between observed numbers of stomach cancers is only 0.05% and deviation between expected numbers of stomach cancers is only 0.1%. The rounding of empirical data used by estimation of crude incidence rates is the reason of such deviation. However, the existence even such small deviations in expected and observed values reflects in some larger deviations in numbers of additional stomach cancers estimated in the present report for the entire Belarus (1,983 and 2,047

cases). Assessment by using these values gives the deviation equal 3.1%. It is clear that such small deviation is practically insignificant for estimation of additional stomach cancers. On the contrary, it is reliable evidence that the "window method" allows describing of additional stomach cancers very correctly.

Table 10.8. *Incidence of stomach cancers in regions of Belarus in 1991-2001.*

Region	Observed	Expected	O - E
Brest	5,455	5,159	296
Gomel	7,001	6,062	939
Grodno	4,739	4,554	185
Minsk	7,417	7,084	333
Mogilev	5,633	5,491	142
Vitebsk	6,675	6,641	34
city-Minsk	5,645	5,591	54
Combined	42,565	40,582	1,983
Belarus	42,587	40,540	2,047

Table 9 presents values of relative risk of additional stomach cancers in different regions of Belarus and in the entire country assessed for the period 1991-2001. As can be seen from these table statistical reliable values of the relative risk were estimated only for Breast, Gomel and Minsk as well as for the entire Belarus. The highest value of the relative risk was established for the Gomel oblast that is the most affected region of Belarus. The other regions of Belarus for which reliable values of relative risk were found were also affected at the Chernobyl accident.

Table 10.9. *Relative risk of additional stomach cancers in regions of Belarus in 1991-2001.*

Region	RR	95% CI of RR	
Brest	1.057	1.018	1.098
Gomel	1.155	1.116	1.195
Grodno	1.041	0.999	1.084
Minsk	1.047	1.013	1.082
Mogilev	1.026	0.988	1.0651
Vitebsk	1.005	0.972	1.040
city Minsk	1.010	0.973	1.048
Belarus	1.050	1.036	1.065

This fact allows to assume that radiation is the main reason for manifestation of additional stomach cancers manifested in regions of Belarus after the accident at the Chernobyl NPP. This conclusion is supported also by existing of linear dependence of relative risk on population dose and of the number of additional stomach cancers on the collective dose of the whole body irradiation. Such linear dependence is shown in Figure -5 and Figure -6.
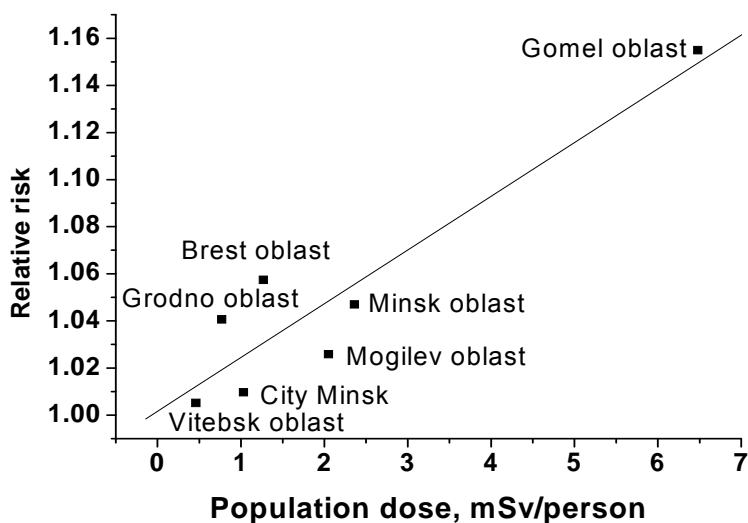
Figure 10.5 - *Time-averaged (1992-1001) relative risk of the incidence in stomach cancers in regions of Belarus.*
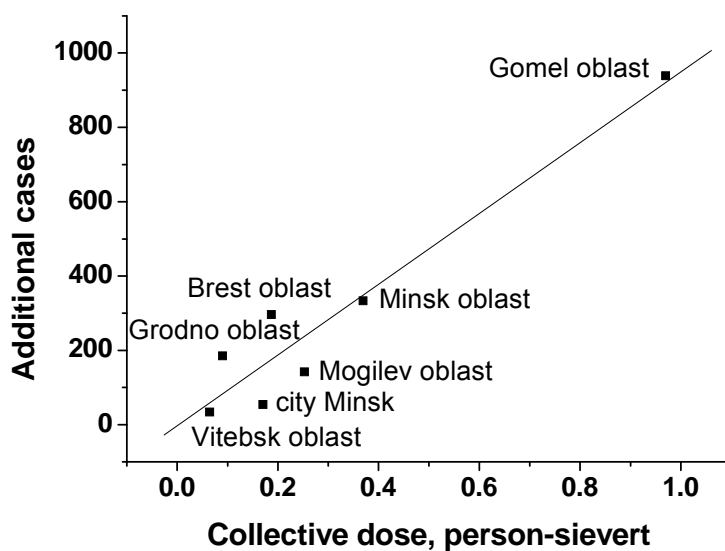
Figure 10.6 - *Numbers of additional stomach cancers in regions of Belarus in 1991-2001.*

Using the least squire method gives the following equation for estimation of values of the time-averaged (1991-2001) relative risk of additional stomach cancers manifested in Belarus after the Chernobyl accident:

$$RR_w = 0.0228 \cdot h_{pop} + 1.00, \ R^2 = 0.865, \ p = 0.0024,$$

where h_{pop} is population dose expressed in millisieverts.

$$N_{add} = 952 \cdot H_w(Coll) - 3, \ R^2 = 0.919, \ p = 0.00064 \cdot$$

In case of additional stomach cancers the following approximation was established in the present report:

$$N_w = 952 \cdot H_w(Coll) - 3,$$

where H_w^{Coll} is the collective dose in the "window period" (1991-2001).

Linear dependence of the relative risk on population dose as well as of the numbers of additional stomach cancers on collective dose of the whole body irradiation indicates that radiation is the main reason for observed change of temporal patterns of the crude incidence in stomach cancers observed in regions of Belarus after the accident at the Chernobyl NPPO.

Coefficients of radiation risks as well as attributable risk of stomach cancers were evaluated in the present report assuming that the radiation origin of discussed change the. This was done by using data established for the entire Belarus in order to diminish the possible deviations of rounding. Results of this evaluation are presented in Table 10.

Table 10.10 *Assessment of radiation risks of stomach cancers in Belarus in 1991-2001*

N_{PY}, person-years	112,314,289
h_{pop}, mSv/person	2.11
$N_{PYSv}/10^4$, person-year-sievert	23.7
Observed cancers, cases	42,587
Expected cancers, cases	40,540
Additional cancers, cases	2,047
RR	1.050
95% CI of RR	from 1.032 to 1.072
$EAR/10^4 PYSV$	86.4
95% CI of EAR	from 11.1 to 161.6
ERR, %/mSv	2.4
95% CI of ERR	from 0.3 to 4,5
AR, %	5.1
95% of AR	From 3.9 to 6.3

Table 11 presents comparison of data on radiation risks of stomach cancers assessed in the present report and data established for atomic bomb survivors [20].

For comparison of values estimated in the present report and values established for atomic bomb survivors coefficients of radiation risks of stomach cancers in Belarus shown in Table 11 were expressed in units of absorbed dose by converting doses. This was done by dividing of population and collective doses of the whole body irradiation used be estimation of values presented in Table 10 0.7 Sv/Gy because this factor was used by evaluation of respective doses in reports [1,4,33].

Data shown in Table 11 demonstrate significant disagreement in coefficients of radiation risks established in the present report and for atomic bomb survivors. It is especially very high in case of excessive relative risk. The value of excessive relative risk estimated in the present report (16.8/Gy) is by factor 49.4 times higher than the excessive relative risk found for atomic bomb survivors (0.34/Gy).

Table 10.11. *Comparison of radiation risks of the incidence in stomach cancers in the Belarusian population and in atomic bomb survivors.*

Sources	This report	Preston et al [20]
Period	1991-2001	1958-1998
N_{PY} , person-years	112,314,289	2,764,732
h_{pop} , mGy/person	3.0	100
$N_{PYGy}/10^4$, person-year-grey	33.8	-
Observed cancers, cases	42,587	4,730
Expected cancers, cases	40,540	4,579
Additional cancers, cases	2,047	151
RR	1.050	1.033
90% CI of RR	From 1.039 to 1.063	-
$EAR/10^4 \, PYGy$	60.6	9.5
90% CI of EAR	From 44.1 to 104.7	From 6.1 to 14
ERR , %/Gy	16.8	0.34
90% CI of ERR	From 4.6 to 29.0	From 0.22 to 0.47
AR , %	5.1	7.2
90% of AR	From 3.9 to 6.3	-

In case of the excessive absolute risk such ratio is 6.3 or by factor 7.8 less than ratio of excessive relative risks. Such big difference of ratios of excessive relative risks and excessive absolute risks is a clear evidence of difference in the crude incidences in stomach cancers. In case if compared population have equal crude incidences in cancers ratios of excessive relative risk and excessive absolute risk have to be the same. Conclusion about difference in incidences in stomach cancers of the Belarusian and Japanese population is supported by comparison of data presented in Table 12 with data given in Tables 3-6.

Table 10.12. *Crude and standardized (World standard) incidence rates of stomach cancers in men and women of Hiroshima prefecture (Japan) [34-37]*

Period	Men		Women	
	Crude	Standardized	Crude	Standardized
1978-1980	74.0	79.9	41.0	35.8
1981-1985	88.9	85.8	49.0	38.9
1986-1990	95.7	83.1	51.1	35.9
1991-1995	113.1	85.5	55.1	33.9
1996-2000	123.8	80.3	57.1	30.2

As can be seen from these data crude and standardized incidences in stomach cancers in men and women of Belarus are by some factors less than in men and women of the Hiroshima Prefecture.

Dependence of the excessive relative risk from the background incidence in cancers requires a special adjustment of relative risk by considering the difference in background incidence in cancers. Simple comparison of excessive relative risks estimated for different population without such adjustment can cause incorrect conclusions about carcinogenic impact of ionizing radiation. In case of data estimated in the present report it were fully unjustified to say that data of this report indicate that radiation risk of stomach cancer is by factor 49.4 higher than radiation risk established for atomic bomb survivors.

In reality results established in the present report allow only to conclude that radiation risk of long-term irradiation of the Belarusian population is only by factor 6 higher than radiation risk found for atomic bomb survivors.

Discussed features of relative and absolute radiation risks show that absolute risk gives more direct evidence of carcinogenic impact of ionizing radiation and this indicates that collective dose of irradiation is useful instrument by assessment of health consequences of some large radiation accident like the accident at the Chernobyl NPP.

It is clear that this six fold difference in radiation risk of stomach cancer can not be explained as a result of six fold underestimation of the whale body dose irradiation of the Belarusian population or as a result of six fold underestimation of numbers of additional stomach cancers established in the present report for the period 1991-2001. A number of other reasons can be responsible for discussed difference of radiation risks.

Firstly this difference can be result of damage of the thyroid gland of the Belarusian population received very high doses of the thyroid gland irradiation. It is well known that there is a very tight link between endocrine, heurohumoral and immune systems. The damage of every of these systems has reflects in distortions in functioning of other related systems.

Secondly, the difference in radiation risks can reflects higher carcinogenic impact of long-term irradiation in comparison with an acute irradiation. In case of acute irradiation only small fractions of cells is in the stage of preparing for dividing or undergo the process of dividing. All cells are very sensitive to impact of ionizing

radiation in this stage. In case of long-term chronic irradiation significant fraction of cells in the high sensitive stage is irradiated.

Thirdly, the difference in radiation risk can reflects some unknown effect of low doses and low dose rates of ionizing radiation. The accident at the Chernobyl NPP caused a quasi acute (some months) irradiation at quite high doses of the thyroid gland and long-term irradiation (many years) of the whole body in case of the affected Belarusian population. On the contrary, irradiation of atomic bomb survivors follows only some seconds [39].

Fourthly, ionizing radiation that affected the Belarusian population as a result of the Chernobyl accident was much softer than radiation of atomic explosions in Hiroshima and Nagasaki and this can contribute to difference in radiation risks of the affected Belarusian population and atomic bomb survivors.

Fifthly, it can be result of internal irradiation of stomach. In case of the Belarusian population external and internal irradiation of the whole body was comparable,. In case of atomic bomb survivors external irradiation caused practically 100% of irradiation dose [39].

All mentioned reasons as well as some other unknown reasons can contribute to disagreement in radiation risk. At present it is clear only that coefficients of radiation risk established for atomic bomb survivors are not relevant for an assessment of health effects in case of normal population irradiated at doses and dose rates like the affected Belarusian population. Using of data established for atomic bomb survivors for assessment of medical populations that have long-term irradiation will cause a significant underestimation of possible medical effects of irradiation. This underestimation increases additionally if so-called DREFF factor (Dose and Dose Rate Effectiveness Factor) suggested by UNSCEAR, BEIR VII and ICPR are used for assessment of radiation effects [40-42]. According to the UNSCERA [40] the value of DDREF for solid cancers is from 2 to 10. BEIR VII recommends for solid cancers the value of DDREFF equal 1.5 [41].

Using the value of the excessive absolute risk of the incidence in stomach cancers established for atomic bomb survivors (9.5 cases per 10^4 PYGy, see Table 11) and the value of DDREF factor recommended by BEIR VII) gives 262 additional stomach cancers in Belarus for the period 1991-2001. This is by factor 7.8 less than the number of additional stomach cancers assessed in the present report (2,047 cases). Using of the excessive relative risk found for atomic bomb survivors and the DDREFF factor equal 1.5 for assessment of radiation-induced stomach

cancers in Belarus in 1991-2001 gives only 28 cases. That is by 73 times less than estimated in the present report.

This assessment show that using data estimated for atomic bomb survivors together with the DDREFF factor underestimates significantly real health effects of radiation accidents and do not allow elaboration of adequate countermeasures for minimizing of their consequences. It was shown in our previous report [43] a significant underestimation of Chernobyl health effects assessed by authors [44] that used radiation risk established for atomic bomb survivors together with the value of the DDREF factor proposed by BEIR VII [41]. In accordance with results estimated in report [44] only 218 additional solid cancers other than thyroid cancers and non-melanoma skin cancers for the period 1986-2005 and 1,666 additional cancers of the same type for the period 1986-2065 can be expected in Belarus as a result of the Chernobyl accident. It is clear correct assessment can be performed only on the basis of an analysis of the incidence in studied cancers in territories affected at accidents. Such analysis diminishes possible underestimation of health effects among affected population. Using the excessive absolute risks seems preferable by performing such assessment. And this indicates that collective dose of irradiation is a very useful tool by assessment of radiological accidents and especially accidents like the accident at the Chernobyl NPP when there is no possibility to assess correctly individual doses of irradiation of all persons affected by the accident. It is much easier to assess in such cases collective doses of irradiation and this requires using of coefficients of absolute risk.

Conclusions.

Results of the analysis of the crude and standardized incidence in stomach cancers in regions of Belarus demonstrate the possibility of the manifestation of the radiation-induced stomach cancers in Belarus as a result of the accident at the Chernobyl NPP. Established linear relation-ship between relative risk and population doses of the whole body irradiation as well as between numbers of additional stomach cancers and collective doses of the whole body irradiation is a strong argument supporting the conclusion that these additional stomach cancers have a radiation origin. Radiation risks assessed in the present report assuming the possible link between additional stomach cancers and radiation are by some factors higher than radiation risks estimated for atomic bomb survivors. A number of reasons can be responsible for this difference. Especially high disagreement was established in the present

report for the excessive absolute risk. This is an indication that using of excessive absolute risk is preferable in case of an assessment of health effects of radiological accident of large scale like the accident at the Chernobyl NPP.

Existence of significant disagreement in radiation risks of thee Belarusian population and atomic bomb survivors demonstrate that using of radiation risks established for survived inhabitants of Hiroshima and Nagasaki underestimates real medical effects of the Chernobyl accident manifested at least in Belarus. This underestimation increases by using of the so-called Dose and Dose Rate Effectiveness Factor (DDREF) proposed by UNSCEAR, BEIR and ICPR. This means that radiation risks found for atomic bomb survivors and the idea of DDREFF using are not relevant at least in case of an assessment of radiation-induced stomach cancers caused in Belarus as a result of the Chernobyl accident.

Appendix

By assessment of the confidence interval of RR_w the simplified method developed in the present report on the basis of the method of Katz et al [45] was used. Applying the method of Katz et al [45] gives for lower and upper limits of the confidence interval of relative risk RR_w the following expressions:

$$RR_w(Upp) = e^V \tag{1}$$

$$RR_w(Low) = e^W \tag{2}$$

Here the values V and W are determined by formulas:

$$V = \log_e RR_w + \left[N_{1-\alpha/2} \times SE\left(\log_e RR_w\right) \right], \tag{3}$$

$$W = \log_e RR_w - \left[N_{1-\alpha/2} \times SE\left(\log_e RR_w\right) \right]. \tag{4}$$

Here $N_{1-\alpha/2}$ is the appropriate value from the standard Normal distribution for the 100(1-α/2) percentile and $SE\left(\log_e RR_w\right)$ is standard error of $\log_e RR_w$:

$$SE\left(\log_e RR_w\right) = \sqrt{\frac{1}{O_w} - \frac{1}{N_{PY}^w} + \frac{1}{E_w} - \frac{1}{N_{PY}^w}} \qquad (5)$$

Introducing the value x:

$$x = N_{1-\alpha/2} \times SE\left(\log_e RR_w\right) \qquad (6)$$

allows rewriting equations (3) and (4) in the form:

$$V = \log_e RR_w + x, \qquad (7)$$

$$W = \log_e RR_w - x. \qquad (8)$$

Inserting (7) and (8) into expressions (1) and (2) gives after some simple operations:

$$RR_w(Upp) = RR_w \cdot e^x, \qquad (8)$$

$$RR_w(Low) = RR_w \cdot e^{-x} \qquad (9)$$

It was found in the present report that for any region of Belarus as well as for the entire country the value of x is much less than 1. This allows using of the following approximations:

$$e^x \approx 1 + x \qquad (10)$$

$$e^{-x} \approx 1 - x \qquad (11)$$

Using these approximations gives instead expressions (10) and (11):

$$RR_w(Upp) \approx RR_w + x \cdot RR_w, \qquad (12)$$

and

$$RR_w(Low) \approx RR_w - x \cdot RR_w. \qquad (13)$$

By inserting the value x determined by formula (6) expressions (13) and (14) can be written in the form:

$$RR_w(Upp) \approx RR_w + N_{1-\alpha/2} \cdot \lfloor SE(\log_e RR_w) \times RR_w \rfloor, \qquad (14)$$

$$RR_w(Upp) \approx RR_w - N_{1-\alpha/2} \cdot \lfloor SE(\log_e RR_w) \times RR_w \rfloor, \qquad (15)$$

or in the form:

$$RR_w(Upp) \approx RR_w + N_{1-\alpha/2} \times SE(RR_w), \tag{16}$$

$$RR_w(Low) \approx RR_w - N_{1-\alpha/2} \times SE(RR_w). \tag{17}$$

Here $SE(RR_w)$ is the standard error of the relative risk : RR_w:

$$SE(RR_w) = SE(\log_e RR_w) \times RR_w. \tag{18}$$

By assessment of the confidence interval of the excessive absolute risk EAR_w the following expression were used:

$$EAR_w(Upp) \approx EAR_w + N_{1-\alpha/2} \times SE(EAR_w), \tag{19}$$

where $SE(EAR_w)$ is the standardized error of EAR. It can be assessed by using the formula:

$$SE(EAR_w) = \delta(EAR_w) \cdot EAR_w. \tag{20}$$

Here $\delta(EAR_w)$ is the relative error of the excessive absolute risk. It is determined by formula:

$$\delta(EAR_w) = \delta(O_w - E_w) + \delta(N_{PYSv}^w), \tag{21}$$

where $\delta\left(O_w - E_w\right)$ is the relative error of the value $\left(O_w - E_w\right)$ and $\delta\left(N_{PYSv}^w\right)$

is the relative error of the collective dose of the whole body irradiation. The last value was taken equal to 30%. This is accuracy of population and collective doses of the whole body irradiation of the Belarusian population affected at the Chernobyl NPP accident [q,4,33].

Similar method was used also for estimation of confidence intervals of the excessive relative risk and the attributive risk.

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11

Risk assessment of radiation-induced thyroid cancer in population of Belarus

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The incidence in thyroid cancer in the Belarusian population are presented in the report. It was found that approximately 8,700 additional thyroid cancers occurred in Belarus in 1990-2006 The number of thyroid cancers registered in Belarus in this period is about 13,300 cases (4,600 expected cases). The relative risk averaged for this period is equal to 2.89 (95% CI from 2.80 to 2.99). The excessive absolute risk of thyroid cancer, EAR, averaged for the same period is assessed as 6.1 case per 104 PYSv (95% CI from 5.8 cases to 6.4 cases per 104 PYSv). The averaged excessive relative risk, ERR, is found equal to 22.7/Sv (95% CI from 21.5 to 23.9/Sv) and the averaged attributive risk, AR, is estimated equal to 65.4% (95% CI from 62.1 to 68.8%). The mean deposition level of iodine isotope 131I on May 4, 1986 or one week after the accident at the Chernobyl Nuclear Power Plant was in some areas of the Gomel region higher than 37,000 kBq/m2. Recalculating with considering of the radioactive decay of this isotope gives the level of contamination higher than 74,000 kBq/m2. Such high levels of contamination with the isotope caused very high doses of the thyroid gland among the Belarusian population. They were by some children higher than 50 Gy (50,000 mGy). The collective equivalent dose of the thyroid gland irradiation of the Belarusian population is about 1,000,000 PGy (assessment of M.Malko).

It is well known that thyroid cancer is a very rare disease by children. According to the data of Prof. Demidchic (Belarus) only 21 cases were registered among the Belarusian children (less than 15 years at the time of diagnose) in 1966-1985 or one case annually. This observed number of thyroid cancers in children corresponds to the number of person-years accumulated in the period 1966-1985 equal to 4.74•107. The last figure was assessed on the basis of demographic data given in handbooks of Belarus. Dividing the number of observed thyroid cancers among by this number of person-years gives the incidence rate of this cancers in children of Belarus equal to 0.443 cases per million persons-years.

Country	Time Period	Crude rate	Standardized rate	Sources
UK, England and Wales	1981-1990	0.6	0.5	IARC
UK, England and Scottish Cancer Register	1981-1990	0.6	0/5	IARC
Poland	1980-1989	0.5	0.5	IARC
Slovakia	1980-1989	0.7	0.6	IARC
Hungary	1985-1990	0.3	0.3	IARC
Ukraine	Before Chernobyl accident	0.5	-	Tronko et al
Belarus	1966-1985	0.44	-	This report

Table 11.1 - *Time-averaged crude and standardized (World standard) incidences in thyroid cancers in children.*
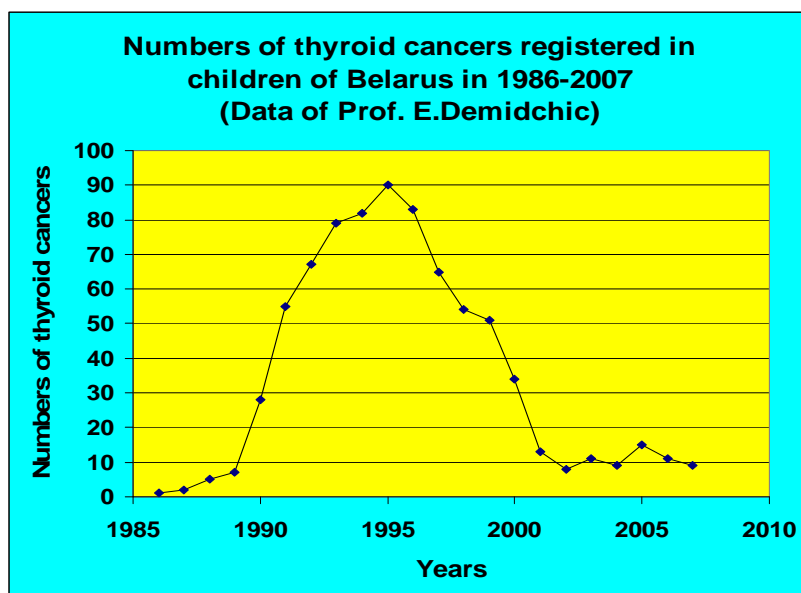
Figure 11.1 – *Thyroid cancer reporting*

Regions	Observed	Expected	O - E	RR
Brest	165	3	162	55
Vitebsk	11	2	9	5.5
Gomel	378	3	375	126
Grodno	43	2	41	21.5
city Minsk	62	3	59	20.7
region Minsk	42	3	39	14
Mogilev	43	2	41	21.5
Together	744	18	726	41.3

Table 11.2 - *Incidence in thyroid cancers in children of Belarussian regions in 1986-2004.*
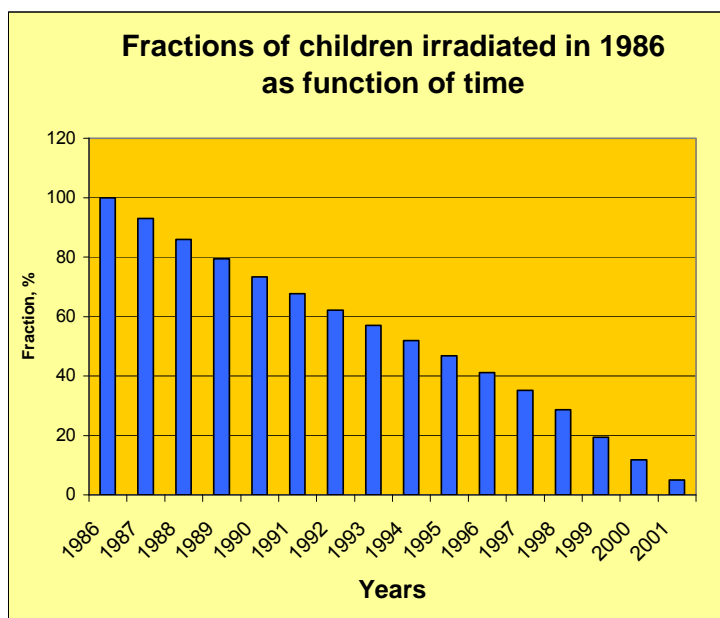
Figure 11.2 – As titled
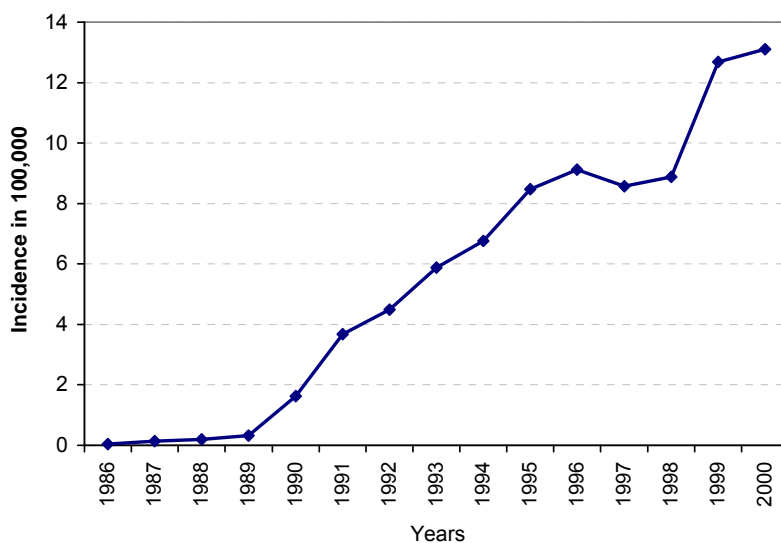
Figure 11.3 - *Incidence rates of thyroid cancer among irradiated children of Belarus*
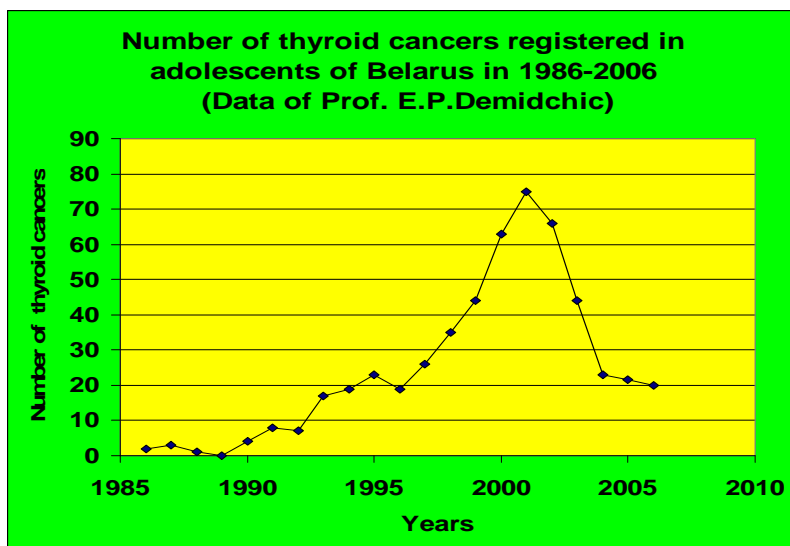
Figure 11.4 *–As titled*
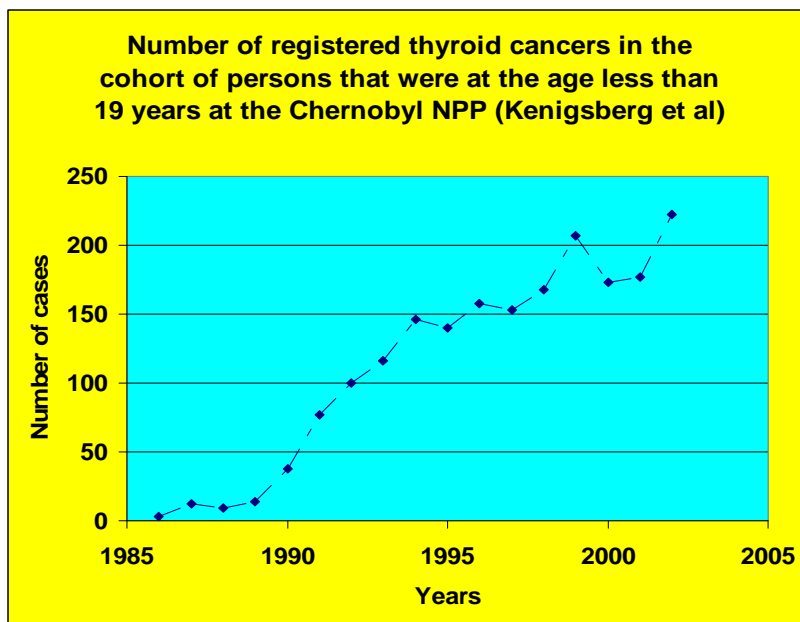
Figure 11.5 – *As titled*

Figure 11.6 – *As titled*

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Excessive absolute risk (with 95%CI) of the incidence in thyroid cancers in Belarus in 1986-2002 in persons irradiated at the age 0-18 years (EAR =2.7/10000 PYGy)

Figure 11.7 – As titled

Incidence rates in thyroid cancers in population of Belarus in 1986-2007

Figure 11.8 – As titled

Age specific incidence rates in thyroid cancer in Belarus in 1991-2006

Figure 11.9 – As titled

Incidence rates of thyroid cancers in males of Latvia in 1985-2005 (IARC data)

$y = 0.0215x - 41.787$

$R^2 = 0.9146$

Figure 11.10 – As titled

Incidence rates in thyroid cancers in females of Latvia in 1985-2002 (IARC data)

$y = 0.1019x - 199.08$
$R^2 = 0.9217$

Figure 11.11 – As titled

Incidence rates of thyroid cancers in the mixed population of Latvia in 1985-2002 (IARC data)

$y = 0.0646x - 126.08$
$R^2 = 0.9166$

Figure 11.12 – As Titled

Figure 11.13 – *As titled*

Figure 11.14 – *As titled*
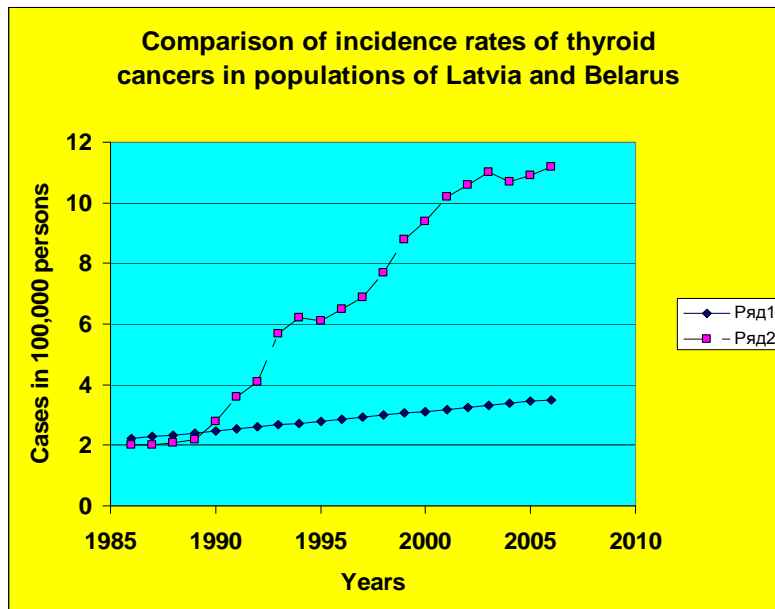
Figure 11.15 *– As Titled*

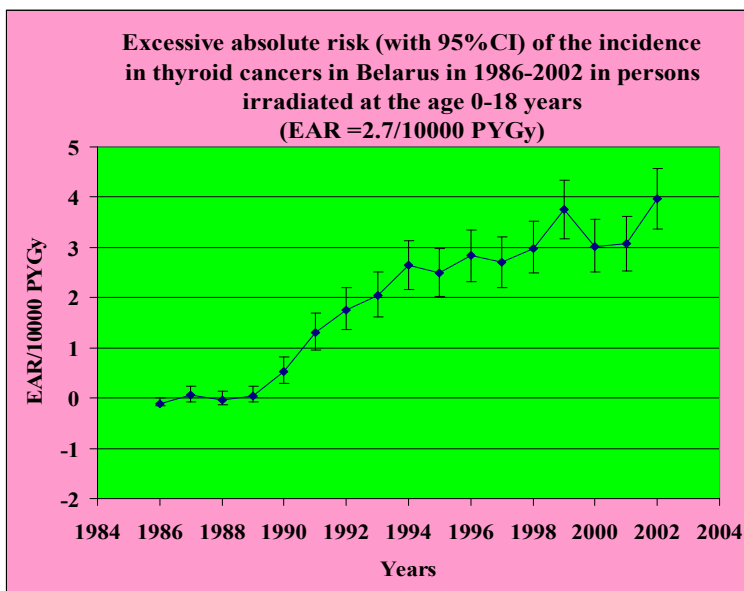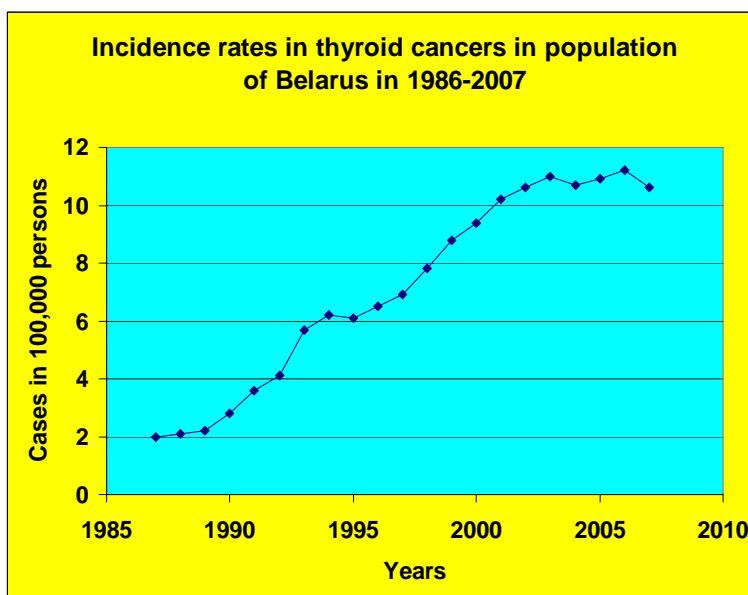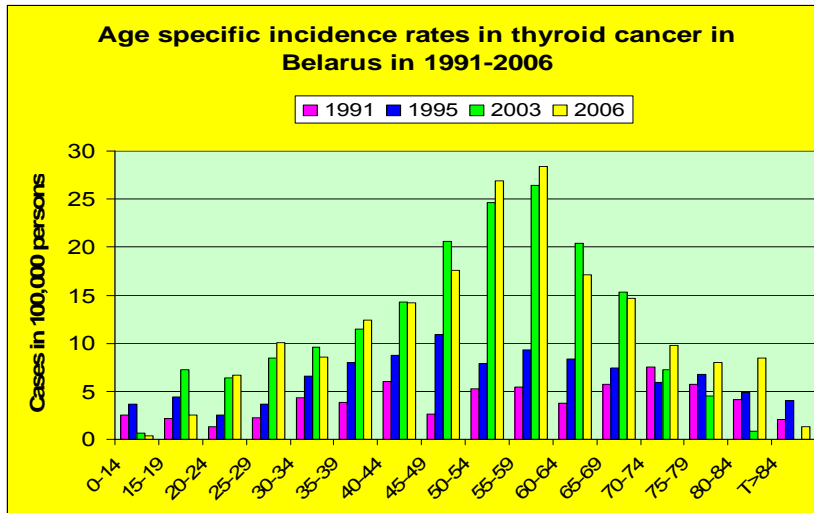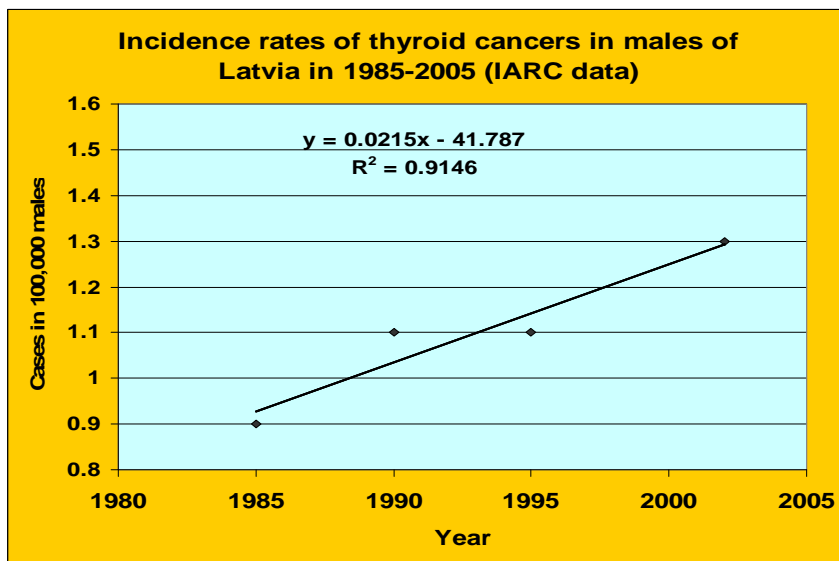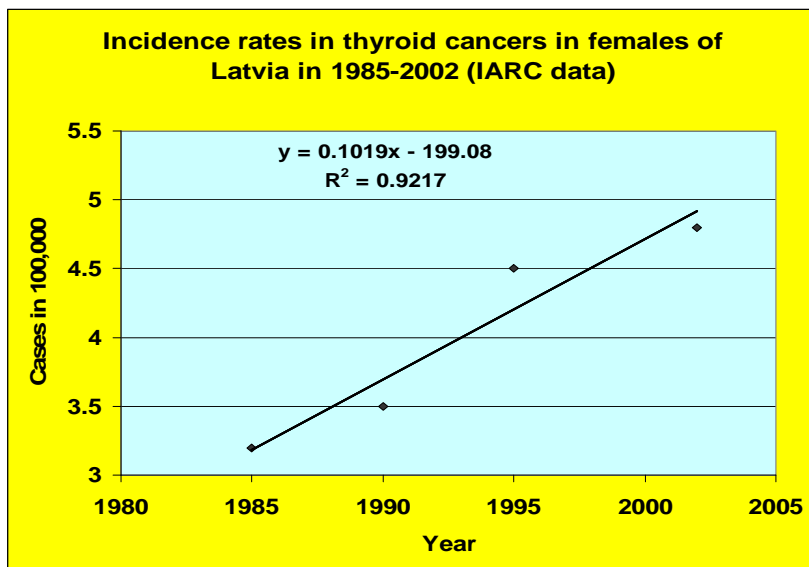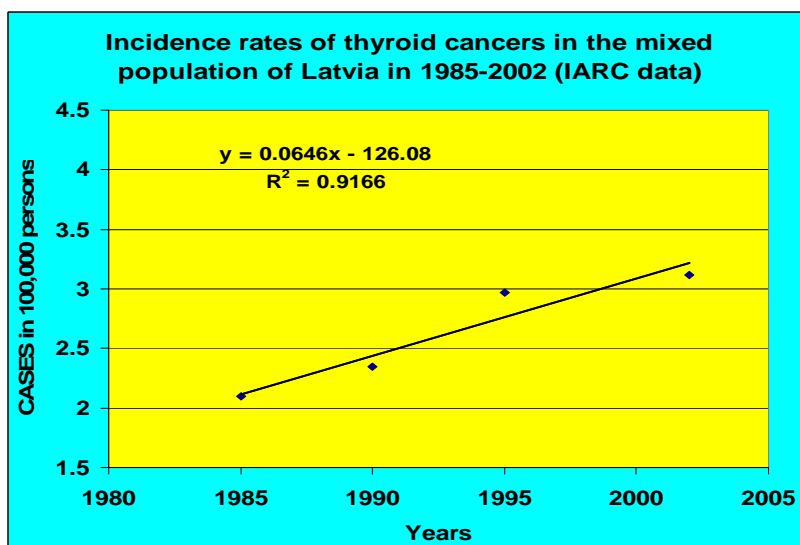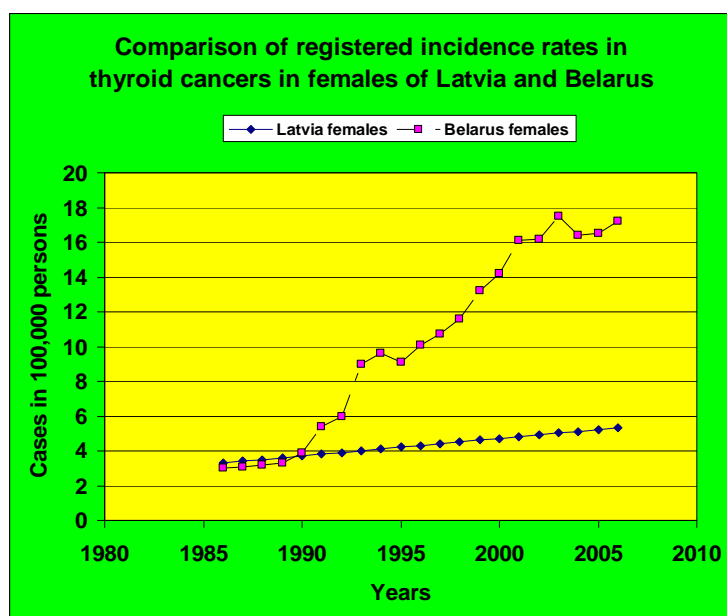|	Belarus			ATB*
Period of time	1990-2006			1958-1998
Contingent	Males	Females	Mixed	Mixed
PY	80,400,000	91,300,000	171,700,000	2,764,731
H(Coll), 10^4 PGy	44 104	50 104		10^4 PGy
h(population), Gy	0.094	0.094	0.094	~0.2
Duration of irradiation	$2.6 \cdot 10^6$ sec	$2.6 \cdot 10^6$ sec	$2.6 \cdot 10^6$ sec	2.6 sec
Dose rate, Gy/sec	$0.036 \cdot 10^{-6}$	$0.036 \cdot 10^{-6}$	$0.036 \cdot 10^{-6}$	0.1
Observed	1560	10,800	13,300	471
Expected	2500	3,660	4,600	408
O - E	940	7,140	8,700	63
RR	2.66	2.95	2.89	1.15
95% CI of RR	2.47 ÷ 2.87	2.83 ÷ 3.06	2.80 ÷ 2.99	
EAR/10^4 PYGy,	2.3	9.3	6.1	1.2**
95% CI of EAR	2.1 ÷ 2.6	8.8 ÷ 9.9	5.8 ÷ 6.4	0.48 ÷ 2.2
ERR/Gy	19.9	23.3	22.6	0.57**
95% CI of EAR	17.6 22.4	22 ÷ 24.7	21.5 ÷ 23.7	0.24 ÷ 1.1
AR%	62.4	66.1	65.4	
95% CI of AR,%	59.5 ÷ 65.1	62.1 ÷ 69.9	64.2 ÷ 66.6	

* *D.L/Preston, E.Ron, S.Tokukoko et al. Solid Cancer Incidence in Atomic Bomb Survivors: 1958 – 1998. Radiation Research, vol.168, pp.1-64 (2007).*

** *Estimates for atomic bomb survivors irradiated at the age 30 years and attained age 70 years.*

Table11. 3 - *Comparison of radiation risks estimated for the Belarusian population and for atomic bomb survivors*

Conclusions

The accident at the Chernobyl NPP caused in Belarus in 1990 – 2006 approximately 8,700 radiation-induced thyroid cancers. The radiation risks of radiation-induced thyroid cancers caused in Belarus by the Chernobyl accident are by some factors higher than observed in atomic bomb survivors. The radiation risks of thyroid cancers established for atomic bomb survivors (acute irradiation) are not relevant for irradiation of normal population. Using radiation risks observed for the surviving inhabitants of Hiroshima and Nagasaki underestimates real number of radiation-

induced thyroid cancers in case of a population exposed to chronic irradiation. Using the Dose and Dose Rate Effectiveness Factor higher than one additionally underestimates number of radiation-induced thyroid cancers caused as a result of a chronic irradiation of the normal population.

12

Tumours of hematopoietic and lymphoid tissues in Chernobyl clean-up workers

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The Chernobyl accident on April 26, 1986 remains the worst ever in the history of the nuclear industry. A dramatic increase in the incidence of thyroid cancer has been observed among those exposed to radioactive iodine in most contaminated areas. The question as to whether the incidence of leukaemias and malignant lymphomas among Chernobyl clean-up workers increased is still a point of much controversy. UN Scientific committee on effects of atomic radiation (report to UN General Assembly, 2001) and Chernobyl Forum (Vienna, 2005) reject the possibility of increasing leukaemia incidence in Chernobyl clean-up workers. Nevertheless, this point of view is inconsistent with the results of several descriptive epidemiologic studies in Ukraine, Byelorussia, and Russia.

In 2006, the standardized incidence of leukaemia, lymphomas and multiple myeloma in adults amounted to 16.5 per 100,000 of population (crude data) (National Cancer Registry of Ukraine). The actual incidence rate is underestimated by about 30% since up to the day several categories of myeloproliferative diseases were not classified as "malignant neoplasms" in IDC-10 (1992) and were not included in Ukrainian Cancer Registry. Various categories of MDS (refractory anemia with and without ringed sideroblasts, refractory cytopenia, refractory anemia with excess of blasts, 5q– syndrome) with total annual incidence of 3.0 per 100,000 also were not accounted. We believe that only precise diagnosis of the major types of hematological malignancies among Chernobyl clean-up workers in comparison with the data in general population will be the basis for estimating the relative contribution of the radiation factor to the overall incidence of such pathologies. The conclusions of other authors are mostly based on crude data without delineation of the incidence according to the biological subtypes of leukaemia and lymphoma. The aim of the study is to present the data on the various forms and variants of leukaemia and lymphoma verified by Western standards in the consecutive group of 281 Ukrainian Chernobyl clean-up workers developed in 10-23 years after Chernobyl accident, diagnosed in the Ukrainian Reference Laboratory in 1996-2008 and

categorized according to the up-to-date classifications (FAB, WHO, EGIL, ICD-10, ICO-O-2).

- **Bebeshko et al. (1999): 96 cases of leukaemia and MDS among clean-up workers enrolled in National Ukrainian Registry**

- **Ledoschuk et al. (2001): 71 cases of acute and chronic leukaemias, 59 cases of malignant lymphomas, 15 cases of other myeloproliferative diseases (polycythemia vera, osteomyelofibrosis, MDS)**

- **Hatch et al. (2006): 87 cases of pathologically confirmed leukaemia (1986-2000)**

- **Kesmiene et al. (2008): 117 cases of neoplasms of lymphoid and hematopoietic tissue (69 leukaemia, 34 NHL, 8 multiple myeloma, 2 MDS, 4 cases of myeloproliferative disease, unclassificable) in Belarus, Russian Federation, Baltic countries**

- **Cardis et al. (1996) estimated about 150 excessive cases of leukaemia within 10 years among 100,000 clean-up workers exposed to an average dose of 10 cSv**

- **Prisyazhniuk et al. (1999) stated statistically significant increment in observed-to-predicted ratio of leukaemia and lymphoma incidence: 2.6 in 1990-1993 and 2.0 in 1994-1997**

- **Ivanov et al. (2003) diagnosed 58 cases of leukaemia in clean-up workers who received doses of 15-30 cGy (twofold increased risk has been shown in a very large cohort of clean-up workers in Russia)**

- **According to the forecasts of Russian scientists, for the cohort of clean-up workers with average dose of 16 cGy about 800 cases of leukaemia are expected, with 17% of cases being associated with radiation exposure (VK Ivanov, AF Tsyb et al.)**

Figure 12.1 - Summary of findings and estimations made by various research teams on leukaemia and lymphoma incidence in Chernobyl clean-up workers

Year	Number of clean-up workers	Average dose in cGy
1986-	207,486	18.5 (14.4)*
1987		11.2 (9.0)*
1988-1989	98,153	4.7 (3.6)*

Figure 12.2 - *Cohort of Ukrainian clean-up workers - 305,639 persons (State Register) predominantly males aged 20-45*

<u>Age groups at time of diagnosis:</u>
  30-39 years – 12 pts.
  40-49 years – 39 pts.
  50-59 years – 89 pts.
  60-69 years – 107 pts.
  70 and above – 34 pts.

Males: 240

Females: 41
Mean age: 62.4 ± 1.6

- Neoplastic diseases of hematopoietic and lymphoid tissues: 281 pts.

- Non-malignant hematopoietic disorders (aplastic anemia, hemolytic anemia, idiopathic thrombocytopenia, neutrophylic leukocytosis, lymphocytosis, dysgranulocytopoiesis etc.) : 117 pts.

- Group of comparison: 2697 consecutive patients of general population diagnosed in 1996-2005

Figure 12.3 - *Chernobyl clean-up workers 1986-1987*

- *MGG staining of blood and bone marrow smears*

- *Cytochemical detection of myeloperoxidase, acid phosphatase, alkaline phosphatase, acid non-specific esterase, naphtol-AS-D-chloroacetate esterase, PAS reaction*

- *Immunocytochemical detection of antigens (ABC-AP, APAAP methods):*

  – *Myeloid cells: CD33, CD13, CD15, CD64, CD16, MPO*

  – *Erythroid and megakaryocytic cells: CD71, CD61, CD62, CD41, CD42, glycophorin A*

  – *T-cells: CD7, CD5, CD3, CD2, CD1a, CD4, CD8, CD45RO, γδTCR*

  – *B-cells: CD19, CD20, CD22, CD10, κ, λ, μ chains*

  – *Stem cell and markers of commitation: CD34, CD38, CD45RA, HLA-DR*

Figure 12.4 – *Diagnostic techniques*

Type of leukaemia	Absolute number and relative frequency (percentage in the brackets)	
	Chernobyl clean-up workers	**General population**
Myelodysplastic syndromes	15 (5.34%)	107 (3.70%)
Acute myeloid leukaemia	44 (15.66%)	732 (27.14%)
Acute lymphoblastic leukaemia	17 (6.03%)	214 (7.93%)

Figure 12.5 - *Summary of malignant diseases of hematopoietic and lymphoid tissues diagnosed in Chernobyl clean-up workers*

|		
Chronic myelogenous leukaemia	25 (8.90%)	178 (6.59%)
Polycythemia vera	6 (2.13%)	3 (0.11%)
Essential thrombocythemia	8 (2.85%)	–
Chronic eosinophylic leukaemia/ Hypereosinophylic syndrome	2 (0.71%)	–
Chronic idiopatic myelofibrosis	4 (1.42%)	2 (0.07%)
Chronic myelomonocytic leukaemia	8 (2.85%)	84 (3.11%)
Chronic lymphocytic leukaemia	75 (26.96%)	791 (29.32%)
B-cell prolymphocytic leukaemia	4 (1.42%)	23 (0.85%)
Hairy cell leukaemia	11 (3.91%)	118 (4.37%)
Multiple myeloma	18 (6.41%)	108 (4.00%)
Non-Hodgkin's lymphoma **in leukemization phase**	34 (12.13%)	296 (10.97%)
Sezary syndrome	3 (1.07%)	8 (0.29%)
T-cell prolymphocytic leukaemia	2 (0.71%)	3 (0.11%)
Large granular lymphocytic leukaemia	5 (1.77%)	3 (0.11%)

Figure 12.6 - *Summary of malignant diseases of hematopoietic and lymphoid tissues diagnosed in Chernobyl clean-up workers*

All of B-Cell Origin:

- ALL with phenotype of stem hematopoietic cell:

- $CD34^+$, $CD38^+$, HLA-DR$^+$, $CD45RO^+$

- pre-pre-B-ALL: $CD19^+$, $CD22^+$, $CD20^-$, $CD10^-$, cym$^-$

- common ALL: $CD19^+$, $CD22^+$, $CD20^{+/-}$, $CD10^+$,   cym$^-$

- pre-B-ALL: $CD19^+$, $CD22^+$, $CD20^{+/-}$, $CD10^+$, cym$^+$

- B-ALL: $CD19^+$, $CD22^+$, $CD20^+$, $CD10^+$, sIg$^+$
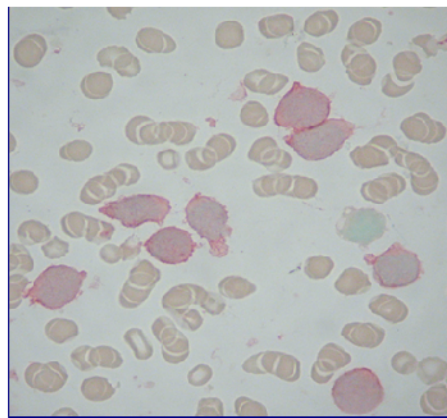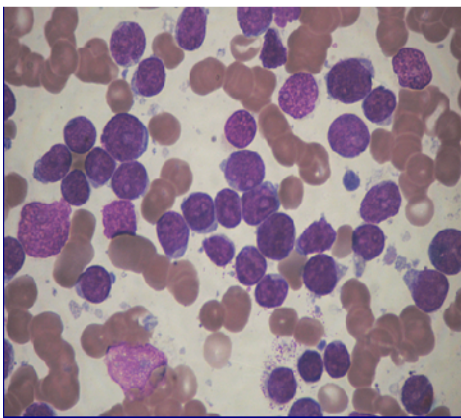
Figure 12.7 - PB smears in pre-B-cell ALL:
a – MGG x 900
b – CD19 positive blast cells

ALL of T-cell origin:

- T1-ALL with a phenotype of subcortical thymocytes: $CD7^+$, $CD2^+$, cyCD3$^+$, $CD5^-$, CD1a$^-$, $CD4^-$, $CD8^-$

- T2-ALL with a phenotype of cortical thymocytes: $CD7^+$, $CD2^+$, sCD3$^+$, $CD5^+$ CD1a$^{+/-}$, $CD4^+$, $CD8^+$

- T3-ALL with a phenotype of medullar thymocytes: $CD7^+$, $CD2^+$, $CD3^+$, $CD5^+$, CD1a$^+$, $CD4^+$ or $CD8^+$

- T4-ALL with gδT-cell receptor:
  gδTCR$^+$, CD7$^+$, cyCD3$^+$, CD2$^+$, CD5$^-$, CD1a$^-$, CD4$^-$, CD8$^-$

Immunophenotype of AML blasts

- M0-AML: HLA-DR$^+$, CD34$^+$, CD33$^+$, CD13$^+$, MPO$^+$

- M1-AML: HLA-DR$^+$, CD34$^{+/-}$, CD33$^+$, CD13$^+$, MPO$^+$, CD15$^+$, CD64$^+$

- M2-AML: HLA-DR$^{+/-}$, CD34$^{+/-}$, CD33$^{+/-}$, CD13$^{+/-}$, MPO$^+$, CD15$^+$, CD64$^+$, CD16$^+$

- M3-AML: HLA-DR$^+$ Expression of pan-myeloid antigens varies

- M4-AML: Presence of myeloblasts and monoblasts

- M5-AML: Three stages of differentiation

  - AcNE^{++}, CD14^{++} > CD15$^{+/-}$

  - AcNE$^+$, CD14^{++}, CD15^{++}

  - AcNE^{low}, CD14$^-$, CD15$^+$, cyHLA-DR$^+$ cyCD7$^+$

- M6-AML: HLA-DR$^+$, CD34$^+$, CD33$^+$, CD13$^+$, CD71$^+$, glycophorin A$^+$

- M7-AML: HLA-DR$^+$, CD34$^+$, CD41$^+$, CD61$^+$
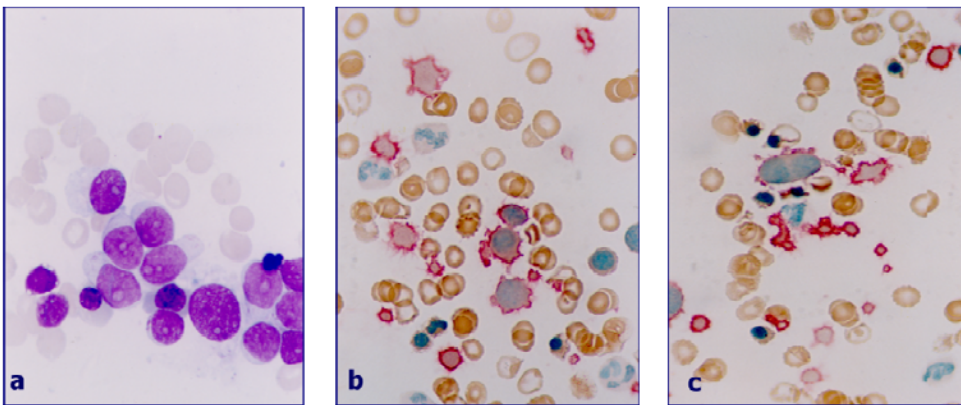
Figure 12.8 - *BM film of patient with acute megakaryoblastic leukaemia (M7AML):*
a – MGG x 900
b – CD41 positive blast cells
c – CD61 positive blast cells
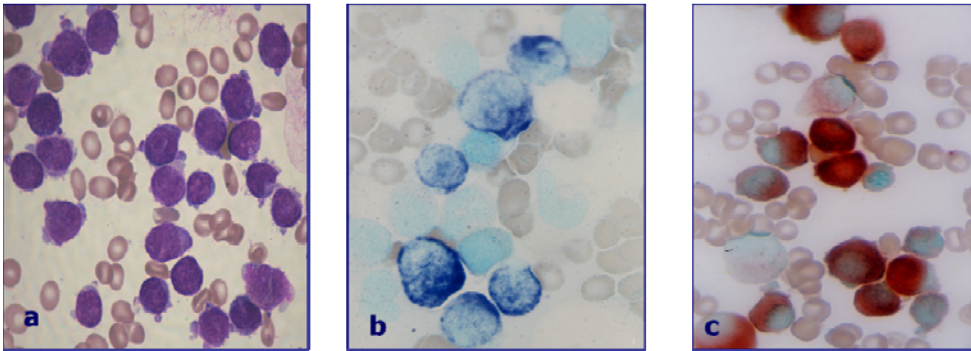
Figure 12.9 - *BM film of patient with acute hypergranular promyelocytic leukaemia (M3 AML):*
a – MGG x 900
b – chloroacetate esterase stain showing a positivity in promyelocytes
c – acid non-specific esterase stain showing a positivity in leukaemic cells

It is worth notice that in seven AML patients (16% of all AML cases) leukaemia was preceded by MDS (including 2 patients with M1 AML, 2 – with M4 AML, 1 – with M4Eo AML; 2 – with M6 AML). At the same time, only 6 cases of preceding MDS were found upon examination of 373 AL patients in general population of Kyiv city and district (1.5%).
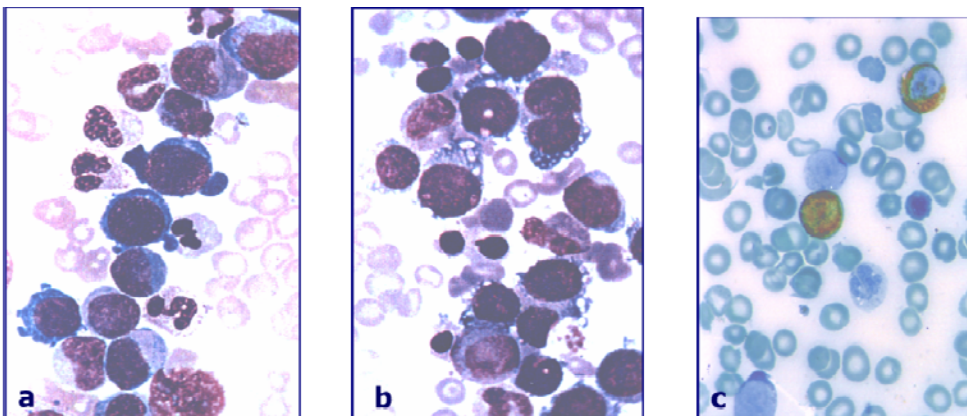
Figure 12.10 - *BM film in refractory anemia (a) an refractory anemia with excess of blasts (b,c): a, b – MGG x 900;*
c – myeloperoxidase stain showing negativity in majority of neutrophils and blasts
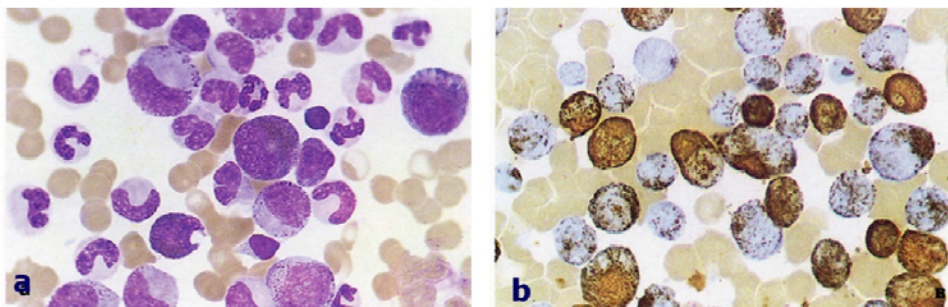
Figure 12.11 - *PB film in Chronic myelogenous leukaemia*
a – MGG x 900
b – positive peroxidase reaction
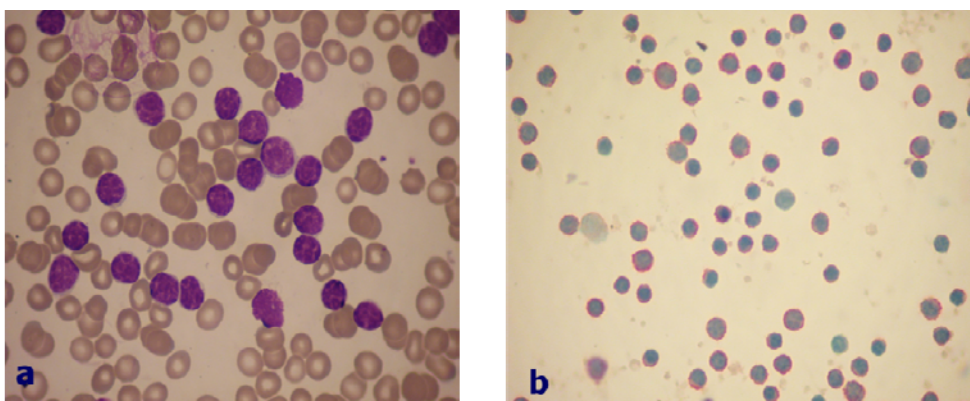
Figure 12.12 - *PB film in B-cell chronic lymphocytic leukaemia:*
a – MGG x 900
b – CD23-positive cells

Advances in molecular biology and our understanding of the pathophysiology of B-CLL provide a strong basis for expecting that exposure to ionizing radiation may increase CLL risk.

Richardson et al., 2005

Silver et al., 2007

Schubauer-Berigam et al., 2007

Vryheid et al., 2008

Hamblin, 2008

Kesminiene et al., 2008

According to our data, up-to-date B-CLL rate in Chernobyl clean-up workers (26.96%) is practically the same as in Ukrainian population in general (29.32%).

Immunophenotypes of verified B-cell non-Hodgkin's lymphoma

- Follicular lymphoma (10 pts.): $CD19^+$, $CD20^+$, $CD22^+$, $CD10^{+/-}$, $CD5^-$, $CD23^{+/-}$, $CD25^-$, $CD43^-$, $CD11c^-$

- Lymphoplasmacytic lymphoma (5 pts.): $CD19^+$, $CD20^+$, $CD22^+$, $CD10^-$, $CD5^-$, $CD23^-$, $CD25^-$, $CD38^+$

- Mantle cell lymphoma (5 pts.): $HLA\text{-}DR^+$, $CD19^+$, $CD20^+$, $CD22^+$, $CD5^+$, $CD23^-$, $CD10^-$, Cyclin D^+

- Splenic marginal zone B-cell lymphoma (3 pts.): $HLA\text{-}DR^+$, $CD19^+$, $CD20^+$, $CD22^+$, $CD5^-$, $CD23^-$, $CD25^-$, $CD10^-$, $CD43^-$, sIg^+

- Diffuse large B-cell lymphoma (8 pts.): $CD19^+$, $CD20^+$, $CD22^+$, $CD79a^+$, $CD5^-$, $CD23^-$

- Extranodal marginal zone B-cell lymphoma of MALT type (3 pts.): $CD19^+$, $CD20^+$, $CD22^+$, $CD79a^+$, $CD23^-$, $CD5^-$, $CD10^-$, $CD43^{+/-}$

Multiple myeloma (diffuse and solitary forms) was diagnosed in 18 patients (mean age 57.9 years). In six patients (35.3%), the disease developed at the age under 50. MM percentage in the patients of Chernobyl clean-up worker group in our study turned out to exceed that in the patients of the general populations studied at the same period (6.41% vs 4.0%).
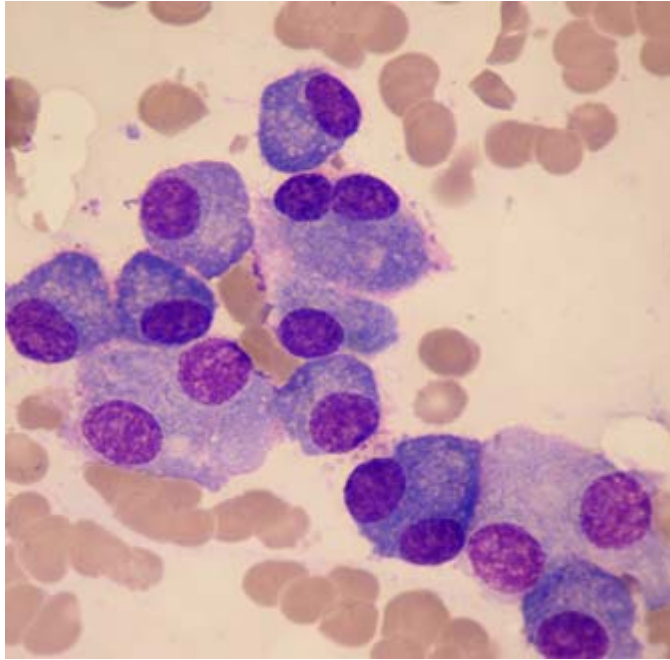
Figure 12.13 - *BM smears in multiple myeloma: MGG x 900*

Tumors from mature (peripheral) T-cells and NK-cells

- T-cell prolymphocytic leukaemia (2 pts.):
  $CD1a^-$, $CD2^+$, $CD3^+$, $CD5^+$, $CD7^+$, $CD4^+$, $CD8^-$

- Sezary syndrome (3 pts.):
  $CD7^+$, $CD3^+$, $CD4^+$, $CD8^-$, $CD25^-$

- Large granular lymphocyte leukaemia

  - T-cell subvariant (3 pts.): $CD3^+$, $CD5^+$, $CD2^+$, $CD7^{low}$, $CD4^-$, $CD8^+$, $CD56^{low}$, $CD57^{+/-}$, $CD16^+$, HLA-DR$^-$

  - NK-cell subvariant (2 pts.): $CD3^-$, $CD5^-$, $CD2^+$, $CD7^+$, $CD4^-$, $CD8^{+/-}$, $CD56^{low}$, $CD57^+$, $CD16^+$, HLA-DR^{low}
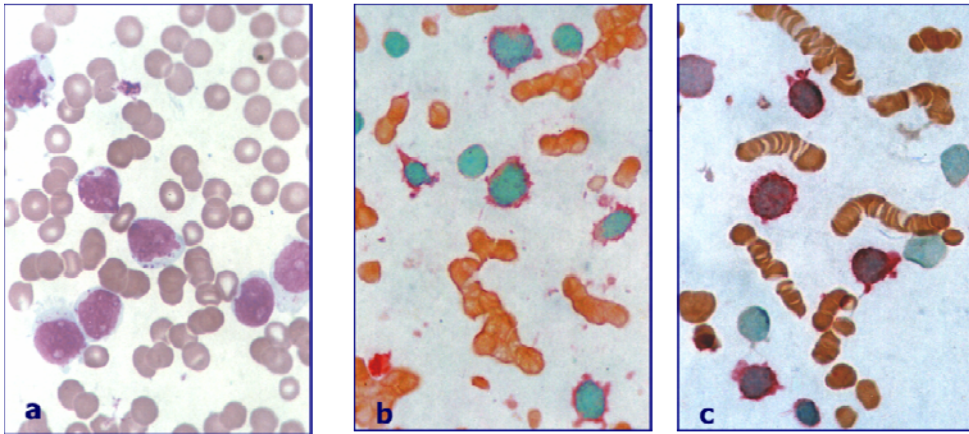
Figure 12.14 - *BM film of patients with LGL leukaemia (NK-cell subtype):*
a – MGG x 900
b – CD16 positive cells
c – CD56 positive cells
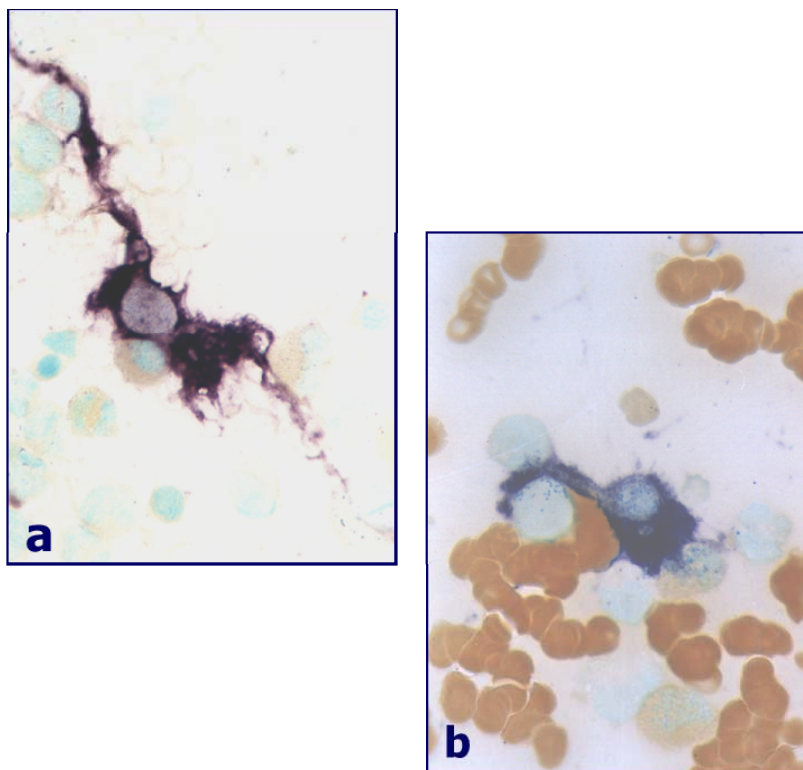
Figure 12.15 - *Reactive responses in bone marrow stroma in clean-up workers*

Cytochemistry and immunophenotype of stromal dendritic cells:

Alkaline phosphatase +++
Acid phosphatase   ++
Acid non-specific esterase ++
PAS-reaction   +
Vimentin   ++
HLA-DR   +
DAKO-DRCL   -
CD34   -

Reactive responses in bone marrow stroma in clean-up workers with malignant diseases of hematopoietic and lymphoid tissue exhibiting the strongly alkaline phosphatase-positive villous cells (endothelium of sinuses or blood vessels? cells precursors of osteoblasts?). The appearance of these cells in bone marrow of clean-up workers (both leukaemia patients and patients with non-malignant diseases of

hematopoietic and lymphoid tissue) could be regarded as a response to incorporation of the osteotropic heavy metals including radionuclides in endostal areas. It is highly probable that such cells that were not evident in the bone marrow of the patients observed in pre-Chernobyl period could serve as the non-specific markers of radiogenic leukaemias. This problem deserves further studying.

All the main forms of malignant diseases of hematopoietic and lymphoid tissues including B-cell chronic lymphocytic leukaemia were registered in the group of Chernobyl clean-up workers diagnosed in 10-23 years after the exposure to radiation. The comparison of the relative distribution of the specified forms of hematopoietic and lymphoid malignancies in the patients diagnosed among Chernobyl clean-up workers demonstrates the increasing multiple myeloma rate and the tendency to the increasing non-Hodgkin's lymphoma in leukaemization phase and CML rates as compared to the group of general population.
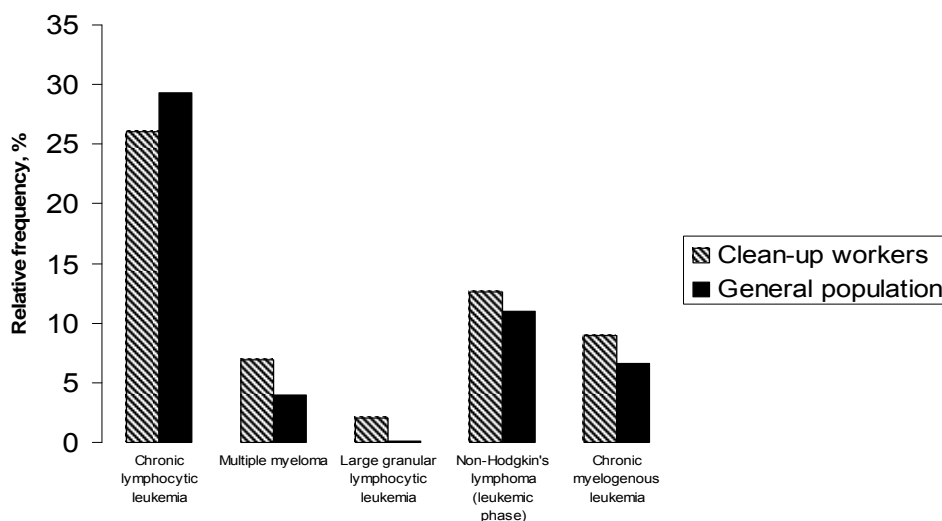
Figure 12.16 - *Relative frequency of selected leukaemia and lymphoma types in clean-up workers and general population*

The peculiar feature of AML in clean-up workers under study was the development of leukaemia on the background of preceding MDS in 19% of all AML cases studied. The high incidence of LGL-leukaemia among clean-up workers with hematopoietic malignancies (1.77%) is of particular importance since until recently this category of T-cell and NK-cell neoplasms was not revealed in oncohematological clinics in Ukraine. Only verified precise diagnosis could be the prerequisite for the advanced studies in analytical epidemiology of different biological types of leukaemias aimed at elucidating the role of the radiogenic factor in the pathogenesis of the malignant diseases of hematopoietic and lymphoid tissue.

13

The ARCH Project and the health effects of the Chernobyl accident

Dr. Keith Baverstock
University of Kuopio, Finland, ARCH Project

Agenda for **R**esearch on **C**hernobyl **H**ealth

A European Commission funded project within FP7.

ARCH will identify and prioritise (short and longer-term) the potential studies, examine their feasibility, cost effectiveness and likelihood of success, and provide a reasoned and comprehensive strategic agenda for future research.

Although primarily concerned with the three most affected countries effects in wider Europe will also be considered

You can find out more at the website

http://arch.iarc.fr

ARCH needs your input

ARCH needs to know what you think needs addressing from the RESEARCH perspective in relation to the HEALTH EFFECTS potentially arising from the **direct effects** of radiation from the Chernobyl accident (i.e., excluding psychosocial health effects). You can make relatively short proposals or comments via the website or longer, more comprehensive proposals via e-mail attachment.

Editors note: October 2011. None of the research proposals suggested by this initiative will be funded according to the EC.

14

Radiation induced genetic effects in Europe after the Chernobyl nuclear power plant catastrophe

Prof Hagen Scherb, Dr Kristina Voigt

Institute of Biomathematics and Biometry, German Research Center for Environmental Health, Neuherberg, Germany

Genetic **Effects**

Muller carried out experiments with varied doses of X-rays to Drosophila, and a connection between radiation and lethal mutations emerged. By 1928, others had replicated his results, expanding them to other model organisms such as wasps and maize. A genetic effect, as a definition, may be the result of radioactivity or substances that cause damage to (the genes of) a reproductive cell (sperm or egg), or a somatic cell, which can then be passed from one generation to another, or may induce disease (e.g. cancer) in an individual. Examples can include Sex odds, birth defects, stillbirths, leukaemia or thyroid cancer.

(http://www.doh.wa.gov/Hanford/publications/overview/genetic.html) Muller HJ (1927). Artificial transmutation of the gene. Science 66: 84-87

Genetic theory for the human sex odds at birth

Irradiated parents and offspring gender

Fathers only   =>   sex odds

Mothers only   ->   sex odds

Both parents   ->   ???

Figure 14.1 – Genetic effects – sex odds (sex ratio)

Schull WJ, Neel JV (1958). Radiation and the sex ratio in man. Science 128: 343-348

Dickinson HO et al. (1996). The sex ratio of children in relation to paternal preconceptional radiation dose. J Epidemiol Community Health 50(6): 645–652 Padmanabhan et al. (2004) Heritable anomalies among the inhabitants of regions of normal and high background radiation in Kerala. Int J Health Serv 34 (3), 483-515

Dosimetry

Working hypothesis

In the first few years after the ChNPP accident, deposition of

$$46.6 \text{ kBq/m2} \quad \text{Cs-137}$$
$$+ 23.3 \text{ kBq/m2} \quad \text{Cs-134}$$

generated an effective dose of   1 mSv/a

Figure 14.2 *– Fallout and dose formation*

Jacob P et al. (1990) Calculation of organ doses from environmental gamma rays using human phantoms and Monte Carlo Methods. GSF-Bericht 12/90

Drozdovitch V et al. (2007) Radiation exposure to the population of Europe following the Chernobyl accident. Radiat Prot Dosimetry 123 (4), 515-528

Bundesamt für Strahlenschutz (2006). Jahresbericht 2005, p. 36. Editor: Bundesamt für Strahlenschutz, Germany, Salzgitter

BStMLU and BStMELF (1987). Radioaktive Kontamination der Böden in Bayern. Munich: Bayerische Staatsministerien für Landesentwicklung und Umweltfragen (BStMLU) und für Ernährung, Landwirtschaft und Forsten (BStMELF)
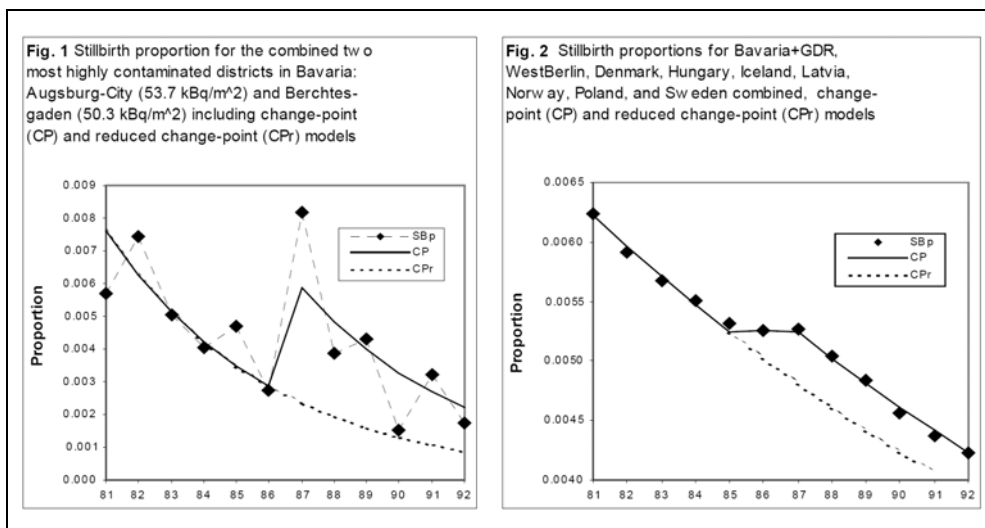
Figure 14.3 - *Stillbirth in Bavaria, Germany, and stillbirth in Europe, 1981 – 1992*
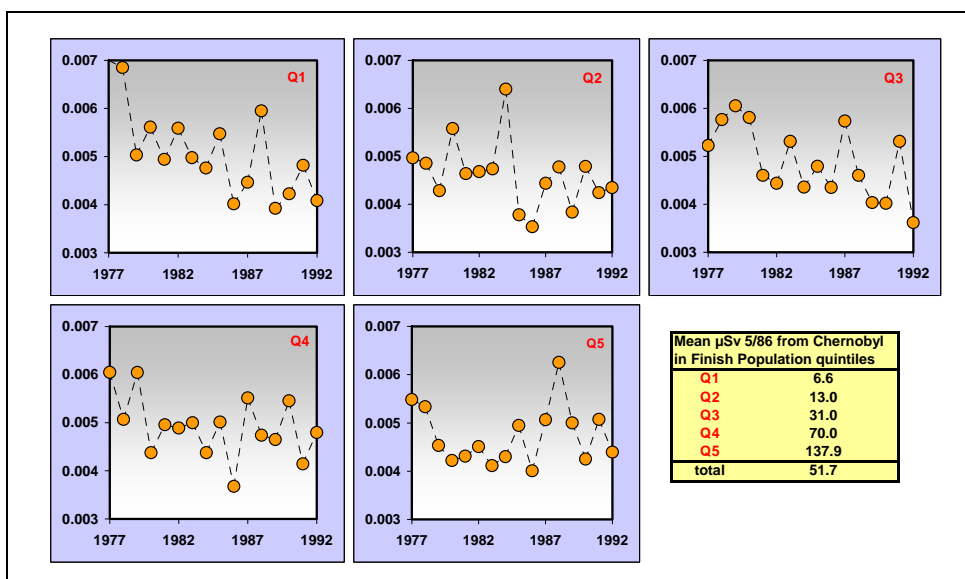
Figure 14.4 - *Stillbirth in Finland, 1977 – 1992 (prevalence data by exposure quintiles)*
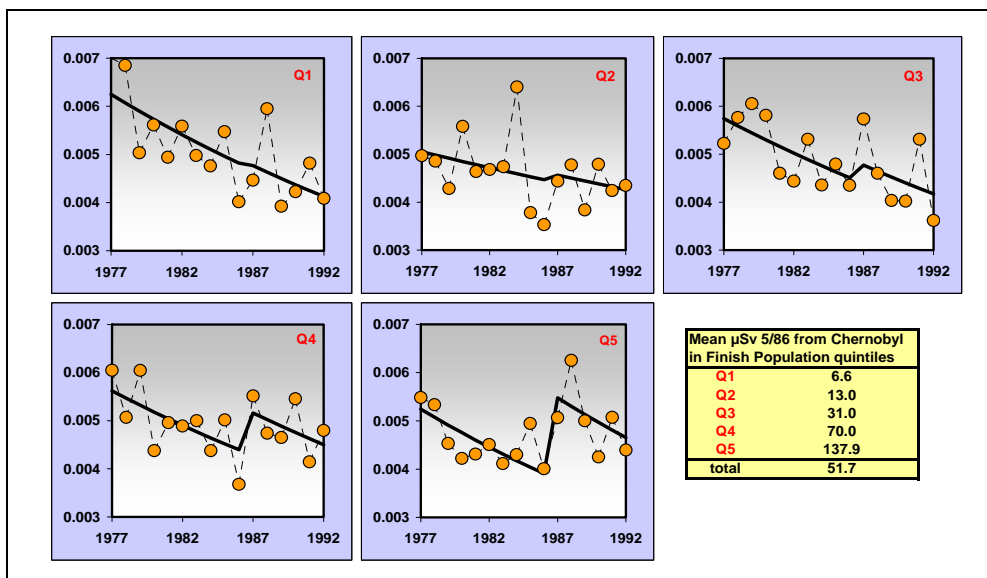
Figure 14.5 - Stillbirth in Finland, 1977 – 1992 (spatial temporal model

Figure 14.6 - Stillbirth in Finland, 1977 – 1992 (dose specific risk

Bavaria

Former GDR
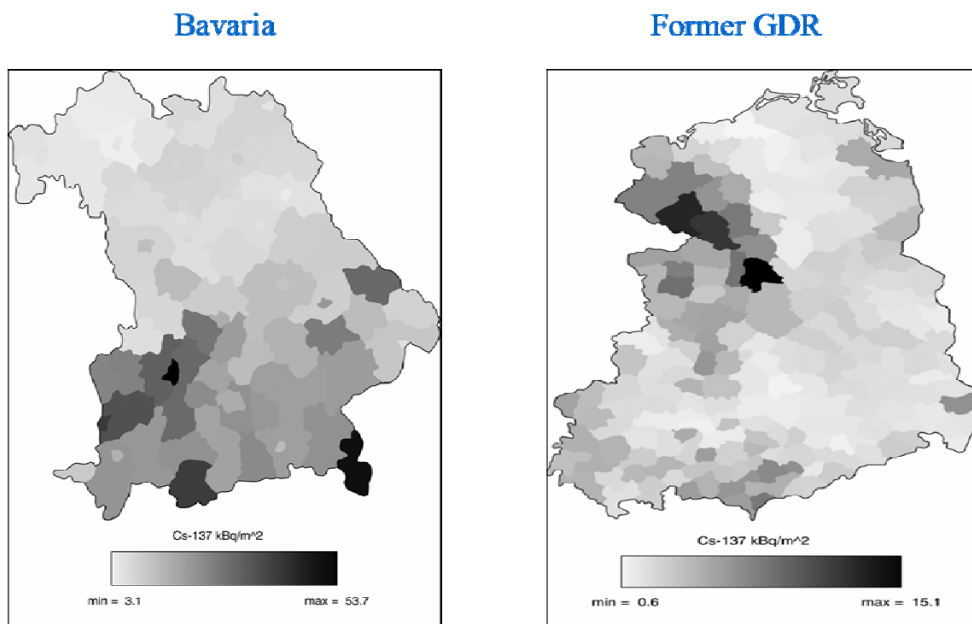
Figure 14.7 - Sex odds and fallout (dose) in Germany (spatial distribution of fallout)

OR/(mSv/a)	1.0380
95%-CI	[1.0126, 1.0640]
p-value	0.0031
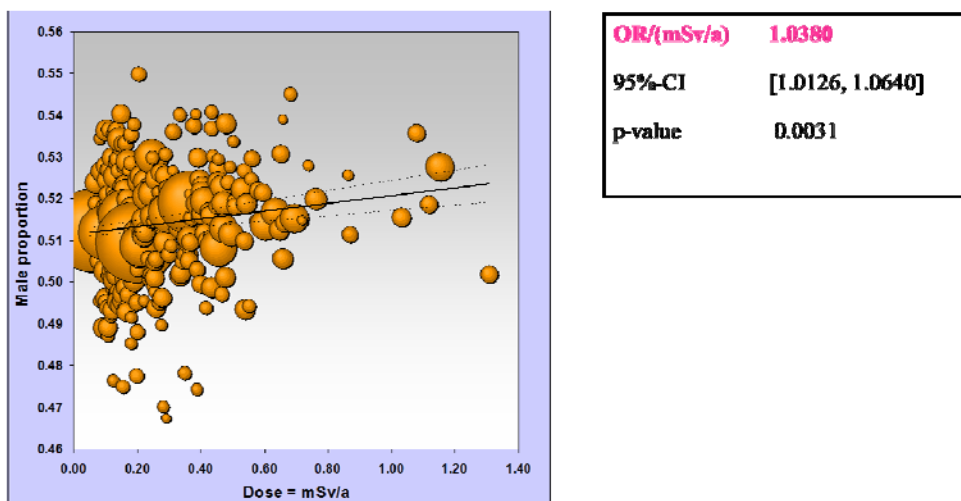
Figure 14.8 - Sex odds and fallout (dose) in Germany (1986+1987 depending on the excess dose by Chernobyl fallout: 0.0143 (mSv/a)/(kBq/m2))

217
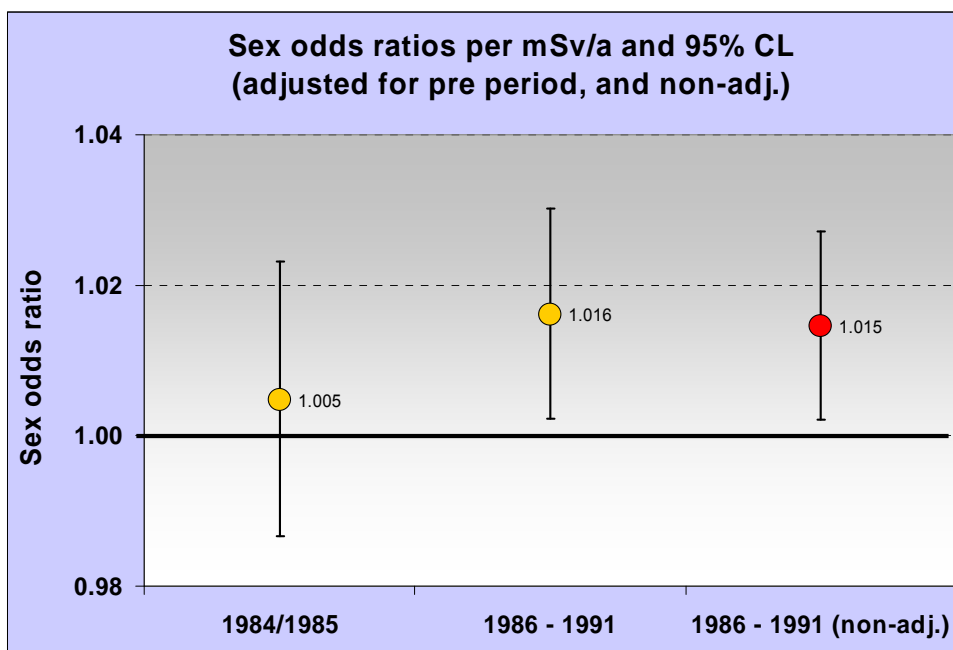
Figure 14.9 - *Sex odds and fallout (dose) in Germany (1984-1991, long-term dose dependent jump heights 1986-1991)*
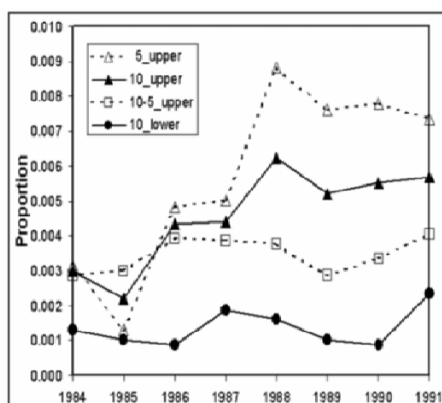
Fig. 5: Birth prevalences of two congenital heart malformations (ICD7454+ICD7455, n = 2797) in Bavaria: stratification according to contamination of districts (see Table 1)

Figure 14.10 - *Congenital malformation of the heart (1984-1991, long-term dose dependent jump heights 1987-1991)*

Similar effects on the sex odds as recently published have already been observed in the USA and in Europe on a global scale in the 1960s and 1970s, but have not yet been acknowledged as possible effects of atmospheric atomic bomb test fallout.

Note, the "missing boys" in the "sex ratio literature" may be "less missing girls" from the 1970s onward, after the atmospheric atomic bomb test ban.
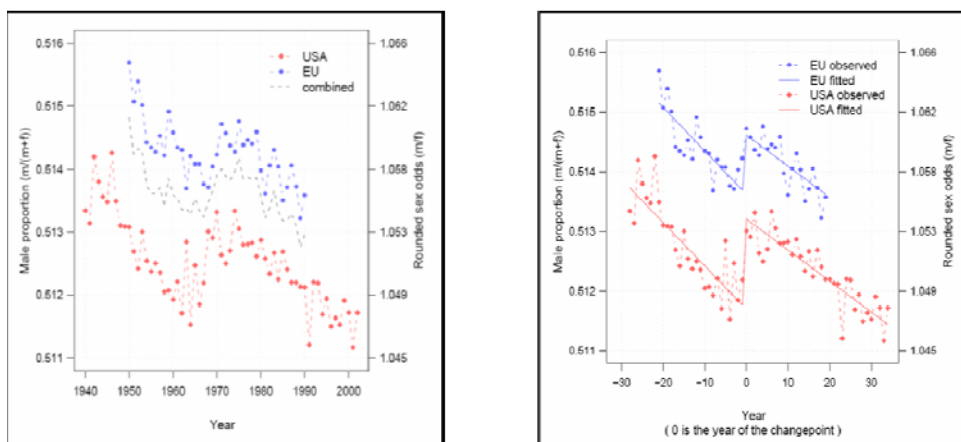
Figure 14.11 *– Sex odds and atmospheric atomic bomb testing*

M Martuzzi, N Di Tanno, R Bertollini. Declining trends of male proportion at birth in Europe. Archives of Environmental Health, 56(4):358 364, Jul- Aug 2001.

TJ Mathews and BE. Hamilton. Trend analysis of the sex ratio at birth in the united states. Nat Vit Stat Rep, 53(20):1 17, Jun 2005. Nat Cent for Health Stat.

S Meyer, H Scherb. Untersuchung des jährlichen Geschlechterverhältnisses der Neugeburten in Europa und den USA auf Changepoints, July 31 2007 (synoptic reanalyses).
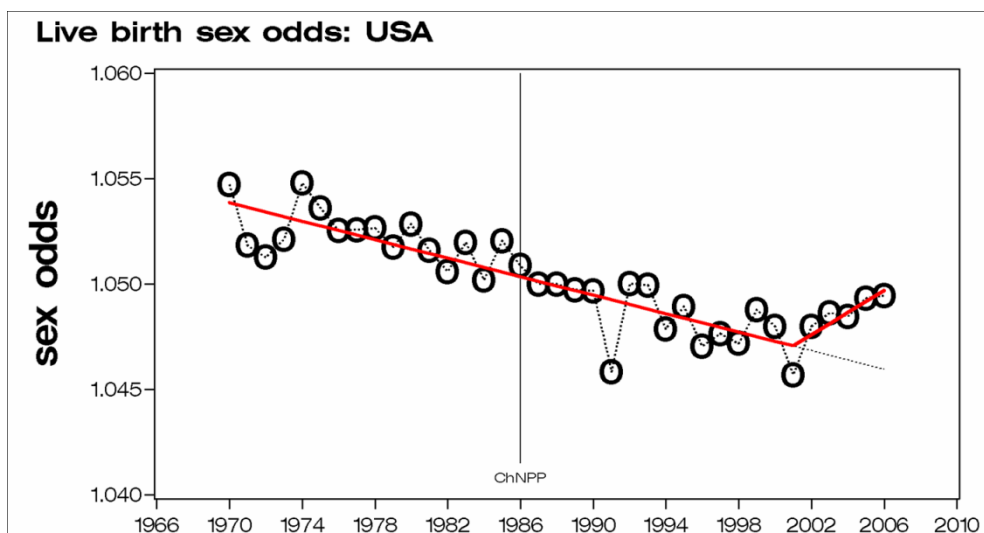
Figure 14.12 - *Sex odds in USA, 1970 – 2007*

Europe IIIa, 1970-2007, complete data			Births and sex odds	
Belgium	Luxembourg	Portugal	total	80,373,314
France	Malta	Switzerland	male	41,249,601
Ireland	Netherlands	UK	sex odds	1.0543

Europe IIIb, 1970-2007, complete data			Births and sex odds	
Albania	Germany	Poland		
Austria	Greece	Romania		
Belarus	Hungary	Russ. Fed.		
Bulgaria	Iceland	San Marino		
Czechoslovakia (f.)	Italy	Sweden		
Denmark	Latvia	Yugoslavia (f.)	total	216,491,268
Estonia	Lithuania		male	111,258,587
Finland	Norway		sex odds	1.0573

Former SU Republics, 1980-2005, incomplete data			Births and sex odds	
Kazakhstan	Tajikistan	Uzbekistan	total	47,655,378
Kyrgyzstan	Turkmenistan		male	24,463,930
Moldova	Ukraine		sex odds	1.0549

40 countries with territory in Europe + 4 Asian countries; Spain omitted because of unusual trend; also ommitted: Andorra, Liechtenstein, Monaco, Turkey, and Vatican due to no data at all, or essentially incomplete data.

Figure 14.13 – *Sex odds in Europe, and parts of Asia, 1970 – 2007*
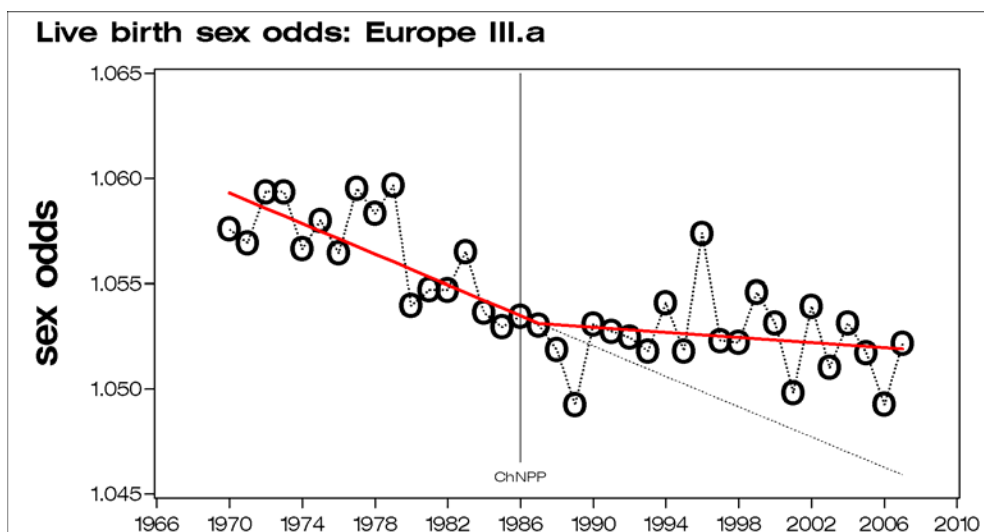
Figure 14.14 – *Sex odds in Western Europe – less exposed*
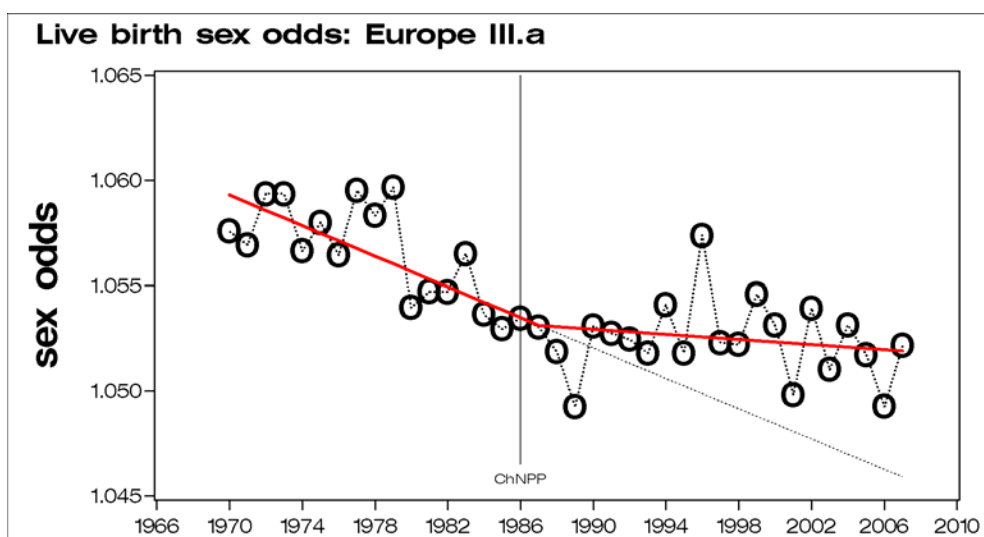
Figure 14.15 – *Sex odds in Central and Eastern Europe – moderately or highly exposed*

221
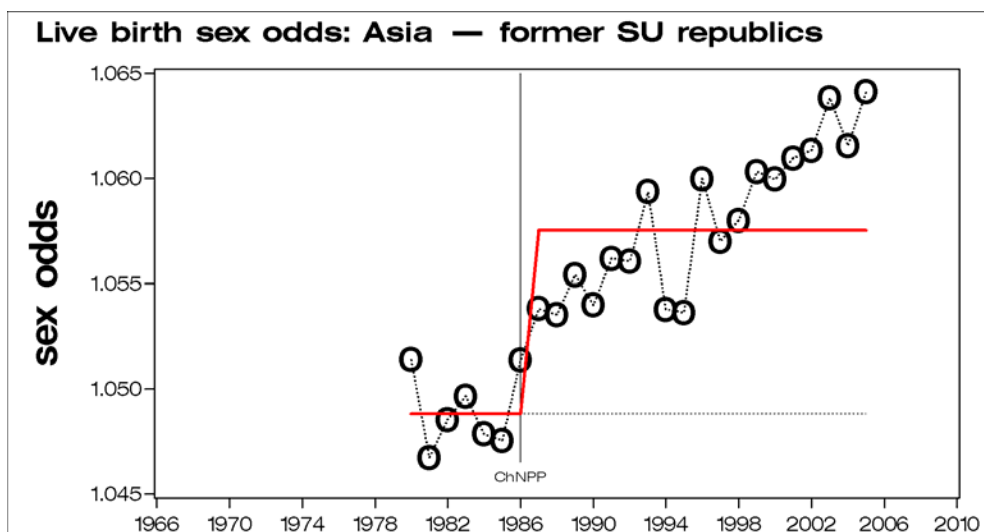
Figure 14.16 – *Sex odds in former SU republics in Asia – high exposure*

I present a hypothesis – that the jump heights in sex odds after Chernobyl depend upon the amount of fallout where the national excess is greater than or equal to average effective doses. As you have seen, I have compared the sex odd ratios in countries with differing levels of fallout after Chernobyl: low fallout in France, intermediate fallout in Denmark, Germany, Italy and the Former Yugoslavia, and highest in Belarus and the Russian Federation.
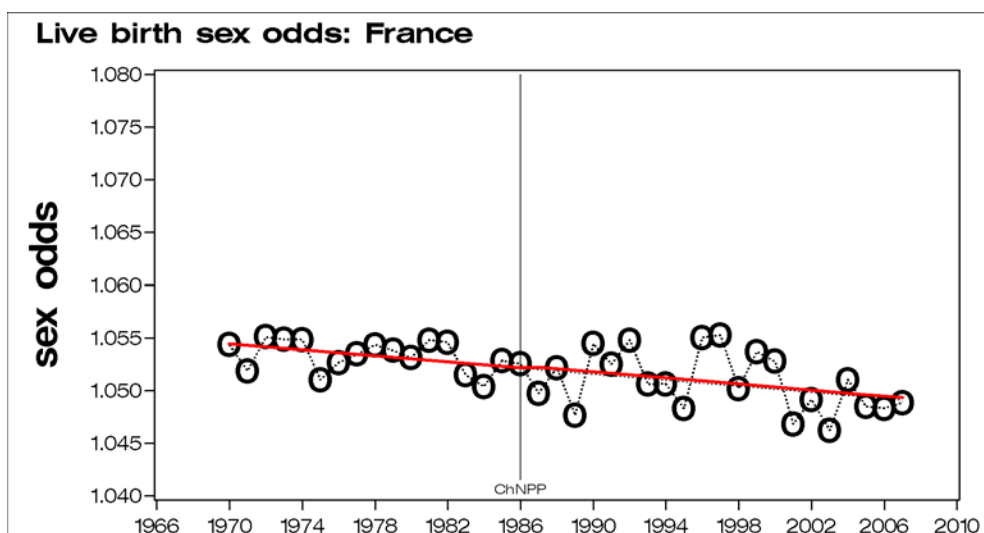
Figure 14.17 – *Sex odds in France*
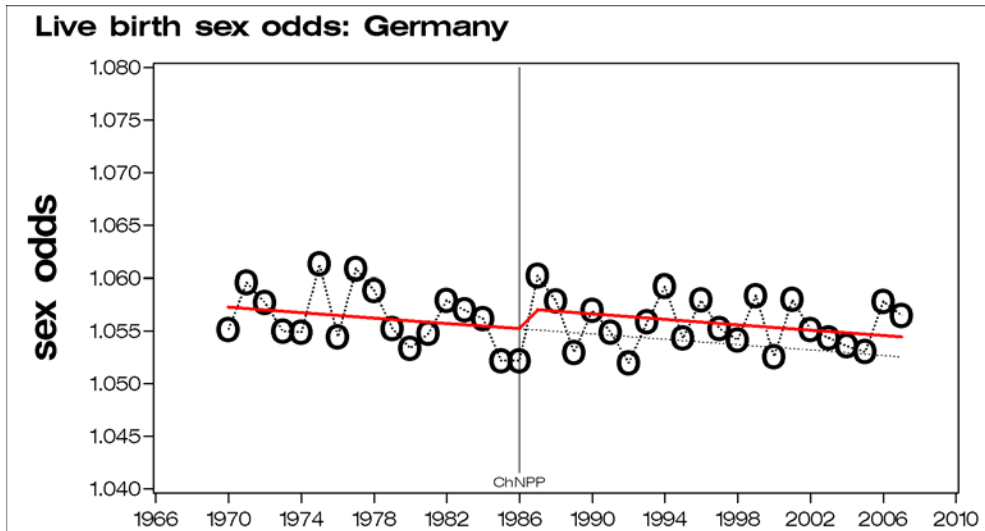
Figure 14.18 – Sex odds in Germany
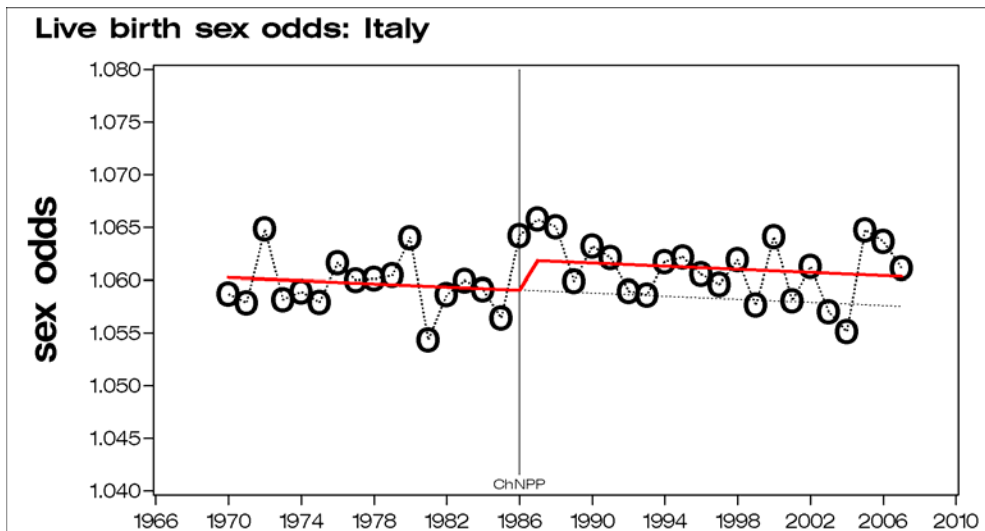
Figure 14.19 – Sex odds in Italy

223
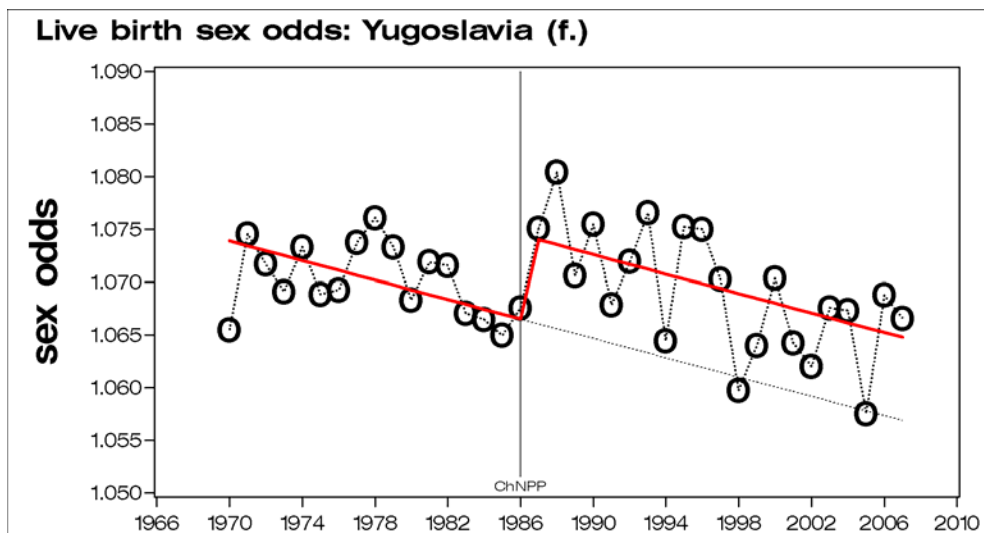
Figure 14.20 – Sex odds in the Former Yugoslavia
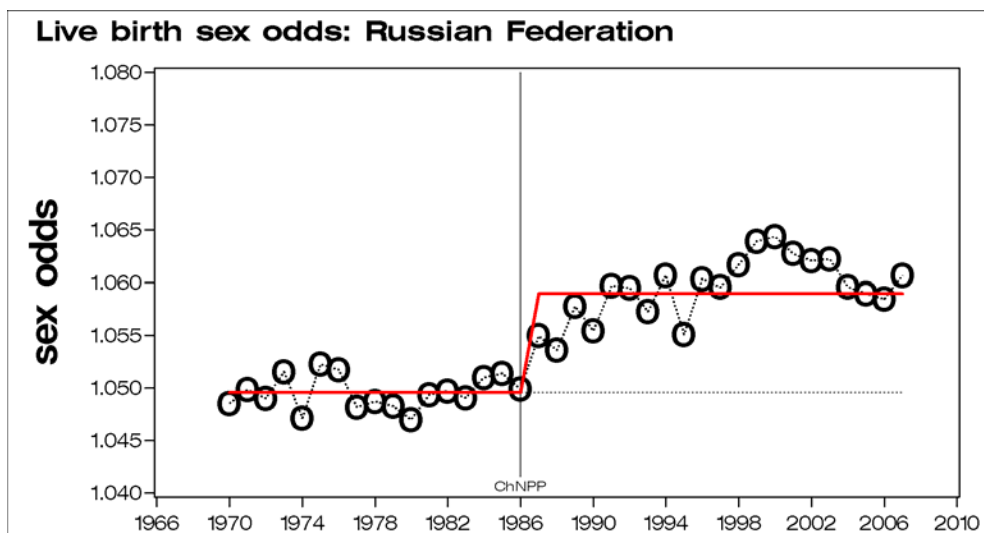
Figure 14.21 – Sex odds in the Russian Federation
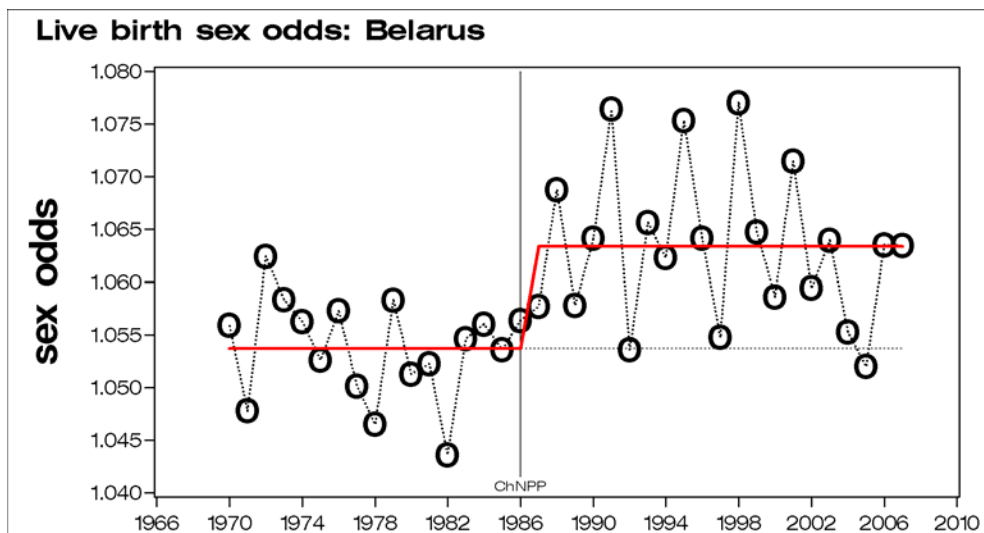
Figure 14.21 – Sex odds in Belarus
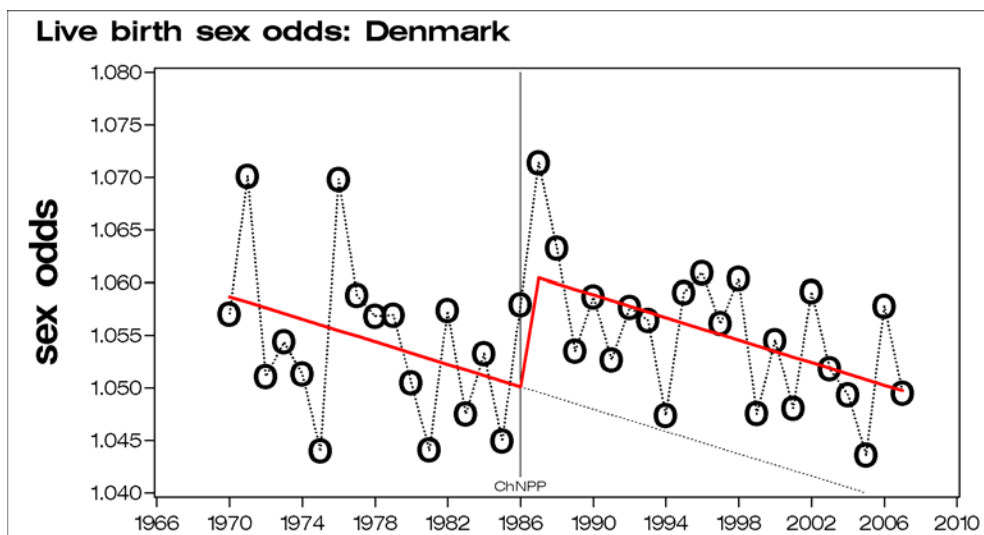
Figure 14.22– Sex odds in Denmark

Vergleich der in den Jahren 1986, 1987, 1996 und 2006 berechneten effektiven Dosen für Erwachsene durch die SSK								
Gebiet	Effektive Dosis im 1. Jahr (mSv)				Gesamte effektive Dosis für die nach dem Unfall folgenden 50 Jahre (mSv)			
	1986	1987	1996	2006	1986	1987	1996	2006
Voralpengebiet		1,2	0,65	0,5		3,8	2,2	2,1
Südlich Donau	0,5-1,1	0,6	0,35	0,3	1,5-4,0	1,9	1,3	1,1
Nördlich Donau		0,2	0,17	0,1		0,6	0,55	0,4

Figure14.23 – *Ecological dose-response (German collective dose data)*
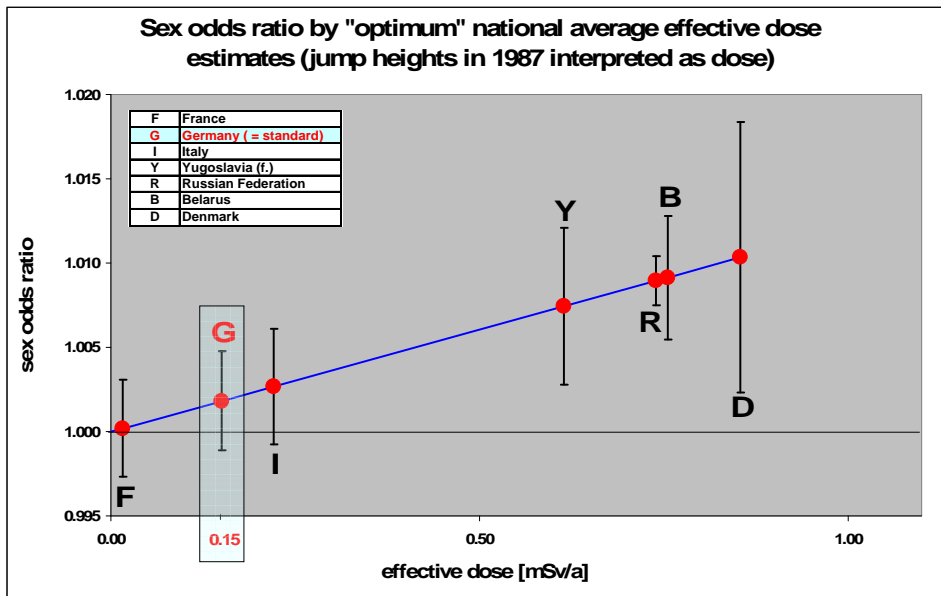
Figure14.24 – *Ecological dose-response ("national dosimetry")*

Country	jump OR	mSv/a
France	1.0002	0.02
Germany	**1.0018**	**0.15**
Italy	1.0027	0.22
Yugoslavia (f.)	1.0074	0.61
Russian Federation	1.0090	0.74
Belarus	1.0092	0.75
Denmark	1.0104	0.85
jump OR per mSv	**1.0121**	

Figure 14.25 - Optimum excess collective doses per year in France, Italy, former Yugoslavia, Russian Federation, Belarus, and Denmark based on the linearity assumption, the jump heights in 1987 and the overall excess collective dose in Germany of 0.15 mSv/year from 1987 to 2007 (Germany serves as a standard)
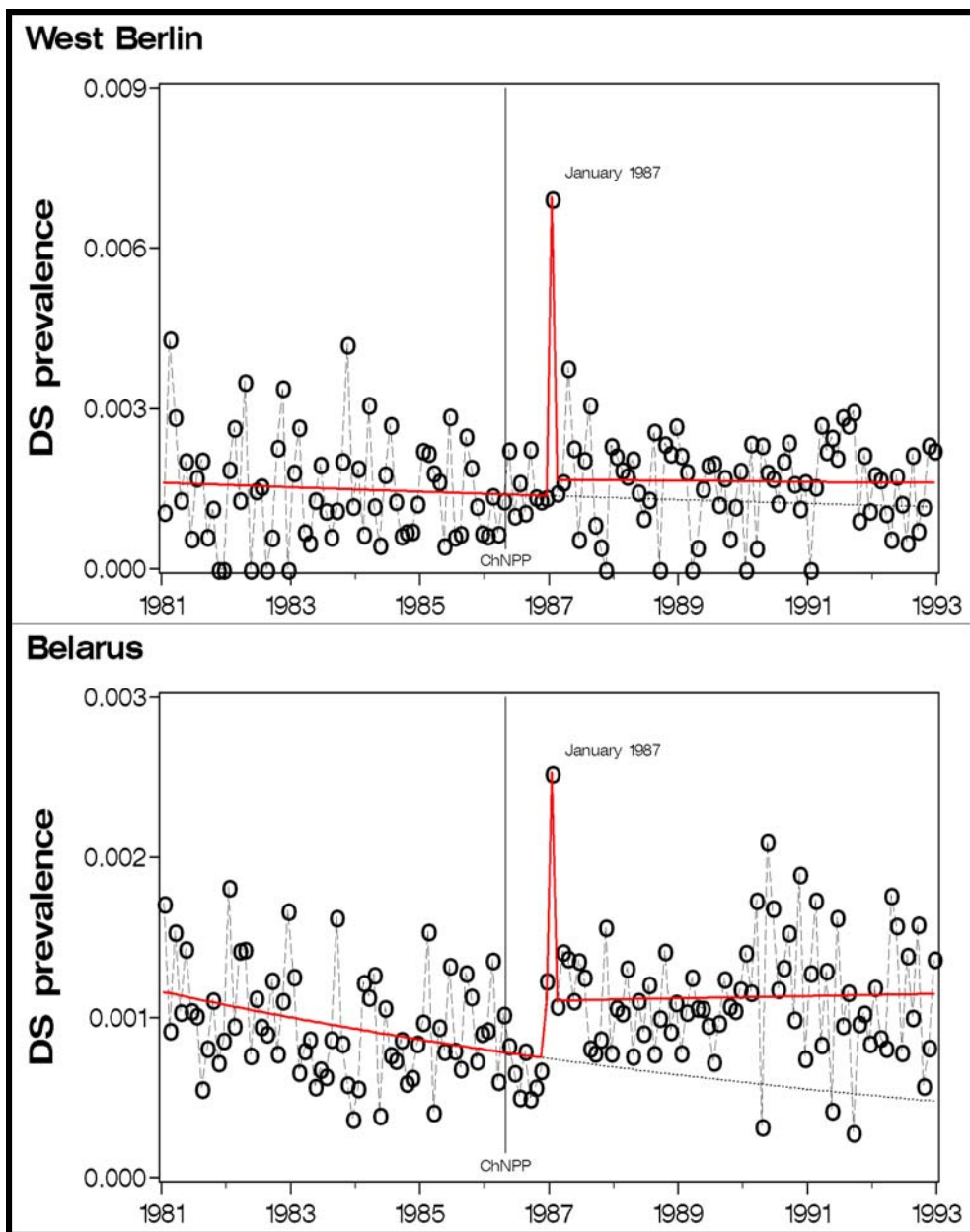
Figure 14.26 – *Down syndrome in Europe before and after Chernobyl (1)*
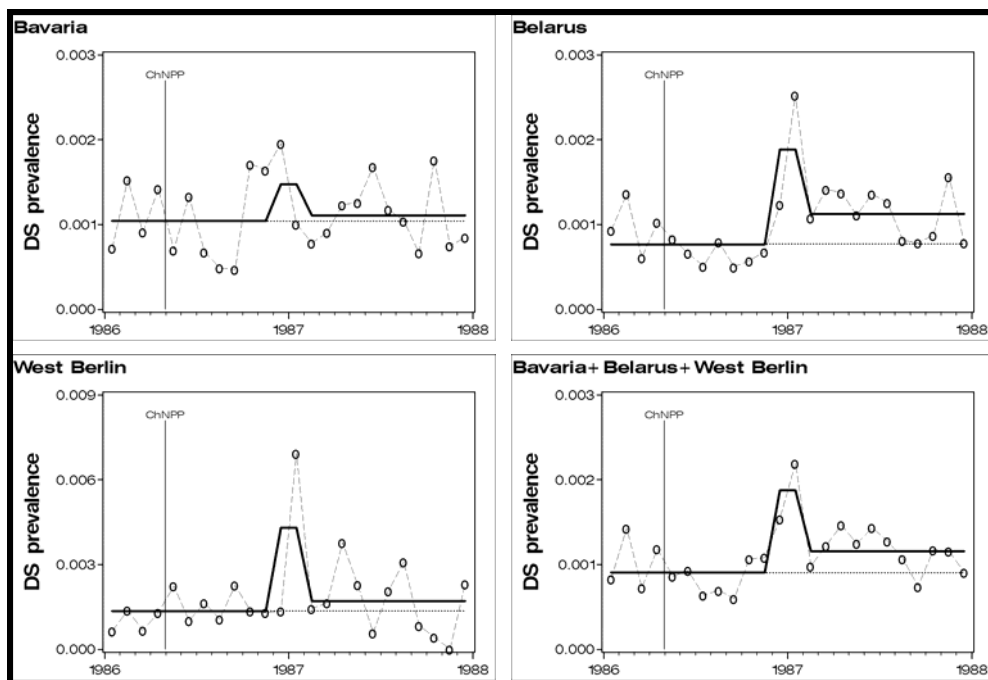
Figure 14.27 – *Down syndrome in Europe before and after Chernobyl (2)*

Average excess per capita effective dose (mSv) in 1986 after Chernobyl, in Bavaria, Belarus and West Berlin combined			
Region	**Population 1986 (1000)**	**mSv 1986**	**Population weighted dose**
Bavaria	10,997	0.47	0.21
Belarus	10,045	0.91	0.38
West Berlin	3,093	0.13	0.02
Total	**24,135**		**0.61**
Doubling dose in mSv		**Estimate**	**95%-CL**
Overall excess dose in 1986		0.6	-
Overall DS odds ratio - 1987 vs. 1986		1.4	1.1 - 1.7
Odds ratio per mSv		1.7	1.2 - 2.5
Doubling dose		**1.3**	**0.8 - 4.0**

Figure 14.28 – *Down syndrome in Europe before and after Chernobyl (3)*

I have submitted these and their related findings under the title "Low dose ionizing radiation increases the rate of nondisjunction in man", with the kind assistance of Sperling K. (*Institute of Human Genetics, Charité - Universitaetsmedizin Berlin, Germany*), Neitzel H. (*Belarus Institute for Hereditary Diseases, Minsk, Republic of Belarus*) and Zatsepin I. (*Institute of Biomathematics and Biometry, Helmholtz Zentrum München –German Research Center for Environmental Health, Neuherberg, Germany*).

Possible scale of lost or impaired children after Chernobyl in all of Europe and the part of Asia covered		
Observed	1987 ≤ Births ≤ 2007	183 802 030
	male	94 446 893
	female	89 355 137
	sex odds	1.0570
	missing boys	249554
	missing girls	831846
Expected	Births	184 883 430
	male	94 696 447
	female	90 186 983
	sex odds	1.0500
	sex OR	**1.0066 (1.0052–1.0079)**
sex OR/mSv		
1.0145 (1.0021–1.0271)		**0.460**
	1987 ≤ Births ≤ 2007	183 802 030
	BD 3%(LB)+0.5%(TB)	6 437 689
	OR/mSv*	1.54
	BD doubling dose	**1.61**
	OR BD+SB	1.22
	Excess BD+SB	**1 415 769**
Lost or impaired children		**2.5 millions**

Chernobyl gender gap

0.6 million missing girls, if only girls were susceptible

1.1 million missing children, if the sex odds of missing children were 1:1

Figure 14.29 *- Possible scale of reproductive detriment due to the Chernobyl accident (Scherb H, Weigelt E. (2003)*

Conclusions
UNSCEAR (*UNSCEAR 2001 Report, Hereditary Effects of Radiation, Scientific Annex, p. 82*) states "The estimate of risk" (at 1 Gray) "for congenital abnormalities is about 2,000 cases per million live births (compared to 60,000 cases per million live births)".

If:
RR/1Gy=62,000/60,000=1.033

This means:
Doubling Dose=21.3 Gy

As we have shown for congenital malformations (*Scherb H, Weigelt E. Congenital Malformation and Stillbirth in Germany and Europe Before and After the Chernobyl Nuclear Power Plant Accident. ESPR - Environ Sci & Pollut Res, 10 Special (1)*

2003 Dec, 117-125) (*Sperling K et al. Low dose irradiation and nondisjunction: Lessons from Chernobyl, 19th Annual Meeting of the German Society of Human Genetics, April 8-10, 2008, Hanover, Germany, Abstractbook, p. 174-175*) e.g. malformations of the heart, deformities, Down syndrome, using data from the Bavarian congenital malformation data set, the doubling dose is in the order of magnitude of below a few mSv. Thus, UNSCEAR is in error at least at 3 orders of magnitude.

The consistency of our results implies that either there is harm of ionizing radiation below 1 mSv, or the dose concept is invalid altogether, or that the exposure after Chernobyl was higher than assumed, or even some combination of these concepts. The genetic effects of ionizing radiation in humans, animals (and plants) should be investigated more objectively and more thoroughly, focusing on birth defects, stillbirths, secondary sex ratio, cancer induction, e.g. leukaemia, combinatory effects (radiation & chemicals) and synergistic effects.

"In our own view, it is quite possible that a permanent doubling of the "background" dose of ionizing radiation, worldwide, would very gradually double mankind's burden of inherited afflictions --- from mental handicaps to predispositions to emotional disorders, cardio-vascular diseases, cancers, immune-system disorders, and so forth. Such a doubling would be the greatest imaginable crime against humanity (nature …)"

Figure14.30 - *A Wake-Up Call for Everyone Who Dislikes Cancer and Inherited Afflictions (Spring 1997) By John W. Gofman, M.D., Ph.D. Egan O'Connor, Executive Director of CNR*

Further publications
I have produced a number of publications on the subject of fallout and its genetic effects for futher reading, they can be found below.

Perinatal mortality and stillbirths
Scherb H, Weigelt E, Bruske-Hohlfeld I European stillbirth proportions before and after the Chernobyl accident. Int J Epidemiol. 1999 Oct;28(5)
Scherb H, Weigelt E, Bruske-Hohlfeld I Regression analysis of time trends in perinatal mortality in Germany 1980-1993. Environ Health Perspect. 2000 Feb;108(2)

Birth defects
Scherb H, Weigelt E Congenital Malformation and Stillbirth in Germany and Europe before and After the Chernobyl Nuclear Power Plant Accident. ESPR - Environ Sci & Pollut Res, 10 Special (1) 2003 Dec, 117-125

Scherb H, Weigelt E Cleft lip and cleft palate birth rate in Bavaria before and after the Chernobyl nuclear power plant accident [Article in German, Abstract in English]. Mund Kiefer Gesichtschir. 2004 Mar;8(2):106-10

Sperling K, Neitzel H, Scherb H (2008) Low dose irradiation and nondisjunction: Lessons from Chernobyl, 19th Annual Meeting of the German Society of Human Genetics, April 8-10, 2008, Hanover, Germany, Abstractbook, p. 174-175

Sex odds in Europe

Scherb H, Voigt K Trends in the human sex odds at birth in Europe and the Chernobyl Nuclear Power Plant accident. Reproductive Toxicology, Volume 23, Issue 4, June 2007, Pages 593-599

Scherb H, Voigt K Analytical ecological epidemiology: Exposure-response relations in spatially stratified time series. Environmetrics, published Online: 12 Sep 2008

Relevant demographic databases

http://data.euro.who.int/hfadb/
http://data.un.org/Data.aspx?d=POP&f=tableCode%3a4
http://data.un.org/Data.aspx?d=POP&f=tableCode%3A54
http://unstats.un.org/unsd/demographic/products/dyb/dyb2.htm
http://www.coe.int/t/e/social_cohesion/population/BELTAB2.xls
http://epp.eurostat.ec.europa.eu/portal/page?_pageid=0,1136184,0_45572595&_dad=portal&_schema=PORTAL
http://www.johnstonsarchive.net/policy/abortion/ab-poland.html

15

In Utero exposure to Chernobyl accident radiation and the health risk assessment

Prof. Angelina Nyagu
President, International Physicians of Chernobyl, Kiev Ukraine

We must first ask a question: what do we know about the qualitative and quantitative effects of ionizing radiation on the developing embryo?
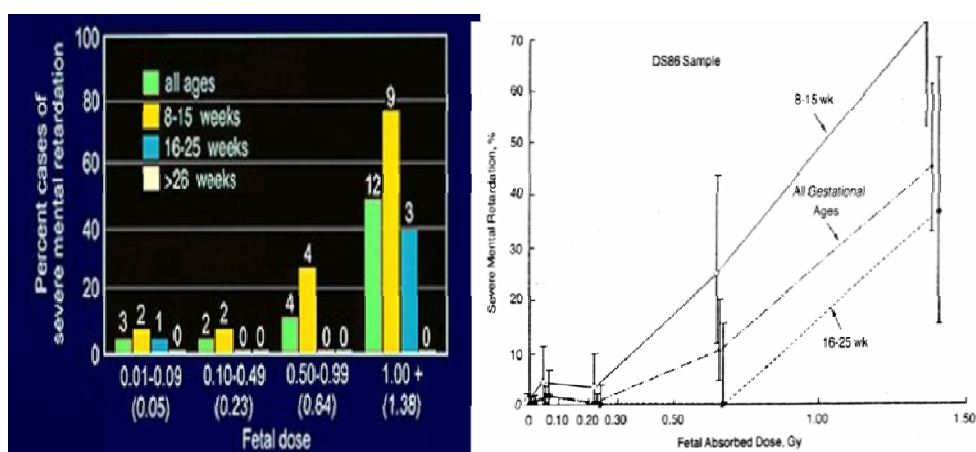
Figure 15.1 *- Specific radiation effects on foetus: mental retardation, microcephaly - Japanese study*

The study shown in Figure 1 shows that those exposed at a gestational age of 8–15 weeks were most at risk. Survivors of the atomic bombing in Japan who were exposed in utero during this sensitive period show a linear increase in the frequency of mental retardation with radiation dose (40% per Gy). There were 2,800 people in this study.

However, there is evidence that radiation affects intelligence (Figs 2-3). John Gofman writes:

"In-utero irradiation during the vulnerable period causes the brilliant to become less brilliant, the average to become "below average," and the retarded to become more retarded. And by pushing more people over the heavy vertical line into the realms of mental retardation and sever retardation, such exposure automatically increases the

percent of a population-sample which is retarded and severely retarded.(John Goffman, 1994)"

Average Fetal Dose	New Percent / Old Percent of	Percent Increase in Rate Mental Retardation
4 rads	(2.63 / 2.28) = 1.15	15 % increase
10 rads	(3.13 / 2.28) = 1.37	37 % increase (at the optimum "hormetic" dose)
15.4 rads	(3.77 / 2.28) = 1.65	65 % increase
23.0 rads	(4.75 / 2.28) = 2.08	2.08-fold increase
30.8 rads	(6.00 / 2.28) = 2.63	2.63-fold increase
46.2 rads	(9.12 / 2.28) = 4.00	4-fold increase
61.5 rads	(13.36 / 2.28) = 5.86	5.86-fold increase
72.0 rads	(16.85 / 2.28) = 7.39	7.39-fold increase

Figure 15.2 - *Tabulations of CNR (John Gofman criticism)*
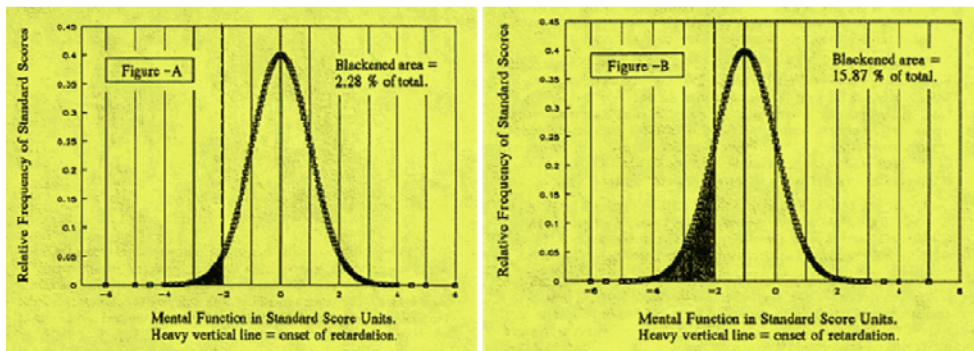
Figure 15.3 - *How Many People Are Mentally Retarded? (Gofman)*

There are widely established effects that radiation has on the embryo: these include intrauterine growth retardation (IUGR), embryonic, foetal, or neonatal death, congenital malformations and cancer.

Gestational	Stage	Radiogenic effects
0-9 days **Embryo contains only few cells which are not specialized.**	Preimplantation Before about 2 weeks gestation the health effect of concern from an exposure of > 0.1 (Gy) or 10 rads is the death of the embryo. Because the embryo is made up of only a few cells, damage to one cell, the progenitor of many other cells, can cause the death of the embryo, and the blastocyst will fail to implant in the uterus. Embryos that survive, however, will exhibit few congenital abnormalities.	If too many cells are damaged - embryo is resorbed. If only few killed - remaining pluripotent cells replace the cells loss within few cell divisions; Atomic Bomb survivors - high incidence of both - normal birth and spontaneous abortion. *For all stages, one has to expect induction of childhood cancers, in particular, childhood leukaemia's. The risk of childhood leukaemia's can be shown to be increased down to doses of 10 mGy. The doubling dose is in the range of 30 mGy. One must keep in mind, however, that the spontaneous risk is small: about 5 per 100.000 children per year. Thus, a very small risk is doubled by about 30 mGy.*
10 days-6 weeks	Organogenesis Radiation risks are most significant during organogenesis and in the early foetal period somewhat less in the 2nd trimester and least in the third trimester	*Most risk* Congenital anomalies, growth retardation, mental retardation
6 weeks- 40 weeks	foetal	Growth retardation, microcephly, mental retardation

Figure 15.4 – *Embryonic risks at each stage of gestation*

Phenomenon	Pathology	Site	Diseases	Risk	Definition
Stochastic	Damage to a single cell may result in disease	DNA	Cancer germ cell mutation	Some risk exists at all doses; at low doses, risk is usually less than the spontaneous risk	Incidence of the disease increases but the severity and nature of the disease increase with dose
Threshold	Multiple cell and tissue injury	Multiple variable etiology, affecting many cellular and organ functions	Birth defects, growth retardation, death, toxity, mental retardation etc.	No increased risk below the threshold dose	Both the severity and incidence of the disease increase with dose

Figure 15.5 - *Stochastic threshold dose-response relationships of diseases produced by environmental agents (Brendt, 1987,1990,1999)*

Organogenesis **2 to 8 weeks**	**Diagnostic radiation**	**No increased risk**
	100 mGy to 200 mGy (10 rad to 20 rad	Mental retardation
	1,000 mGy (100 rad)	Reduction of IQ (25 to 30 points); Severe mental retardation in 40% of case
	1,500 mGy (150 rad)	Severe mental retardation in 60% of cases
Fetal development **Early 8/9 to 15 weeks**	**Diagnostic radiation**	**No increased risk**
	200 mGy (20 rad)	Malformation of forebrain producing mental retardation
	1,000 mGy (100 rad)	Reduction of IQ (25 to 30 points); Severe mental retardation in 40% of cases
	1,500 mGy (150 rad)	Severe mental retardation in 60% of cases
Mid **16 to 25 weeks**	**Diagnostic radiation**	**No increased risk**
	Above diagnostic radiation	Less risk of IQ reduction and severe me retardation
Late 26 to delivery		Central nervous system is radioresistent

Figure 15. 6 - *Foetal Effects of Ionizing Radiation: Severe Mental Retardation*

Sources: *ACOG Committee on Obstetric Practice. ACOG Committee Opinion. Number 299, September 2004 (replaces No. 158, September1995). Guidelines for diagnostic imaging during pregnancy. Obstet Gynecol 2004 Sep;104(3):647-51; De Santis M, Di Gianantonio E, Straface G, et al. Ionizing radiation in pregnancy and teratogenesis: a review of literature. Reprod Toxicol 2005 Sep-Oct;20(3):323-9; Harding LK, Thomson WH. Radiation and pregnancy. Q J Nucl Med 2000 Dec;44(4):317-24; Henshaw SK. Unintended pregnancy in the United States. FamPlann Perspect 1998 Jan-Feb;30(1):24-9, 46; International Atomic Energy Agency. Radiologic protection of patients: pregnancy and radiationin diagnostic radiology. [online]. [cited 2008 Jan 21]. Available from Internet: http://rpop.iaea.org/RPoP/RPoP/Content/SpecialGroups/1_PregnantWomen/Pregn ancyAndRadiology.htm; International Commission on Radiological Protection. Radiation and your patient: a guide formedical practitioners. Ann IRCP 2001;31(4):5-31; International Commission on Radiological Protection (ICRP). Biological effects after prenatal rradiation (embryo and foetus). ICRP Publication No. 90. Kidlington, Oxford (United Kingdom): Elsevier; 2003; International Commission on*

Radiological Protection (ICRP). Pregnancy and medical radiation. ICRP Publication No. 84. Kidlington, Oxford (United Kingdom): Elsevier; 2000;Timins JK. Radiation during pregnancy. N J Med 2001 Jun;98(6):29-33; Toppenberg KS, Hill DA, Miller DP. Safety of radiographic imaging duringpregnancy. Am Fam Physician [online]. 1999 Apr 1 [cited 2008 Jan 21]. Available from Internet: http://www.aafp.org/afp/990401ap/1813.html

Spontaneous incidence of major malformations	Approximately 1% to 3%
Intrauterine growth restriction	4%
Spontaneous abortion	At least 15%
Genetic disease	8% to 10%
Mental retardation (intelligence quotient less than 70)	Approximately 3%
Severe mental retardation (unable to care for self)	0.5%
Heritable effects	1% to 6%
Spontaneous risk of childhood leukemia and cancer (ages 0 to 15)	0.16%
Children developing cancer up to age 15 (United Kingdom)	0.15%
Children developing leukemia only to age 15 (United Kingdom)	0.03%
Lifetime risk of contracting fatal cancer	20%
Lifetime risk of contracting cancer	33%

Figure 15.7 - *Background Incidence of Conceptus Complications without Diagnostic Imaging Radiation*

Source; *ACOG Committee on Obstetric Practice. ACOG Committee Opinion. Number 299, September 2004 (replaces No. 158, Septembe1995)Guidelines for diagnostic imaging during pregnancy. Obstet Gynecol 2004 Sep;104(3):647-51; Brent RL. The effects of embryonic and foetal exposure to x-ray, microwaves, and ultrasoundIn: Brent RL, Beckman DA, editors. Clinics of perinatology, teratology. Vol 13. Philadelphia (PA): Saunders;1986:613-48; Coakley F, Gould R. Guidelines for the use of CT and MRI during pregnancy and lactation. Chapter 5. In: UCSF imaging of retained surgical objects in the abdomen and pelvis section handbook [online]. University of California, San Francisco Department of Radiology. 2005 [cited 2007 Jun 6]. Available from Internet: http://www.radiology.ucsf.edu/instruction/abdominal/ab_handbook/05-CT_MRI_preg.html;Harding LK, Thomson WH. Radiation and pregnancy. Q J Nucl Med 2000 Dec;44(4):317-24; International Commission on Radiological Protection.*

Radiation and your patient: a guide for medical practitioners. Ann IRCP 2001;31(4):5-31; International Commission on Radiological Protection(ICRP). Biological effects after prenatal irradiation (embryo and foetus). ICRP Publication No. 90. Kidlington, Oxford (United Kingdom): Elsevier; 2003;International Commission on Radiological Protection (ICRP). Pregnancy and medical radiation. ICRP Publication No. 84. Kidlington, Oxford (United Kingdom): Elsevier; 2000; Ratnapalan S, Bona N, Chandra K, et al. Physician's perceptions of teratogenic risk associated with radiography and CT during early pregnancy. AJR Am J Roentgenol 2004 May;182(5):1107-9; Ratnapalan S, Bona N, Koren G. Ionizing radiation during pregnancy. Can Fam Physician 2003 Jul;49:873-4; Sharp C, Shrimpton JA, Bury RF. Diagnostic medical exposures: advice on exposure to ionizing radiation during pregnancy [online]. Chilton, Didcot, Oxon (UK): National Radiological Protection Board. 1998 [cited 2007 Jul 19].

Available from Internet: http://www.e radiography.net/regsetc/nrpb_asp8/Diagnostic Medical Exposures Advice on Exposure to Ionising Radiation during Pregnancy.htm; Timins JK. Radiation during pregnancy. N J Med 2001 Jun;98(6):29-33; Toppenberg KS, Hill DA, Miller DP. Safety of radiographic imaging duringpregnancy. Am Fam Physician [online]. 1999 Apr 1 [cited 2008 Jan 21]. Available from Internet: http://www.aafp.org/afp/990401ap/1813.html.

Threshold dose for developmental effects approximately 0.1 Gy.

At 0.1 Gy , increase of 0.1-1%. ICRP (1990 Recommendations of the International Commission on Radiological Protection. Report 60.) recommends a limit of radiation exposure to a member of the general public as 100 mrem/y (1 mSv/y) and the limit for the foetus of an occupationally exposed individual to 200 mrem (2 mSv) during the gestation period. There was a long-standing debate on whether a threshold dose exists for the weeks 8 to 15, whereas it was comparatively clear from the beginning that a threshold dose is present for weeks 16 to 25. Biology always pointed to threshold doses for both time periods, because many cells have to be killed or impaired in their migration behaviour in order to cause a severe mental retardation. ICRP meanwhile suggests a threshold dose of about 300 mGy for both time intervals. It is not clear whether a threshold dose exists for IQ reduction. This question will be hard to answer in any case, because even if one assumes linear dose dependence without a threshold, the risk in the low dose range will be so low that it is impossible to detect it. ICRP estimates the risk to be a reduction of 21 IQ-points per Gray for the weeks 8 to 15, and 13 IQ-points per Gray for weeks 16 to 25. Both numbers do not include the cases of severe mental retardation. Chernobyl caused significantly lower external foetal doses, but it caused the high doses on the

foetal thyroid by the incorporation of the radioiodine and other radionuclides in first stage of accident.

A Ukrainian investigation

A recent investigation in the Ukraine showed promise. The objectives of the study was the psychometric, neurophysiological and neuropsychiatric (ICD-10) criteria) characterization of acutely prenatally irradiated children. This study involves acutely prenatally exposed children — born between April 26th, 1986 and February 26th 1987 from pregnant women at the time of the accident who had been evacuated from the 30-kilometer zone surrounding the Chernobyl NPP to Kiev — and their classmates. This sample seems to be optimal for examination of possible distinguished effects of exposure in different periods of cerebrogenesis. During the first stage (1990-1992) it was examined children five-six years old. At the second stage (1994-1996) the epidemiological WHO project "Brain Damage in Utero" (IPHECA) was implemented. At the third stage (2002-2004) it was examined a cohort of 154 children born between April 26th 1986 and February 26th 1987 to mothers who had been evacuated from Chernobyl exclusion zone to Kiev and 143 classmates from Kiev. In the third stage reconstruction of individual doses of children born to mothers evacuated from the Chernobyl exclusion zone was carried out at taking internal and external exposure. Children were profoundly medically examined by general paediatrist, paediatrist-psychoneurologist, paediatrist-endocrinologist, paediatrist-Ear-Nose-Throat (ENT), paediatrist-ophtalmologist, paediatristcardiologist, paediatrist-haematologists, paediatrist-pulmonologists, paediatrist-gastroenterologists, paediatrist-surgeon, paediatrist-gynecologist (for girls), general and biochemical blood tests, immunological tests, urine tests, coprogram, thyroid and visceral ultrasonography, Electrocardiogram (ECG), electroencephalogram (EEG), rheoencephalogram (RhEG) as well as fibrogastoscopy, cardiac ultrasonography, and magnetoresonance imaging (MRI) for diagnostic reasons. It should be emphasised that neuropsychiatric assessments presented here are based on neurological and psychiatric examinations, psychometry of both children and their mothers.

In order to avoid uncertainties concerning the estimation of prenatal age at the time of the Chernobyl accident we used the formulas offered for estimation of prenatal age at atomic bombing in Hiroshima and Nagasaki: Days of pregnancy (Y) = 280 — (date of birth — April 26th, 1986), where the day of birth has been obtained by interviewing the mothers of the children. The mean duration of pregnancy is taken to be 280 days. The days from birth were counted back until the accident and subtracted from the 280 days, the duration of a pregnancy. Since the duration is calculated from the beginning of the last menstrual cycle, additionally 14 days have

to be subtracted. Gestational weeks after fertilization at the time of the accident were thus calculated by the following equation: Gestational weeks $(G) = (Y — 14 \text{ days}) / 7 \text{ days}$, where G was taken to be zero if G<0. According to different radiosensitivity of the foetus the gestational time is divided into 4 periods in relation to the Chernobyl accident. In the exposed groups there are fewer children who were at the earliest stages of prenatal development. A possible explanation is increased numbers of abortions and miscarriages due to the Chernobyl accident.

Individual reconstruction of total foetal doses, foetal thyroid doses and foetal doses on the brain has been carried out using 2 methods:

1) foetal thyroid dose is assumed to be equal to the thyroid dose of the mother, and 2) according to the model by ICRP Publication 88 (2001).

The main irradiation sources of the pregnant women were: 1) external irradiation of the whole body; 2) irradiation of thyroid by radioactive iodine isotopes; 3) internal irradiation by inhaled radionuclides; 4) internal irradiation by ingestion of radioactively contaminated food. The doses were reconstructed for the exposed children from Pripyat and also for the control group in Kiev by Professor   Victor REPIN (Laboratory of dosimetry RCRM in Ukraine).

First stage
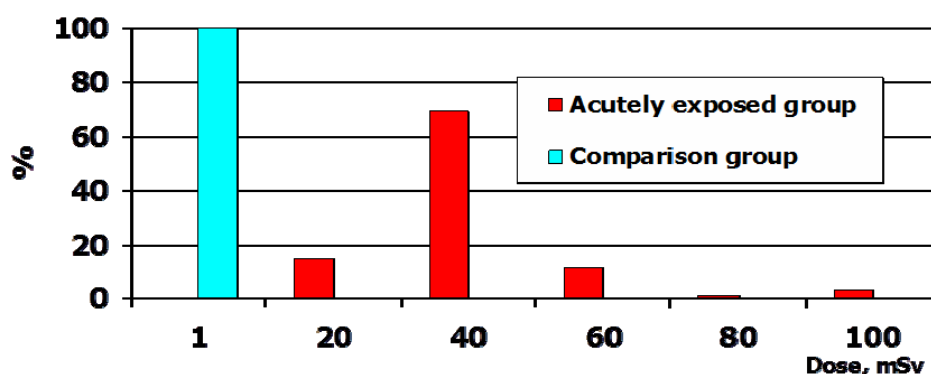
Distribution of foetal dose of external irradiation
Acutely exposed group (M±SD) 31.7±14.4 mSv
Comparison group — 1.9±8.1 mSv

Figure 15.8 - *Dose on embryo and foetus distribution (ICRP-88)*

There are 20 children from Pripyat (13.2%) who had been exposed in utero >100 mSv – the threshold for medical abortion due to prenatal irradiation (European Commission, 1998; ICRP Publication 84, 2000).
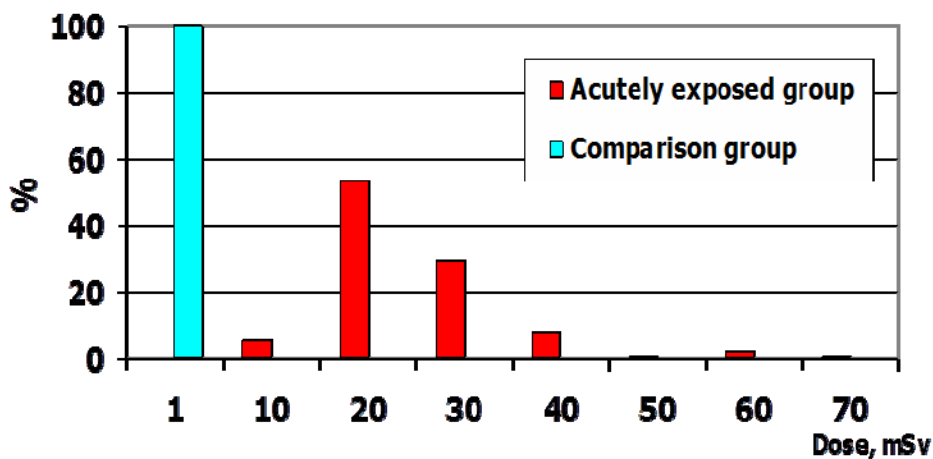
Distribution of equivalent doses on the foetal brain
Acutely exposed group (M±SD) 20.5±9.4 mSv
Comparison group — 0.7±1.5 mSv

Figure 15.9 *- Dose on embryo and foetus distribution (ICRP-88)*
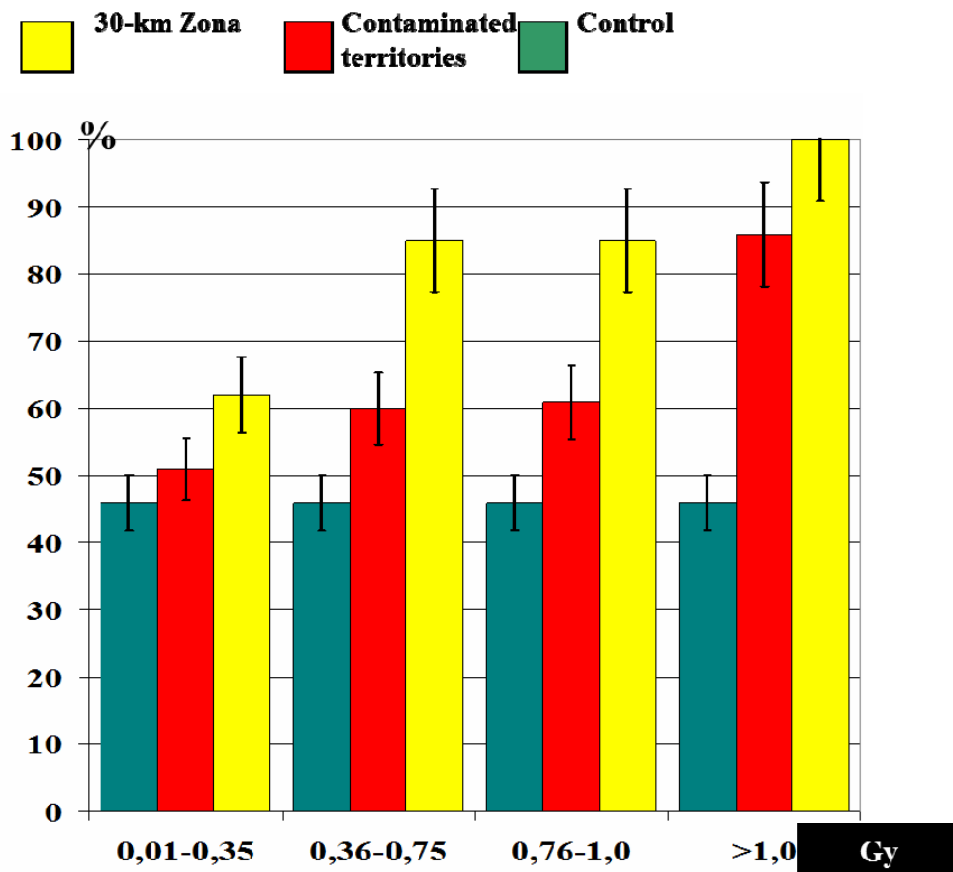
Figure 15.10 - *In UTERO Thyroid doses were estimated 0,01 - 3,34 Gy.*
The mean doses according trimester of gestation:
Until 8 weeks – 0,0 Gy;
of 8 to 15 week – 0,31Gy;
of 16 to 25 week - 0,8Gy;
More than 25 weeks – 0,62 Gy.
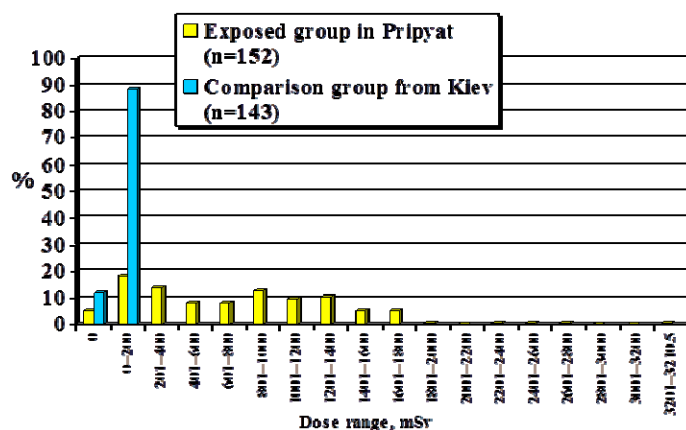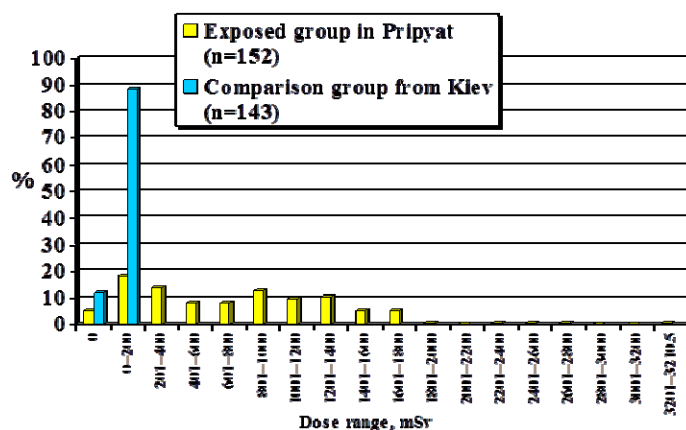
Figure 15.11 - *Dose on thyroid in utero distribution (ICRP-88): There are (35.5%) children from Pripyat who received in utero thyroid doses >1 Sv*
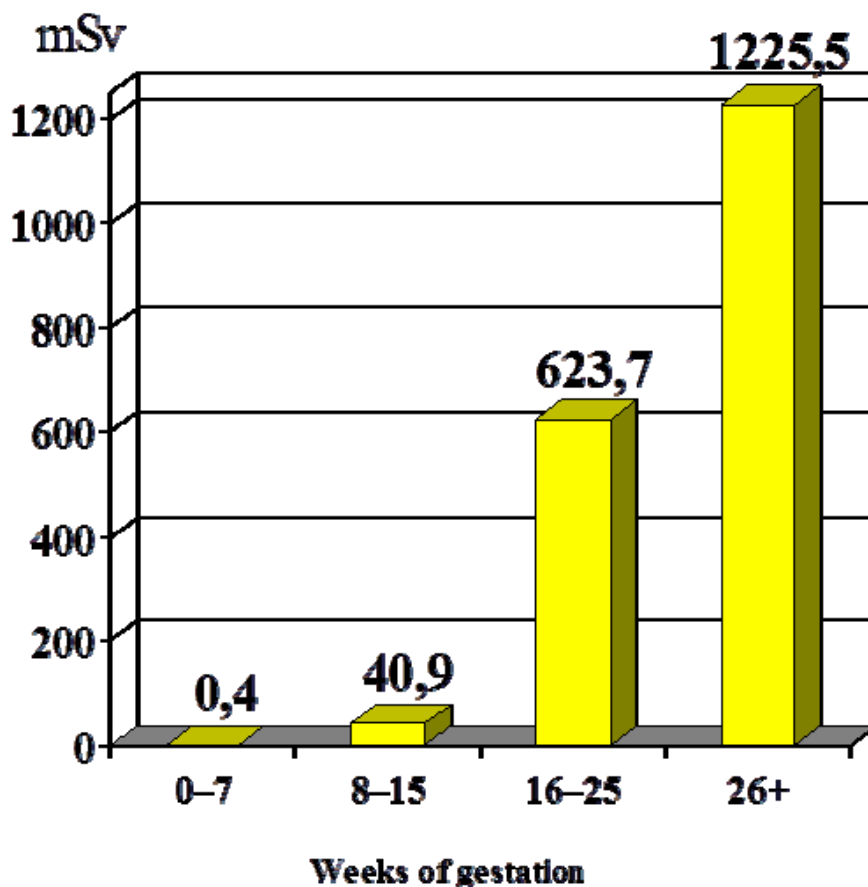
*Figure 15.12 - Geometric means of the thyroid doses in utero related to the periods
of cerebrogenesis at 26.04.1986 in exposed group in Pripyat*

According to the model by ICRP-88 there is a strong influence of gestational age on
the thyroid doses in utero: later intrauterine period at the time of exposure — higher
the thyroid doses in utero. It is concluded that multifactor impact of Chernobyl
disaster unfavourable factors defined health deterioration in children irradiated in
prenatal period shortening amount of practically healthy kids down to 5%. The
results showed much more somatic diseases and neurovegetative mental disorders.
At the same time it was clearly recognized   the decrease of immunity (hypo
immunoglobulin level and increase of T-lymphocytes, T-helpers), neurological,
gastrointestinal and endocrine diseases.

Health groups Average doses of gamma-irradiation varied as 7mSv-13 mSv (Monte-Carlo dose reconstruction method for foetus).Individual dose of Thyroid – varied within 10-120cSv.	Main group (n=147) (Evac. From 30-km Zone)		Control group (n=101-city. Kiev)	
	a	b(%)	a	b(%)
1-st -healthy children	12	8,2	2	2
2-nd –dynamic diseases	68	46,3	67	67
3-rd –chronic relapsing diseases	55	37,4	30	30
4-th – chronic decompensate diseases, congenital defects, anomalies	7	4,8	2	2

Figure 15.13 - *First Stage (children 5-6 years old)*
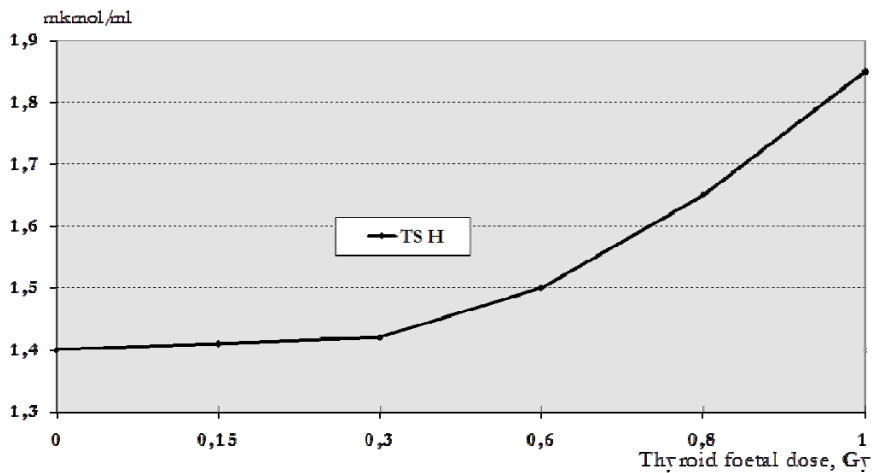
Figure 15.14 - *Thyroid-stimulating hormone (TSH)*

It was also established in this cohort that starting with the 0.3 Gy threshold dose thyroid-stimulating hormone (TSH) level grew along with foetal thyroid dose increase. Thereupon the radiation-induced malfunction of the thyroid-pituitary system on this stage was suggested as important biological mechanism in the genesis of health risk assessment and mental disorders of prenatally irradiated children.
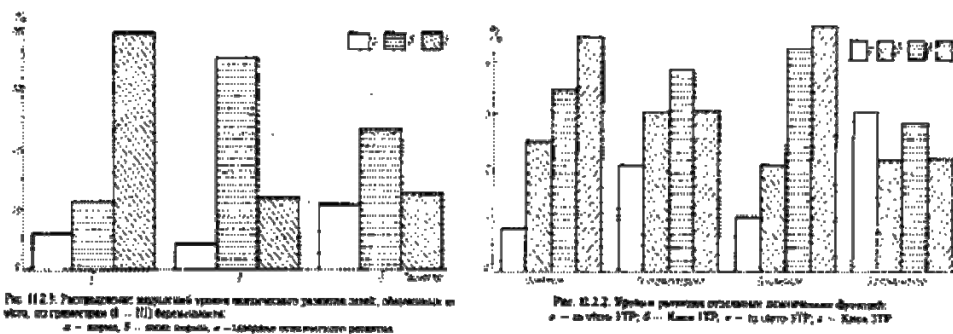
Figure 15.15 -
(1) Distribution of the psychic development level disturbances in children irradiated in utero during the pregnancy 1-3 trimesters: a – the norm; b- below the norm ; c- psychic development delay.

(2) The levels of separate psychic functions development (6 years old): 1- notions;

2-psychomotor system; 3-attention; 4-memorizing. a ,b - 1 trimester, b,c - 3 trimester (control and irradiated children accordingly). The Kern-Jeracika and verbal tests of willingness to teaching (school education) were used.

Signs of mental progress retardation were met in 77% of kids from Pripyat city exposed in utero within first pregnancy trimester, in 69% of those exposed in second trimester and in 45% — in third one. Among kids resident in Kiev city the percent of persons with decreased mental development value was substantially lower (p<0.05). In 25.5% of cases in Pripyat group the brain organic pathology signs were revealed. Brain circulation disorders according to the rheoencephalography data were observed a bit more often in children from Pripyat city exposed to radiation within first pregnancy trimester. The low induces of psychic development in utero irradiated children are largely determined by the irradiation factor.

Second Stage: WHO project "Brain Damage in Utero" (IPHECA)

An analysis of the results in three countries (Belarus, Russian and Ukraine) has shown the following: An incidence of mild mental retardation in prenatally irradiated children is higher when compared with the control group; an upward trend was detected in cases of behavioral disorders and in changes in the emotional problems in children exposed in utero; incidence of borderline nervous and psychological disorders in the parents of prenatally irradiated children is higher than that of controls. In the frame of the WHO Pilot Project «Brain Damage in Utero» we have previously revealed a significant increase of borderline and low range IQ, emotional and behavioural disorders. Since possible dose correlations were not investigated and contradictory results of the mental health assessment of the in utero exposed children and the aetiology of the observed neuropsychiatric disorders were found.

Groups	Number of children with revealed mental retardation IQ<70. A decrease in high (IQ>110), as well as statistically significant higher prevalence of mental retardation (IQ<70) in Ukrainian prenatally irradiated children compared to the controls: 21 (3.9%) vs. 12 (1.6%) correspondingly (χ2=6.27; df=1; P<.05).					Number of kids with emotional, behavioural and non-differentiated disorders		Indices characterising degree of mental health in mothers	
Methods	Non-verbal intellect (Draw-a-Man)	Verbal intellect (BPVS)	Non-verbal intellect (Raven Coloured Matrices)	General intellect lowering (A)*	General intellect lowering (B)**	Ratter scale À(2)	Ratter scale Â(2)	General Health Question-naire GHQ-28	IQ
«Experimental» n=544	11 (2.06 %) n=535	61 (11.34 %) n=538	59 (10.95 %) n=539	19 (3.49 %) n=544	23 (4.34%) n=544	152 (41.76%) n=364	137 (34.86%) n=393	24.26±0,4 n=382	33.6± 0,6 n=377
PFor c2 or Student's criteria	>0.05	>0.05	>0.05	<0.05	<0.05	<0.01	>0.05	<0.01	<0.05

| Control, N=759 | 8 (1.06 %) n=755 | 66 (8.87 %) n=744 | 92 (12.12 %) n=759 | 8 (1.05 %) n =759 | 16 (2.10 %) n=759 | 214 (28.69 %) n=746 | 269 (38.93 %) n=691 | 20.73±0,5 n=639 | 43.6± 0,5 n=750 |

Figure 15.16 - Mental health in children exposed to radiation in prenatal period and their mothers
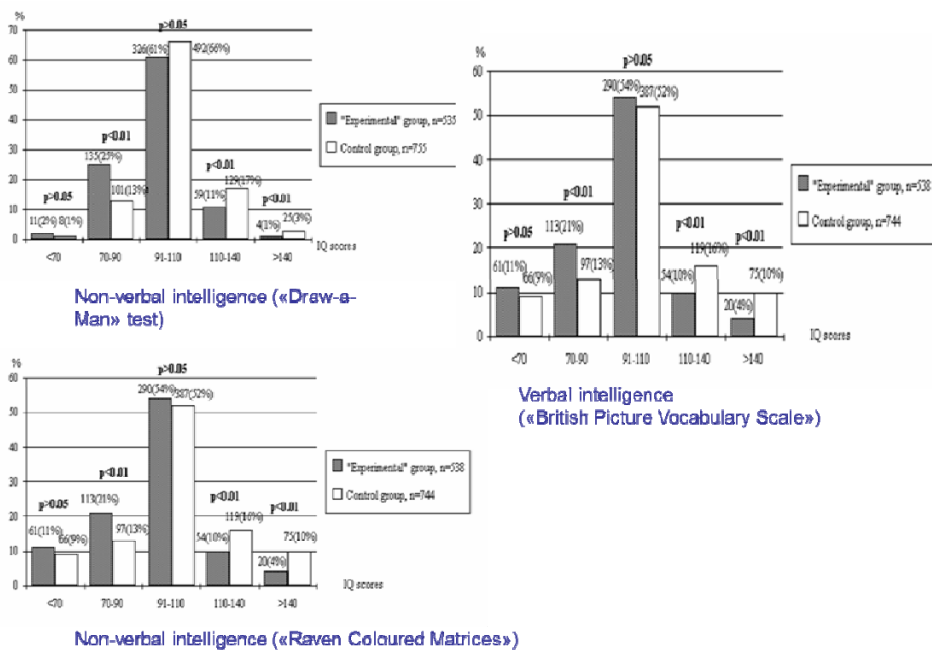
Figure 15.17 - *Distribution of IQ scores in the prenatally irradiated children («Experimental» group) and non-exposed control children*
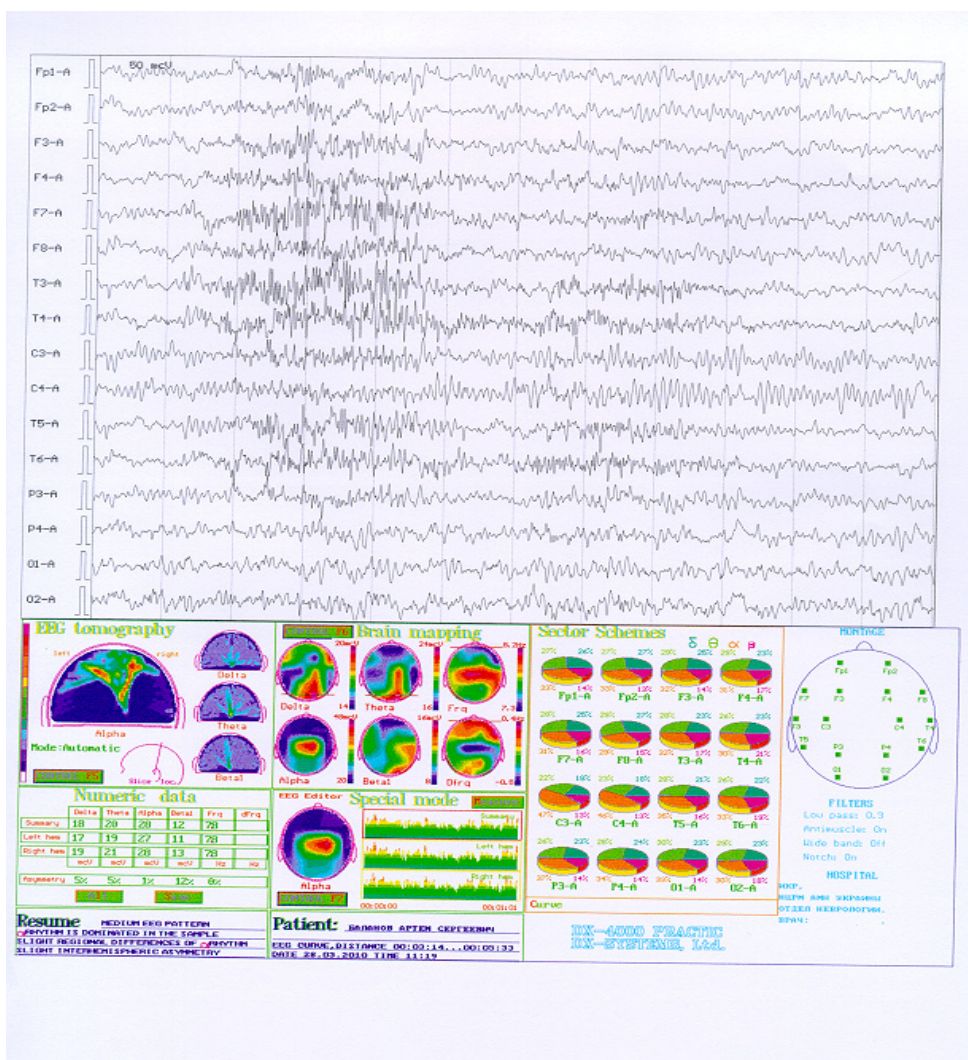
Figure 15.18 *- Conventional EEG of B-v 23.12.1998. Without anticonvulsants. The 3rd minute of hyperventilation — paroxysmal activity (like «spike-waves») in the fronto-temporal area shifted to the left (leads F7,T3, T4, T5, T6).-MRI (1998&1999).*

EEG-pattern	Children exposed to radiation in prenatal period n=50	p c2	Children from control group n=50
Age norm:	8 (16.0 %)	<0.05	24 (48.0 %)
Pathological: Disorganized slow	23 (46.0 %)	<0.05	8 (16.0 %)
Disorganized with paroxysmal activity	14 (28.0 %)	<0.05	2 (4.0 %)
Laterality: Left-hemisphere	20 (40.0 %)	<0.05	6 (12.0 %)
Disorganized with α-activity predominance Hypersynchronous	5 (10.0 %)	>0.05	16 (32.0 %)
Right-hemisphere	13 (26.0 %)	>0.05	10 (20.0 %)
Symmetry	7 (14.0 %)	<0.01	32 (64.0 %)
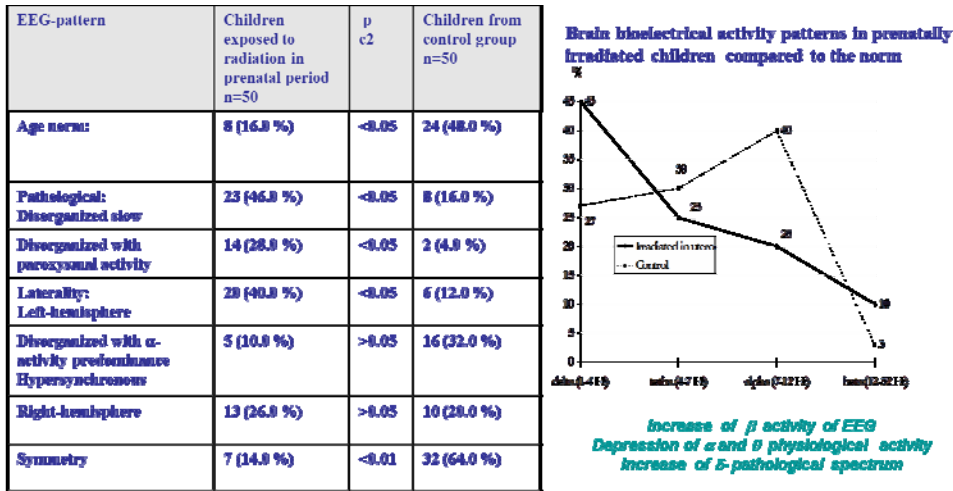
Low-voltage EEG (20–25 µV) with excess of slow (δ) and fast (β) activity together with depression of normal physiological α- and θ-activity with paroxysmal activity;
Disorganised slow EEG-pattern with δ-activity domination;
Disorganised EEG-pattern with paroxysmal activity;
Epileptiformal EEG with «spike» or «polyspike—wave» complexes in the fronto-temporal region, mainly of the left hemisphere.

Figure 15.19 – *Bioelectrical patterns in prenatally irradiated children*

Abnormal EEG patterns in irradiated children displayed themselves in a number of ways. Low-voltage EEG (20–25 µV) with excess of slow (δ) and fast (β) activity together with depression of α- and θ-activity with paroxysmal activity shifted to the left fronto-temporal region was one of the most distinguished conventional EEG-pattern in the children of the acutely exposed group (31% vs. 8%, $\chi2=16.85$, P<.001). Disorganised slow EEG-pattern with δ-activity domination characterised by disorganised activity of moderate (40–55 µV) or high (70–80 µV) amplitude with a mainly δ-range slow activity domination and non-regular α-activity where hyperventilation led to bilateral paroxysmal activity discharges, as well as disorganised EEG-pattern with paroxysmal activity, similar in general to the one described above, but characterised by generalised paroxysmal discharges and bursts of acute, θ- and δ-waves of high amplitude where the hyperventilation led to the bilateral paroxysmal activity increase, were found equally in the both groups. Finally, an epileptiformal EEG with «spike» or «polyspike—wave» complexes in the fronto-temporal region, mainly of the left hemisphere, and bilateral paroxysmal activity in the form of δ-waves of very high amplitude (higher than 100 µV) was

another of the most distinguished conventional EEG-pattern among the children of the acutely exposed groups.

NON-RADIATION FACTORS				RADIATION FACTORS
Mother low education level	h=0.8	VERBAL IQ DECREASE	h=0.3	Residence territory ^{137}Cs – contamination level in prenatal period
		h=0.8		
Delivery complications	h=0.3	NON-VERBAL IQ DECREASE	h=0.4	Cerebrogenesis most critical period (8–15 weeks of prenatal progress) at the time of Chernobyl disaster (04.26.1986)
Mental health worsening in mother	h=0.5	EMOTIONAL-BEHAVIOURAL DISORDERS	h=0.6	Internal radiation dose on thyroid

Figure 15.20 - *Factors making impact on mental health in children exposed to radiation in prenatal period*

Third Stage

A number of assessments were carried out here, these included:

- Intelligence Assessment by the adapted and normalised version for the Ukrainian children of the Wechsler Intelligence Scale for Children, WISC (the verbal, performance and full scale IQs).
- Additional Psychological and Demographic Measurements
- Russian translation of Achenbach's Child Behaviour Checklist (CBCL)
- Rutter A (2) Behaviour Rating Scale
- General Health Questionnaire (GHQ-28)

- The vocabulary subtest of the Wechsler Adult Intelligence Scales (WAIS)
- Impact of Events Scale (IES) and Irritability, Depression Anxiety Scale (IDA)
- Self-rating Depression Scale (Zung's)
- Questionnaire on stress-factors related to the Chernobyl accident
- School performance
- Demographic background, family history, educational level of the family, social and economical status as well as they completed a standardised questionnaire on radiation history

Clinical Psychiatric and Neurological assessment according to ICD-10
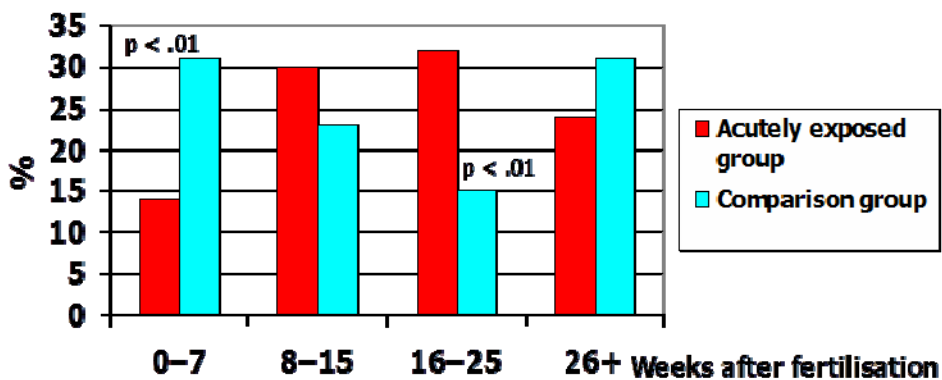
Distribution of children by prenatal age at the time of explosion (April 26th, 1986)

Figure 15.21 – *As titled*

In the exposed group there are fewer children who were at the earliest stages of prenatal development (0–7 weeks after conception) that could be explained with abortions and miscarriages due to the Chernobyl accident.

Distribution of children by the health groups
1st — absolutely healthy; 2nd — practically healthy; 3rd — remission of chronic diseases; 4th — handicapped children with chronic diseases; 5th — handicapped children with decompensated diseases
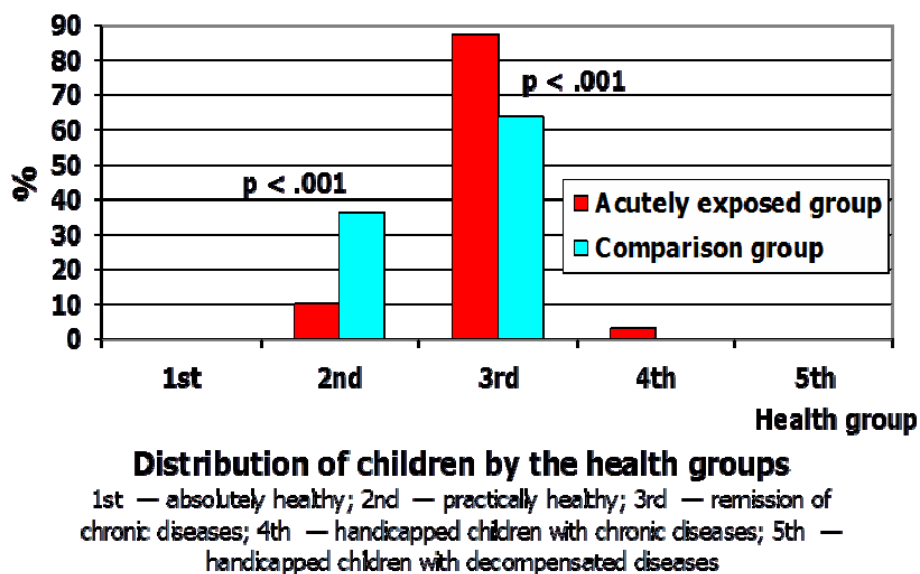
Figure 15.22 – *Health groups*
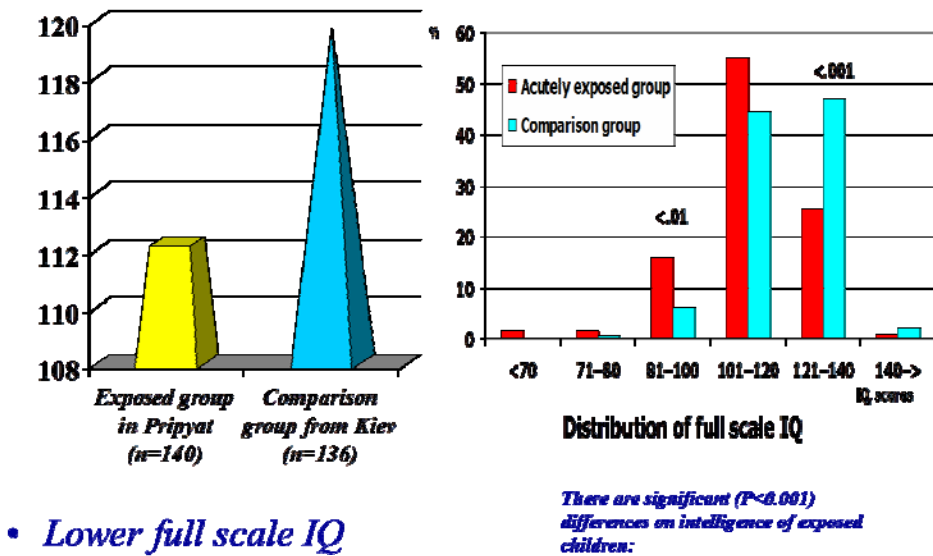
Figure 15.23 - *Wechsler Intelligence Scale for Children (WISC): Full scale IQ*
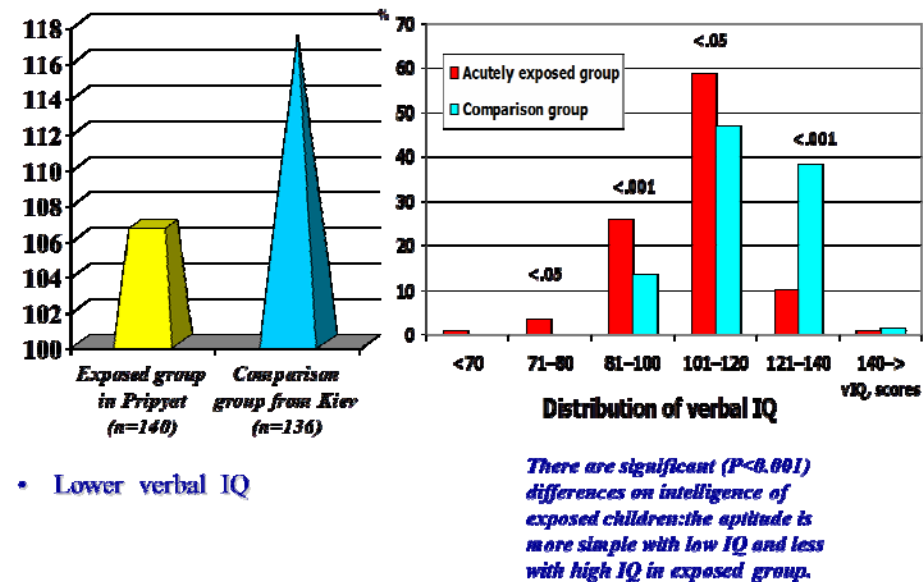
Figure 15.24 - *Intelligence of children (WISC): Verbal IQ*
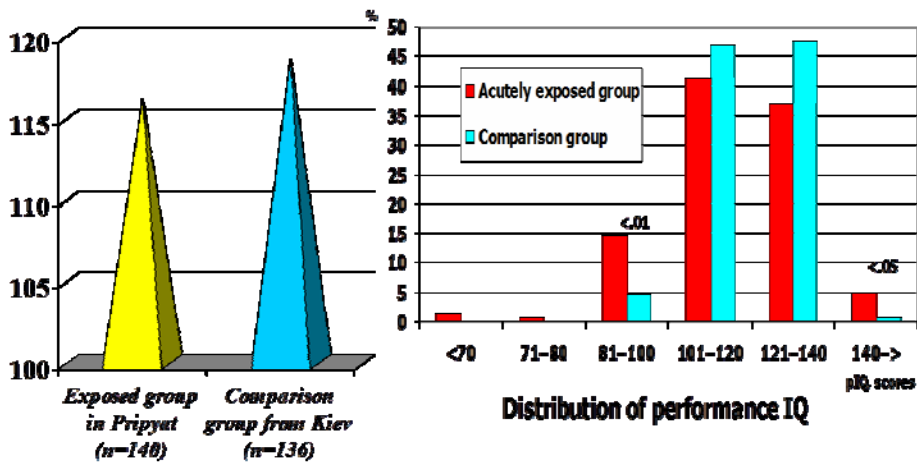
Figure 15.25 *- Intelligence of children (WISC: Performance IQ)*
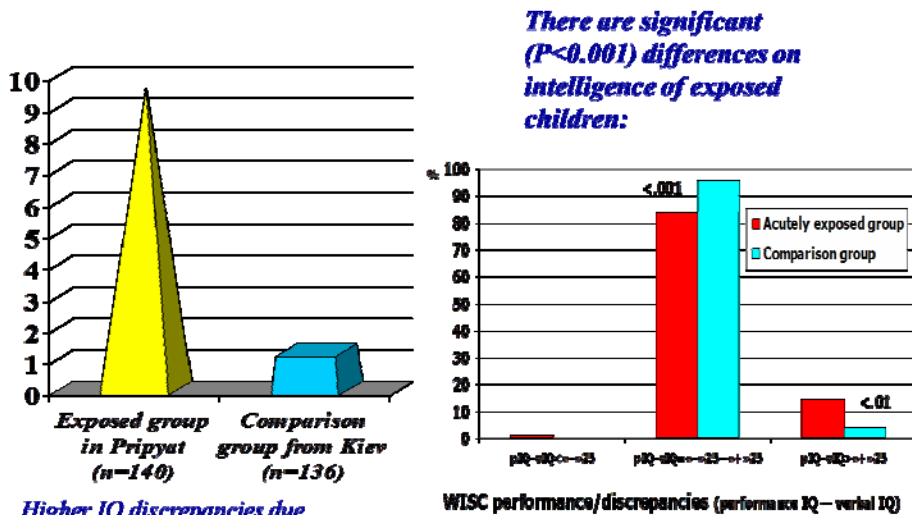
Figure 15.26 *- Intelligence of children (WISC):Discrepancies IQp–IQv*
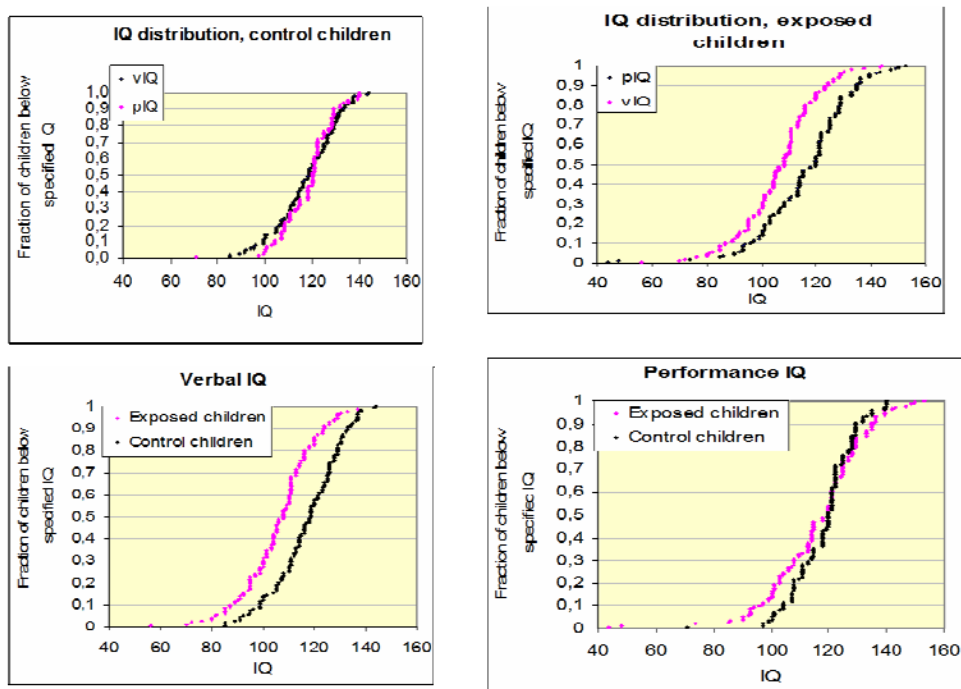
Figure 15.27 *- Fraction of control and exposed children below specific verbal and performance IQ,*
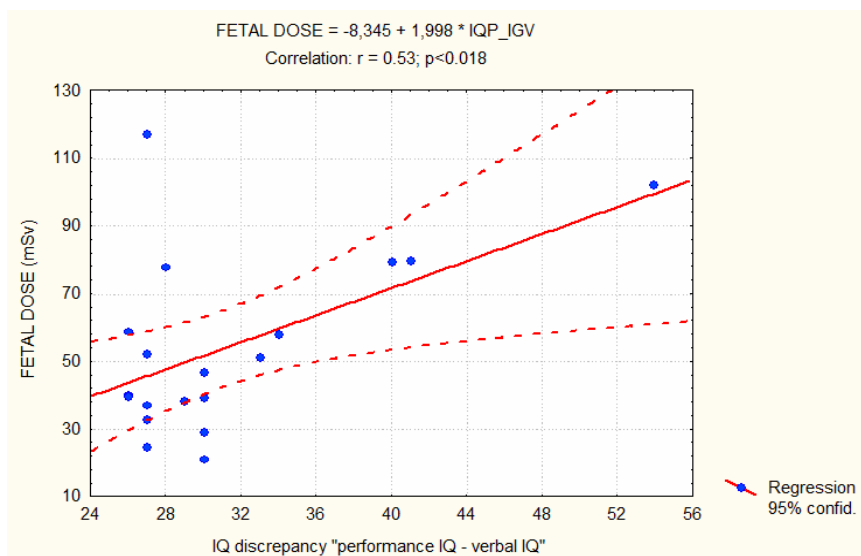
Figure 15.28 *- Correlation between IQ discrepancy «performance IQ - verbal IQ» and foetal dose in children irradiated in utero, who have IQ discrepancy >25 point*
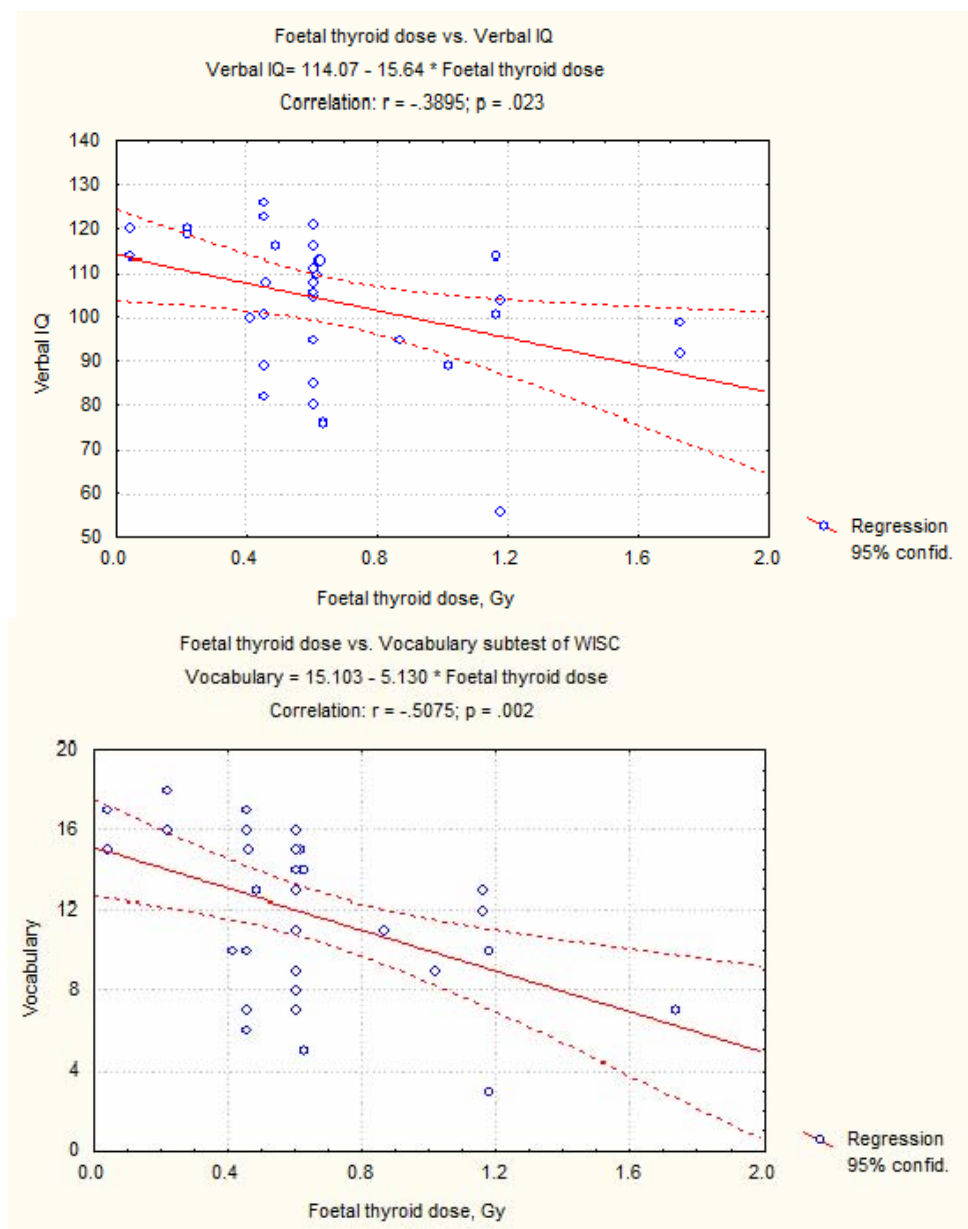
Figure 15.29 - *Relationships between Verbal IQ and Vocabulary subtest of WISC vs foetal thyroid dose, in children of the both groups (n=47) exposed at 16–25 weeks after fertilisation*
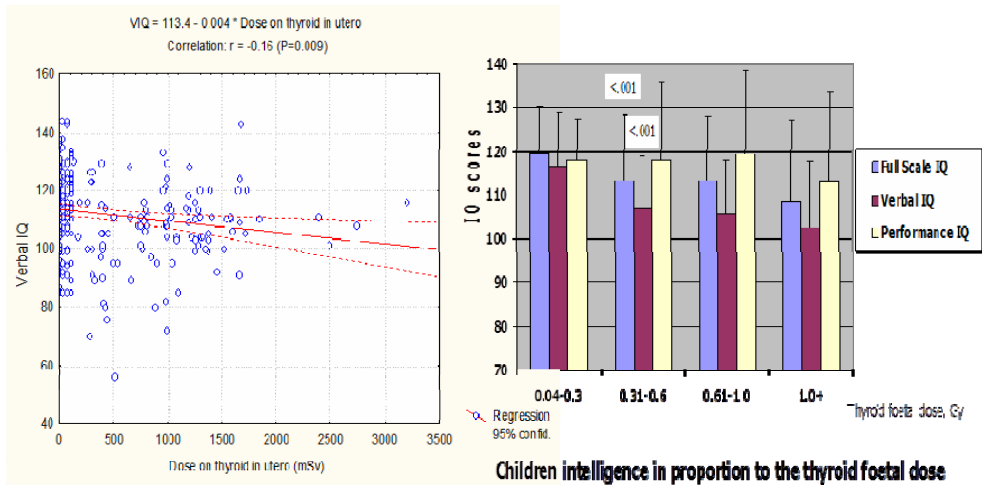
Figure 15.30 - *Correlations between verbal IQ of children of both groups and dose on thyroid in utero (ICRP-88)*
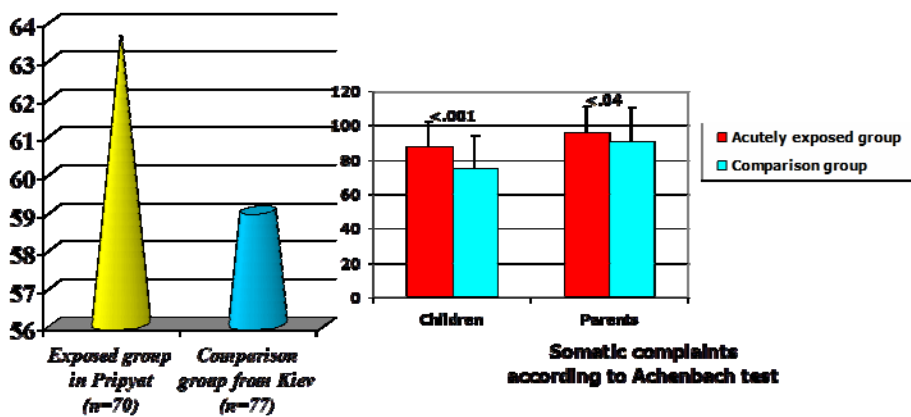
Figure 15.31- *Behavioral and emotional problems. Children. Achenbach test (Youth Self-Report). Somatic complaints (T)*
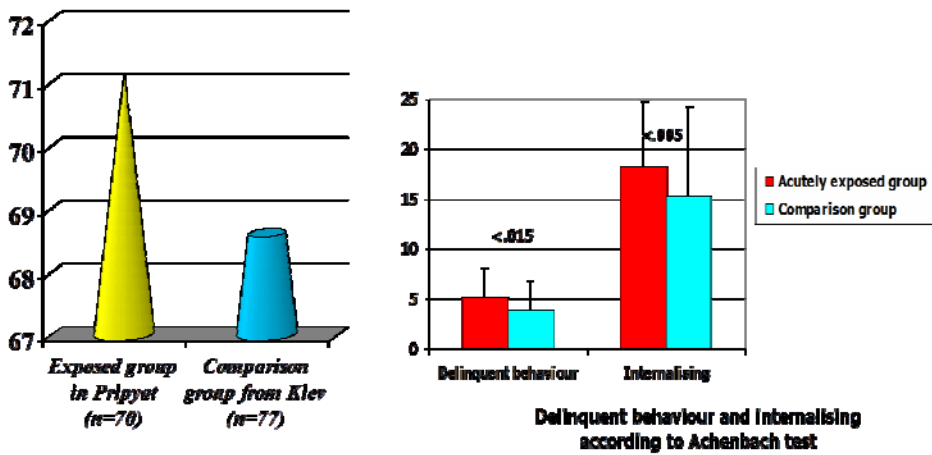
Children of the exposed group show an increased level of emotional and behavioural problems in comparison with children from Kiev (P<0.05)

Figure 15 32 - *Achenbach test (Youth Self-Report): Total score (T)*
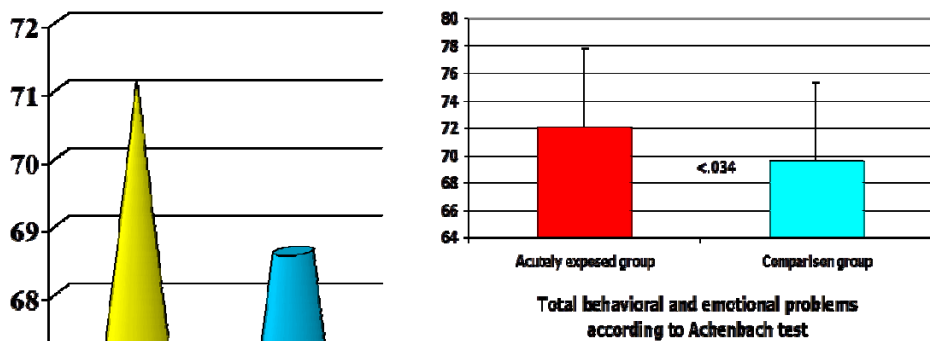
Children of the exposed group show an increased level of emotional and behavioural problems in comparison with children from Kiev (P<0.05)

Figure 15.33 - *Achenbach test (Youth Self-Report): Total score (T)*
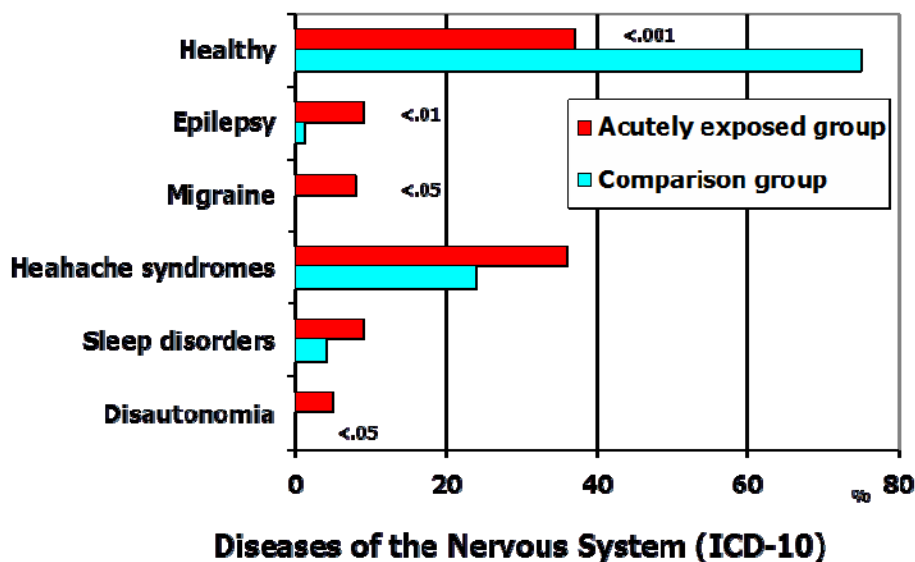
Figure 15.34 – *As titled*

Figure 15.35 – *As titled*

Mothers of children evacuated from Pripyat experienced much more (P<0.001) real stress events (evacuation, lack of information about relatives, migration, difficulties of medical care, etc.)

There is a significant (P<0.001) mental health problems in mothers of children evacuated from Pripyat: PTSD (0,001)
Depression (0,001)
Somatoform disorders (0,001)
anxiety, insomnia (0,001)
Social dysfunction (0,04)
Severe depression(0,01)

Figure 15.36 – *Mother's stress events*

The results of this study agree with the Japanese studies concerning the critical periods of cerebrogenesis — 8–15 and, especially, 16–25 week after fertilisation, the dose related full scale IQ reduction and the increase of paroxysmal disorders. The highest vulnerability of the brain under exposure at 16–25, but not 8–15 weeks after fertilisation as in the Japanese sample, we can explain this through maximal radioiodine transfer rate in foetal thyroid at about 20–25 weeks and more «delicate» examination of intelligence disturbances that corresponds exactly to the events of the brain creation at 16–25 weeks after fertilisation (apoptosis and its underlying molecular mechanisms; growth factor gene expression, cell formation and migration; neuronal differentiation, gross anatomical parameters in cortical and commissural diameters, synaptogenesis and synaptic remodelling limbic system and brain asymmetry forming, etc.). An absence of dramatic increase of mental retardation, especially its severe form, as well as microcephalia obviously can be explained by significantly lower foetal doses of irradiation than that in the atomic bomb survivors and lack of information about all in utero survivors. It is need the strong epidemiological investigation of the whole of this cohort. The «dose—effects» relationships concerning both intelligence and EEG-parameters, which are the most marked at the critical periods of cerebrogenesis, testify to significant contribution of prenatal irradiation into the brain damage.

Thus, the neuromental health of the acutely prenatally irradiated children at the Chernobyl exclusion zone is deteriorated in comparison with the non-evacuee classmates living in Kiev due to more frequency of episodic and paroxysmal

disorders, organic, including symptomatic, mental disorders, somatoform autonomic dysfunction, disorders of psychological development, and behavioural and emotional disorders with onset usually occurring in childhood and adolescence. Obviously, their neuromental health disorders are etiologically heterogeneous including psycho-social and economic factors, medical problems in their families; however an effect of real stress events (but not only their perception) during pregnancy together with prenatal irradiation cannot be excluded. Intelligence of the acutely prenatally irradiated children is deteriorated due to reduction of full scale and verbal IQ, as well as WISC performance/verbal discrepancies, with verbal decrements. In spite of the children's intelligence is multifactorial, the contribution of prenatal irradiation was revealed. Characteristic neurophysiological changes of the acutely prenatally irradiated children are also etiologically heterogeneous, but the dose—effect relationship, especially at critical periods of cerebrogenesis, can testify the impact of prenatal irradiation. This study suggests that prenatal exposure to ionising radiation at thyroid foetal dose 0.2–2 Gy and foetal dose 11–92 mSv can result in detectable brain damage. The data obtained reflect great importance, interdisciplinarity, and complexity of such problem as brain damage in utero following radio ecological disaster and a necessity to integrate international efforts to its solving. Thus this integrate research conducted in this area has made a valuable contribution to radiological protection by reinforcing the view that functionally significant radiation effects on the developing brain are most likely to occur at the low doses.

Finally, the TSH level grows with foetal thyroid dose increase with a 0.3 Sv threshold. Probably, these children had been affected by intrauterine hypothyroidism resulted in intelligence disturbances during the life. Obviously, an international psychoendocrine study should be organise for exploration of functions of the pituitary-thyroid system as a possible biological basis of mental health problem in children irradiated in utero as a result of the Chernobyl disaster. Neurophysiological abnormalities together with intelligence disturbances, both dose-related, especially at 16–25 weeks after fertilisation, as well as a «concentration» of the most severe neuropsychiatric disorders among the children exposed at the critical periods of cerebrogenesis, can testify to the developing brain abnormalities due to multiple factors with effects of prenatal irradiation. Consideration must to given to deterministic effects prevail during the initial phase of damage may subsequently be modified by compensation within the brain.

In this view this study should be continued. We must study the whole of this cohort of children irradiated in utero in Ukraine, identify further children irradiated in utero and children exposed at the age of 0–1 years is necessary; identify and form

cohorts of age-, gender- and urban/rural-matched children from radioactively clean areas of the Ukraine; verify and develop the currently available dosimetric models; assess and verify the multifarious neuropsychiatric disorders; carry out a risk analysis of the influence of radioiodine in prenatal period and during the 1st year of life on brain development and a risk assessment of other stochastic and non-stochastic diseases on this base. A large-scale epidemiological investigation on this cohort only will give us the answer on open question on low dose risk after in utero radiation. It seems that the acutely prenatally exposed children at the Chernobyl exclusion zone are a unique sample that should be used for the reassessment of the risks of prenatal irradiation at radiation accidents on nuclear reactors.

16

The real effects of the Chernobyl accident and their political implications

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I start by calling to attention our publication in Volume #1171 of the Annals of the New York Academy of Sciences, which will be published in English (enlarged and revised) in the book "Chernobyl: Consequences of the Catastrophe for People and Nature" by A. Yablokov, M. Nesterenko and A.Nesterenko (St. Petersburg, "Nauka" Publ.,2007, 372 p.)   Hundreds of individuals and organizations help us made this mega-review. This is very likely the broadest scope and undoubtedly the most up-to-date monograph about the Chernobyl consequences.

Among reasons complicating an estimation of the impact of the Catastrophe on health, singular is the Official secrecy and falsification of the USSR medical statistics for the first 3½ years after the Catastrophe. These created difficulties in estimating true individual doses in view of a reconstruction of doses in the first days, weeks, and months; uncertainty as to the influence of "hot particles"; problems accounting for spotty contamination and an inability to determine the influence of each of many radionuclides, singly and in combination.   The demand by IAEA and WHO experts to require "significant correlation" between the imprecisely calculated levels of individual radiation (and thus groups of individuals) and precisely diagnosed illnesses as the only iron-clad proof to associate illness with Chernobyl radiation is not scientifically valid.

Objective information on the impact of the Catastrophe on health can be obtained comparing: morbidity / mortality of territories having identical physiographic, social, and economic backgrounds and differ only in radioactive contamination; the health of the same group of individuals during specific periods after the Catastrophe; the health of the same individual in regard to disorders specifically linked to radiation (e.g., stable chromosomal aberrations); health of individuals living in contaminated territories by the level of incorporated radionuclides; and by correlating pathological changes in particular organs by measuring their levels of incorporated radionuclides.
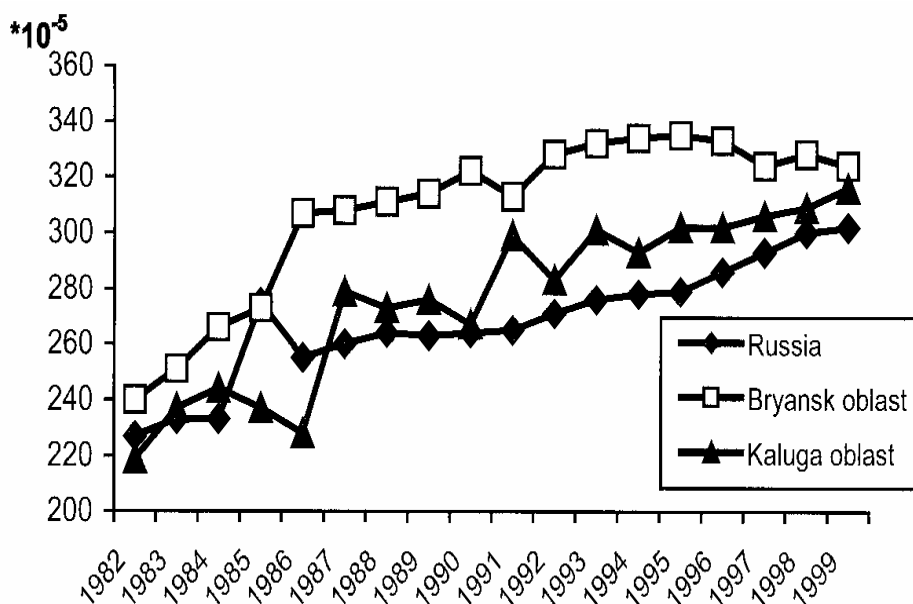
Figure 16.1 - *All solid cancers in Bryansk and Kaluga provinces and Russia (Ivanov et al., 2004)*

Among specific disorders associated with Chernobyl radiation, there is increased morbidity and prevalence in the blood and the circulatory system; endocrine system; immune system ("Chernobyl aids," increased incidence and seriousness of all illnesses); respiratory system; urogenital tract and reproductive disorders; musculoskeletal system (including composition of bones: osteopenia and osteoporosis); central nervous system (changes in frontal, temporal, and occipitoparietal lobes of the brain, leading to diminished intelligence and behavioural and mental disorders);eyes (cataracts, vitreous destruction, refraction anomalies);digestive tract; congenital malformations and anomalies (including previously rare multiple defects of limbs and head); thyroid cancer (Chernobyl thyroid cancers rapid and aggressive, striking children and adults); leukaemia (not only in children and liquidators, but adult population) and other malignant neoplasms. Amongst other health consequences of the Catastrophe, exist Intensified infectious and parasitic diseases (e.g., viral hepatitis and respiratory viruses), premature aging in both adults and children, multiple somatic and genetic mutations and most common within these is polymorbidity (people are often afflicted by many illnesses at the same time).

Chernobyl has "enriched" medicine with terms and syndromes never seen before:

"Cancer rejuvenescence,"

"Vegeto-vascular dystonia",
 "Incorporated long-life radionuclides",
"Acute inhalation lesions of the upper respiratory tract".
"Chronic fatigue syndrome,"
"Lingering radiating illness syndrome",
"Early aging syndrome".
 "Radiation in utero,"
"Chernobyl AIDS," "Chernobyl heart," "Chernobyl limbs," etc.

But most importantly the full picture of the deteriorating health of those in the contaminated territories is still far from complete. Medical, biological, and radiological research must expand and be supported to provide the full picture of Chernobyl's consequences. Instead this research has been cut back in Russia, Ukraine, and Belarus. Psychological factors ("radiation phobia") simply cannot be the defining reason because morbidity continued to increase after the Catastrophe, whereas radiation concerns have decreased. What is the level of radiation phobia among voles, swallows, frogs, and pine trees, which demonstrate similar health disorders, including increased mutation rates?

The Chernobyl Forum (2005) declared that the total death toll from the Catastrophe would be about 9000 and the number of sick about 200,000. Soon after the catastrophe the average life expectancy decreased noticeably and morbidity and mortality increased in infants and the elderly in the Soviet Union. Analyses of official demographic statistics in the contaminated territories of Belarus, Ukraine, and European Russia, give the Chernobyl death toll here for the first 15 years after the Catastrophe amounted to nearly 237,000 people. It is safe to assume that the total Chernobyl death toll for the period from 1987 to 2004 has reached nearly 417,000 in other parts of Europe, Asia, and Africa, and nearly 170,000 in North America, accounting for nearly 824,000 deaths worldwide.
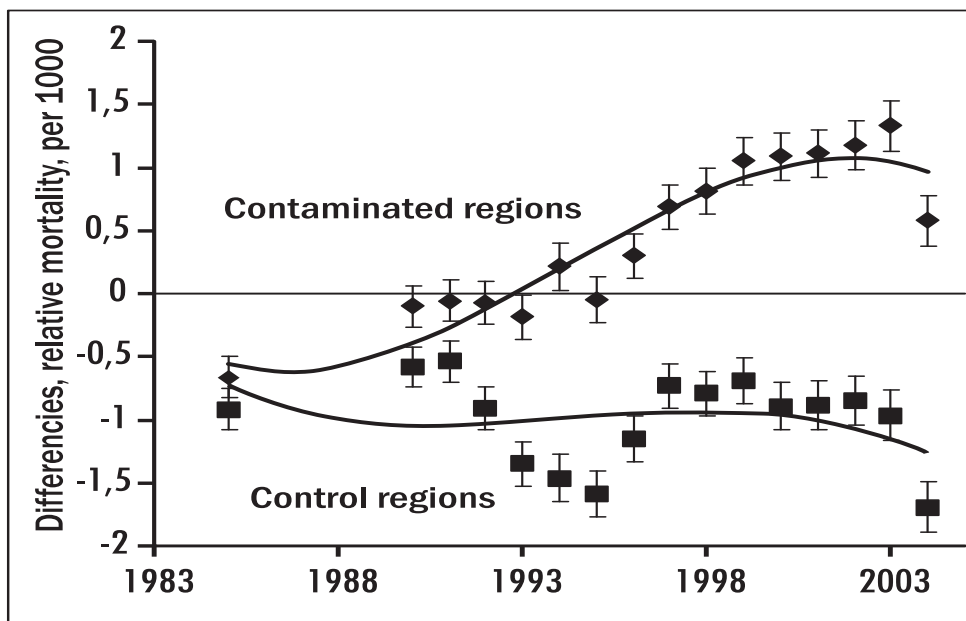
Figure 16.2 - *Comparison of the relative level of mortality in six Russian areas contaminated by the Catastrophe provinces with the six less contaminated neighboring areas (Khudoley et al, 2006)*
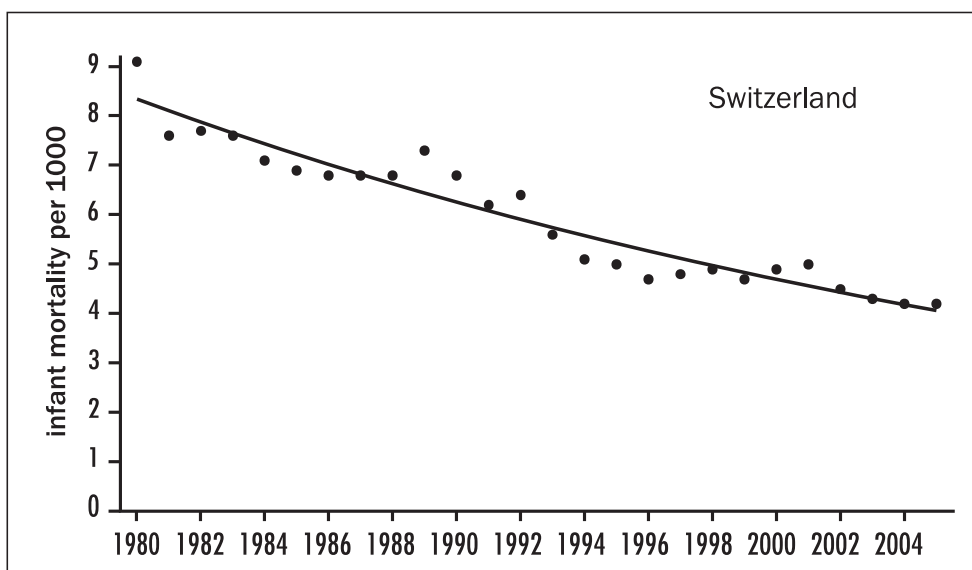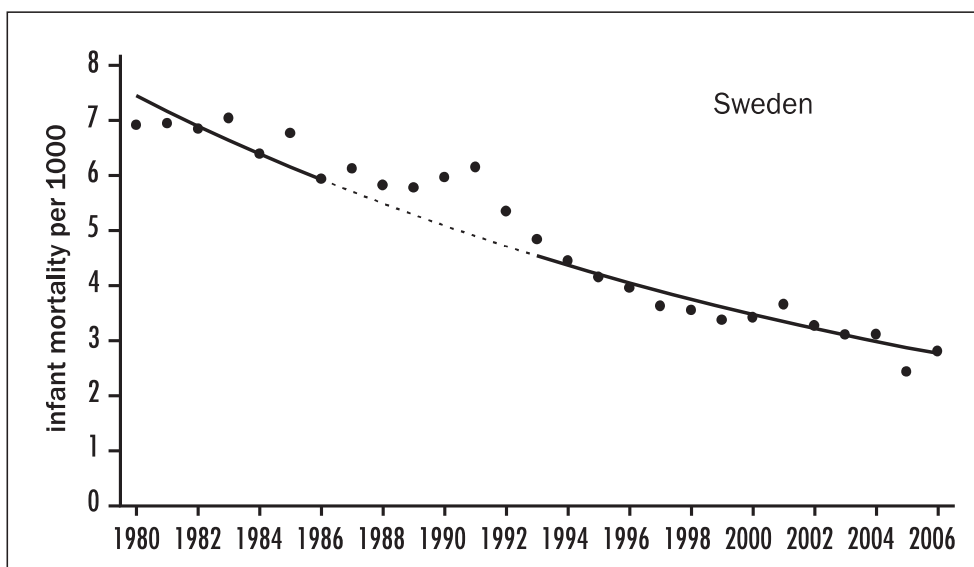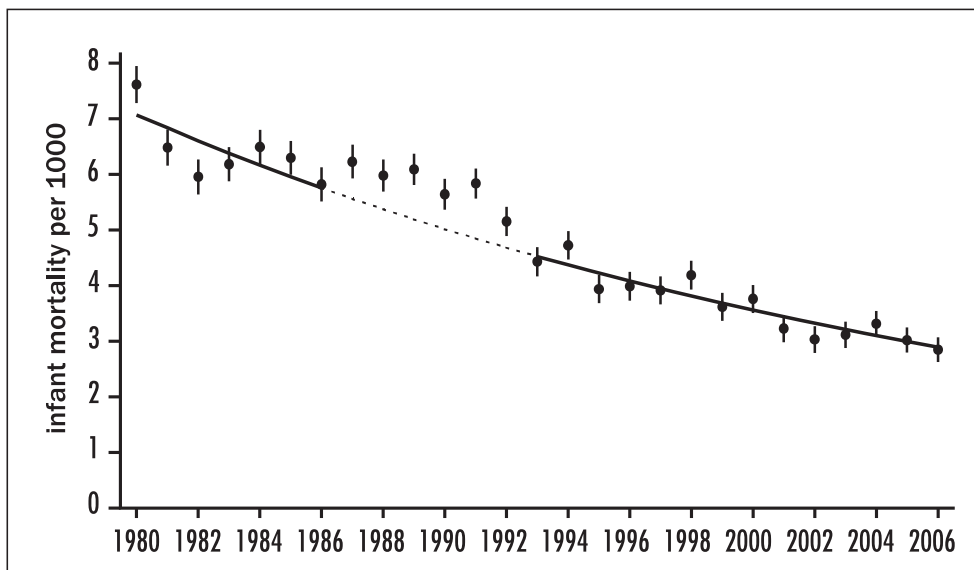
Figures 16.3, 4, 5 - Trend of infant mortality rates in (top to bottom) Finland, Switzerland and Sweden, 1980 - 2006, and undisturbed trend line. Based on official statistical data (Korblein, in litt., 2008)

All affected populations of plants and animals (that have been the subjects of detailed studies) exhibit of morphological deformities that were rare prior to the Catastrophe. In the contaminated territories all plants, fishes, amphibians, birds, and mammals that were studied presented lower stability of individual development (determined by level of fluctuating symmetry). The number of the genetically anomalous and underdeveloped pollen grains and spores in the Chernobyl radioactively contaminated soils indicates geobotanical disturbance. All the plants, animals, and microorganisms (that were studied in the Chernobyl territories) have higher levels of mutations than those in less contaminated areas.

The chronic low-dose exposure in Chernobyl territories results in a trans-generational accumulation of genomic instability, manifested in cellular and systemic effects. Wildlife in the heavily contaminated Chernobyl zone sometimes appears to flourish, but the appearance is deceptive. According to morphogenetic, cytogenetic, and immunological tests, all of the populations of plants, fishes, amphibians, and mammals that were studied there are in poor condition. This zone is analogous to a "black hole"—some species may only persist there via immigration from uncontaminated areas. The tragedy of Chernobyl showed that societies everywhere (especially in Japan, France, India, China, the United States, and Germany) have to have of independent radiation monitoring of both food and individual irradiation levels Monitoring of incorporated radionuclides, especially in children, is necessary around every NPP. This monitoring must be independent of the nuclear industry and the data results must be made available to the public. The WHO diminished the impression of the catastrophe's consequences because it is tightly tied to IAEA by agreement, allowing the nuclear industry to hide from the public any information that they want kept secret.

- **Article III - Exchange of information and documents[**
- 1. The International Atomic Energy Agency (IAEA) and the World Health Organization (WHO) recognize that they might have to take <u>certain restrictive measures to ensure the confidentiality of information that were provided to them</u>.

Figure 16.6 *- Agreement WHO-IAE from May 28, 1959 (Resolution WHA 12-40)*

The Chernobyl catastrophe demonstrates that the nuclear industry's willingness to risk our planet with nuclear power plants will result, not only theoretically but practically, in the same level of hazard to humanity and the Earth as nuclear weapons. What happened to voles and frogs in the Chernobyl zone shows what can happen to humans in coming generations: increasing mutation rates, increasing morbidity and mortality, reduced life expectancy, decreased intensity of reproduction, and changes in male/female sex ratios.

17

Sex ratio of offspring of A-bomb survivors – Evidence of Radiation-induced X-linked lethal mutations

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Abstract.

According to genetic theory, females exposed to ionizing radiation before conception will have lower proportion of boys in their offspring. Likewise, males' exposure will result in fewer girls. In 1953, Neel and Schull reported changes in sex ratio (SR- males per 1000 females) in the children born during 1948-53 (Phase I) to parents exposed to radiation from the atom bombs in Hiroshima and Nagasaki. As the findings were in line with the theory, the study was extended for another eleven years (Phase II). According to the latest paper published in 1981, the findings in the second phase contradicted those of the first phase and hence the observed deviations were dismissed as accidental and biologically insignificant. A closer look at two papers of the same study published in 1965 and 1981 reveals that 1819 boys and 753 girls were added to the Phase II database in the 1981 report without any explanation. SR of all children born during 1954-65 was 1071 in 1965 report and 1100 in 1981 report. Even though there were changes in data for the period 1948-53, these were minimal and the effect on SR was marginal. There were two control groups in this study and SR of these groups during Phase I were 1034 and 1089. SR of all children born in Japan during 1950-55 was 1055. Reanalysis of data using the Japanese SR as the reference shows that (a) SR of all children in the study was 1075, significantly different from the reference (Chi square 6.36, p=0.0117) (b) SR of one of the 'unexposed' control groups was 1089, significantly different from the national SR (Chi square 8.54, p=0.0034), (c) the other 'control' group had a lower SR of 1034 and (d) all the nine cohorts in the reanalysis had deviant SR, four of them pro-theory. The deviances in (b) and (c) above could have been due to the inclusion of fathers and mothers exposed to residual radiation from neutron activation products and fission products respectively. Incidentally, these two groups were treated as control groups in all the genetic studies conducted in the target cities. All genetic studies done in Hiroshima-Nagasaki need be reviewed.

Introduction

In 1927, Herman J Muller observed that female fruit flies (Drosophila Melanogaster) exposed to ionizing radiation (IR) had more female progenies [1]. This was the first experimental demonstration that IR can induce genetic mutation. Further experiments showed that there were more males among the offspring of exposed males. The deficit of boys and girls have been attributed to lethal mutations on the X chromosome in ova and sperms respectively. A dominant lethal mutation of the X chromosome in the sperm will be lethal for the female zygotes as only the daughters inherit the paternal X chromosome. The same mutation on the ovum will be lethal for both male and female zygotes. A recessive lethal mutation on X chromosome of the ovum will be lethal to male progeny only, since the male has only one copy of that chromosome. A female receiving an X chromosome with a recessive lethal mutation may grow up and reproduce, but all her male zygotes receiving the mutated chromosome will be unviable. Therefore, the genetic expectation is that lethal mutation on X chromosome of the sperm and the egg will cause a deficit of girls and boys respectively in the F1 generation (Fig 1). As the exposure of the population to IR was increasing since World War II, an expert committee of the World Health Organization (WHO) in 1957 recommended a study of the sex ratio (SR – number of boys per 1000 girls) of children of those exposed as this endpoint can be studied with limited resources [2].

EFFECTS ON IMMEDIATE POST-EXPOSURE (TWO YEARS) EXCLUDED

THE X-LINKED LETHALITY

- **DOMINANT LETHAL MUTATION IN SPERM LETHAL FOR FEMALE ZYGOTES ONLY**
- **RECESSIVE LETHAL MUTATION IN OVA LETHAL FOR MALE ZYGOTES ONLY**
- **ALL OTHER LETHAL MUTATIONS GENDER NEUTRAL**

Fig 17.1. Genetic effects of ionizing radiation

Few studies of children born to radiation workers [3], down-winders [4] and residents of high natural background radiation regions [5] have demonstrated a significant increase in the incidence of chromosomal and genetic disorders. These findings are not accepted by the radiation standard setting agencies because there

was no significant increase in any of the genetic endpoints among the children born to the Hibakushas in the bombed cities of Hiroshima and Nagasaki.

Study of Genetic Effects in Children of the Bombed Cities

The Atomic Bomb Casualty Commission (ABCC) was constituted in 1945 to conduct short and long term human health studies of the bombs in the target cities. ABCC was disbanded in 1975 and its structures and functions were transferred to the Radiation Effects Research Foundation (RERF), a private foundation funded by the governments of the USA and Japan. The first attempt (GE-3 study) to assess the radiation-induced genetic effects was initiated by ABCC in 1948. This focused on five pregnancy outcomes- still birth, congenital anomalies, birth-weight, perinatal mortality and sex ratio at birth (Fig 2).

METHODOLOGY -GE- 3 STUDY

- **WOMEN 20 WEEK GESTATION, INTERVIEWED WHILE REGISTERING FOR RATIONS**
- **MIDWIFE VISITS AFTER TERMINATION**
- **ALL "NOT NORMAL" AND A THIRD OF THE NORMAL CHILDREN SEEN BY A DOCTOR**
-

LIMITATIONS OF GE-3 STUDY

- **EXCLUSION OF THE RICH**
- **ABORTION < 20 WEEKS NOT DETECTED**

Fig 17.2 GE3 Study protocols

 Analysis of data of 75,000 children born during 1948-53 showed a statistically significant decrease in SR of children born to the exposed women (p <0.05%) and an insignificant increase in SR of children sired by the exposed men [6]. Since this finding was pro-genetic theory, ABCC launched the second phase of SR study, based on births between 1954 and 1965. In the latest report of the study published in 1981, the authors concluded that the results of Phase II were opposite to that of phase I and the earlier finding was fortuitous and of no significance [7] (Fig 3-6)
We will take a closer look at the data and the analysis and see if there were any real changes in SR that can be attributed to radiation-induced mutation.

"THE FINDINGS OF PHASE II (1954-62) OPPOSITE IN DIRECTION OF 1948-53

THE CHANGES OBSERVED IN PHASE I FORTUTIOUS AND BIOLOGICALLY INSIGNIFICANT."

"SEX-LINKED DOMINANT MUTATION MAY NOT KILL FEMALE ZYGOTES BECAUSE OF LYONIZATION (INACTIVATION OF THE SECOND X CHROMOSOME)"

Fig 17.3 Sex ratio 1948-53 in two reports, 1966 and 1981
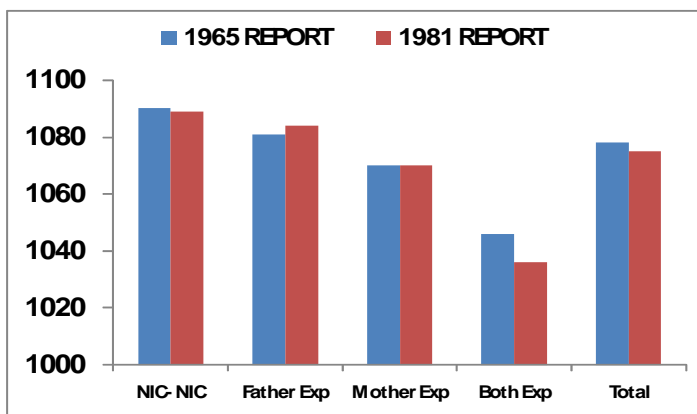
Fig 17.4 Sex ratio 1948-53 (Phase I) for different groups in the RERF studies in 1965 and 1981.
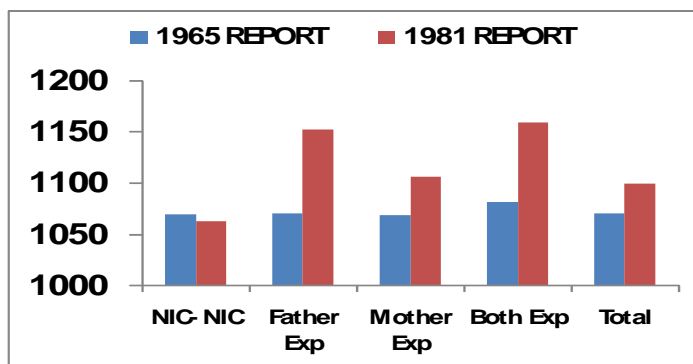
Fig 17.5 *Sex ratio 1954-62 (Phase II) in the RERF studies in 1965 and 1981*
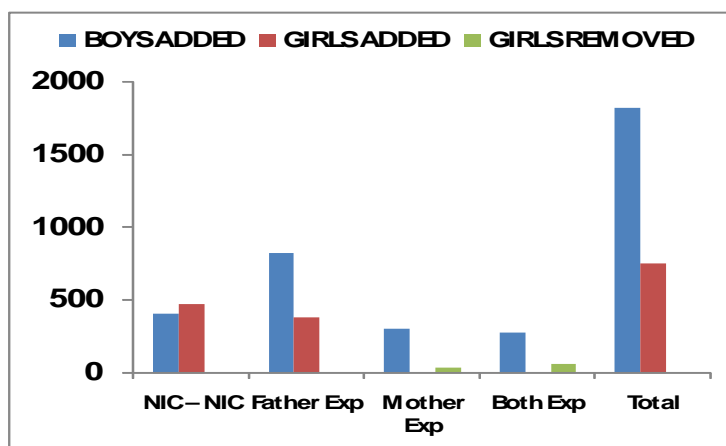
Fig 17.6 *Boys and girls added to the 1954-62 birth group*

Radiations from the bombs – Gamma Rays, Fission Products and Neutron Activation Products

A short narration of the physics of the bombs will be essential for reviewing the health studies in the bombed cities. The explosive yields of the uranium235 (U235) bomb dropped in Hiroshima on 6th Aug 1945 was 15,000 tons (15 kilotons – KT) of trinitrotoluene (TNT) equivalent. The yield of the plutonium239 (Pu239) bomb used in Nagasaki on 9th August was 21 KT [8]. One ton of yield is generated from fission of about 1.45×10^{20} atoms. Fission of one atom generates about one free neutron that does not take part in the chain-reaction, two fission products (FP) and 200 MeV of energy in the forms of photon, heat and blast. The free neutron will

enter the nucleus of the atom it encounters and transform it into neutron activation product (NAP). Neutrons, FP and NAP are radioactive. FP yield was 4.35x1024 in Hiroshima and 6.09x1024 in Nagasaki. Less than 10% of the fissile materials in a bomb will undergo fission, the remaining fuel and other materials will evaporate in the inferno. The bomb debris and materials consumed in the fire will be lofted into the air and drifted by wind and return to the ground as fallout in due course.

People were exposed to the gamma rays, neutrons, particles of unfissioned uranium and plutonium, FP and NAP. The exposure to gamma rays was external and instantaneous and was confined to a circle of about 3000 meters radius from the hypocenters. FP and NAP also delivered internal doses through air, water and food on a chronic basis till all of them decayed to their stable isotopes. NAP intensity was the highest near the ground zeros while the fallout was dispersed in a wider area. Koi-Takasu (off Hiroshima) and Nishiyama (off Nagasaki), which are about 3 km away from the hypocenters, got drenched in the fall-out, which was referred to by the local people as black rain. NAP and FP were sources of chronic internal and external radiations for those who worked and lived around the hypocenters and the fall-out areas. The radioactivity recorded on 1st November 1945 was four times the background level at Koi Takasu, eight times at the Hiroshima hypocenter and ten times at Nishiyama. Arakawa estimated the maximum exposure to a resident at Nishiyama at 10-rad [9] (Fig 7,8). He took into account only the external exposure; the internal doses from inhaling the radioactive dust and eating foods harvested from the contaminated soil and waters were not included in the estimate.
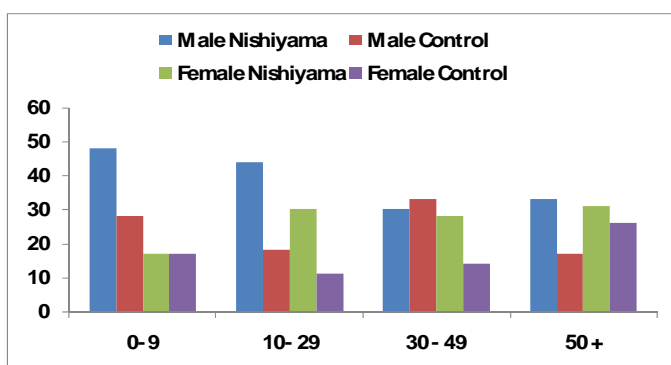
Fig 17.7 *Cs137 in Nishiyama residents & Controls 1969 by Sex and Age ATB (pCi/ kg body weight); Internal body burden higher 24 yrs after bomb*
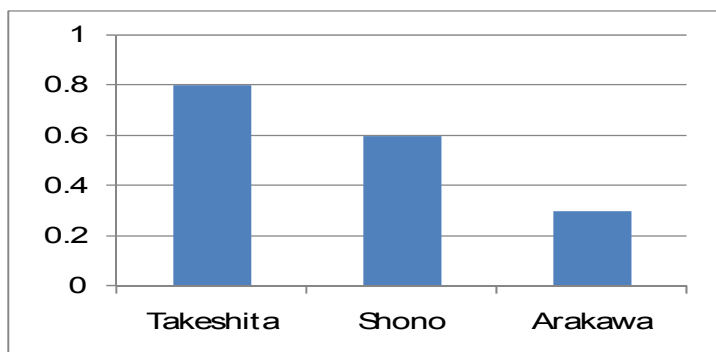
Fig17.8 *Estimated doses for Nishiamaites in Sv.*

Bomb Dosimetry and Dose Groups

Till 1957, survivors were grouped on the basis of twin criteria of (a) distance from the hypocenters at the time of bombing (ATB) and (b) history of symptoms of acute radiation syndromes like loss of hair, bloody diarrhea etc. The first dosimetry in which all survivors within 2000 meters from the hypocentres were allotted their individual doses was created in 1957. Since then, there have been four revisions. Initially, the exposed group consisted of survivors who were within a radius of 2,000 meters from the hypocentres. Those who were beyond 10,000 meters from the hypocentres, labeled as 'Not-In-City (NIC) ATB', were treated as the unexposed control group. NIC included two sub-cohorts: (a) the residents who were temporarily away from the cities ATB and (b) the immigrants from other prefectures and expatriates from the oversea colonies who settled down in the cities after the bombings and before the initiation of the study. Many among group (a) above returned to the cities immediately after the bombs and participated in search, rescue and rehabilitation works. They were exposed to residual radiations from NAP and some of them experienced symptoms of acute radiation. Recognizing this, the government classified the people who returned to the cities within 15 days of the explosions as bomb survivors under the Atomic Bomb Survivors' Medical Treatment Law of 1957. ABCC did not bother to remove the exposed early entrants from NIC. Since there were differences in income and health status between the expatriates and the resident population, ABCC treated NIC as the 'external' control group and carved out an 'internal' control group consisting of residents who were beyond 3,000 meters from the hypocenters ATB. As the latter had received some

prompt radiations from the bombs, estimated to be less than 5 milliSievert (mSv), it is also known as the distally exposed (DE) group.

Besides the prompt radiation, some residents in the fall-out areas located beyond 3 km were exposed to chronic external and internal radiations from fission products and bomb debris. In other words, both the internal and external control groups included subjects who were exposed to residual radiations. The radiation measurements at the hypocenters and the fall-out areas were not incorporated in the bomb dosimetry. As we shall see later, this 'contamination' has seriously jeopardized the results of the health studies. (Fig 9)

Between the years 1950 and 1981, ABCC/RERF researchers published 10 papers on SR as journal articles and technical reports. All the papers published before 1965 highlighted the pro-genetic theory deviations in SR during 1948-53. One paper had a provocative title- "Sex ratio among children of survivors of atomic bombings suggests induced sex-linked lethal mutations"[10]. This position was reversed and the question of bomb radiation causing visible and measurable genomic changes was settled forever in 1981.

In order to see if the reversal of the results is real, I compared the data published in 1965 and 1981. Since each revision in dosimetry also involves inter-group shifting of survivors, comparison of dataset is problematic. Since the subjects in NIC group were not affected by the revisions, their numbers should be the same in all reports. For the comparison of data, we have used two groups – NIC and Exposed, the latter comprises of proximally (<2000 meters) and distally (3000-10000 meters) exposed persons. There are four groups in this comparison; (i) both parents NIC, (ii) both exposed, (iii) mother exposed and (iv) father exposed. Data on children born during the two phases as given in 1965 and 1981 reports are in the data appendix [*].

CONTROL GROUPS IN BOMB
EFFECT STUDIES

THERE WERE 2 CONTROL   GROUPS IN ALL STUDIES OF ABCC

1. 10 KM AWAY FROM HYPOCENTRES   ATB -   EXTERNAL CONTROL GROUP - LABEL = NIC ATB
2. RESIDENTS BEYOND 3 KM FROM HYPOCENTRES - KNOWN INTERNAL CONTROL GROUP - LABEL = DISTALLY EXPOSED

BOTH INCLUDED EXPOSED PERSONS

EXPOSURE DETAILS OF NIC

NIC ATB (10 KM AWAY FROM GROUND ZERO)

RESIDENTS, TEMPORARILY AWAY ATB,

RETURNED ASAP IN SEARCH OF RELATIVES.

EXPOSED TO RESIDUAL RADIATION FROM NEUTRON ACTIVATION PRODUCTS

INCLUSION OF EXPOSED IN CONTROL GROUP

- 1967 - GOVT   CONSIDERS PEOPLE RETURNING TO THE CITIES WITHIN 15 DAYS OF BOMBS (NIC EARLY ENTRANTS) AS BOMB SURVIVORS.
- 20% OF NICS IN ABCC SAMPLES WERE EARLY ENTRANTS. SOME OF THEM HEAVILY EXPOSED.

INTERNAL CONTROL GROUP – SURVIVORS > 3 KM FROM GROUND ZERO

- WITHIN SIX HOURS AFTER DETONATION, BLACK RAINS OF FISSION PRODUCTS IN OUTSKIRTS OF BOMBED CITIES – 3 KMS AWAY FROM GROUND ZEROS.

THIS CONTROL GROUP INCLUDED PEOPLE LIVING IN FALL OUT AREAS ALSO

Fig 17.9. The controls groups for the radiation genetic studies

In Phase I there were 70,212 births as per 1965 report and 70,082 births as per 1981 report. The second report is short 103 boys and 27 girls. Besides this exclusion, there were shifts between exposure groups. In the 1981 report 490 children were removed from NIC-NIC and father-exposed groups, while 360 children were added to mother-exposed and both-exposed groups. After these modifications, SR of the entire cohort declined from 1078 in 1965 report to 1075 in 1981 report. All the exposed groups also underwent such marginal changes.

As per the 1981 report, 72,902 children were born in Phase II and their SR was 1,100(df =1, chi sq 49.44, p= 0.0000). SR was even higher (1,132) among the 39,995 children born to proximally and distally exposed parents (df =1, chi sq 49.44, p= 0.0000). Likewise, during the first phase SR of the total sample and NIC-NIC cohort was significantly higher than the Japanese SR. Changes are changes, even though they do not follow the theories. RERF has a responsibility towards their subjects to probe the reasons for the observed difference.

In the data for phase II (1954-65), 1819 boys and 753 girls were added in the 1981 report. Boys were added to all the four cohorts. 856 girls were added to NIC-NIC and father-exposed cohorts, while 103 girls were removed from mother-exposed and both-exposed groups. SR for all children born during 1954-65 was 1071 in 1965 report and 1100 in 1981 report as more boys than girls were added. NIC-NIC group's SR declined from 1070 in the 1965 report to 1063 in the 1981. There were increases in SR in the other three cohorts. SR of two groups is above 1,150, incredibly high ratios, not reported in any normal population so far. In a long term epidemiological study involving large number of events, data cleaning and removal of bad data is inevitable. In such a situation, the authors have to give convincing arguments supporting the changes. The data modifications are not mentioned in the 1981 paper. Total number of children added for 1954-65 is 2,572 and its impact on SR of all cohorts is very high. As the changes for the period 1948-53 is minimal and the impact on SR marginal, this reanalysis is confined to Phase I data only.

Reanalysis of SR data for 1948-53

In TR-7/81, there are five dose groups - NIC, <5 mSv, 5 mSv to 0.1 Sv, 0.1 – 1 Sv and <1 Sv. (1 Sv = 100 Rem). The first two groups represent the external and internal control groups respectively. Considering the exposure of both parents, there are 25 exposure groups in the analysis. Of the 70,082 children in the study, 83%

were born to parents in four 'control' groups – NIC-NIC = 49%, NIC-DE/DE-NIC = 26% and DE-DE = 8%. That leaves 11,914 children of exposed parents to be placed in 21 cells. Since the chance of being born as a boy or a girl is (almost) 50-50, large numbers of births are required for detecting any real change in SR. The data under consideration simply do not permit disaggregation into 21 exposure groups. Therefore we have compressed the dose groups into three, – NIC, <5 mSv and 5 mSv+, corresponding to the external control group, the distally exposed (DE) internal control group and the proximally exposed (PE) group respectively. When the exposures of father and mother are considered, there are nine dose groups. The results are given in Fig 10.

I REDUCED THE EXPOSURE GROUPS INTO THREE

- **NIC   - EXTERNAL CONTROL**
- **DISTALLY EXPOSED – INTERNAL CONTROL**
- **PROXIMALLY EXPOSED – ALL SURVIVORS <2.5 KM**
- **THERE ARE NINE PARENTAL DOSE GROUPS IN THIS REANALYSIS**

DEVIANT SR IN CONTROL GPS

- **SR OF CONTROL GP 1 (NIC-NIC) =   1089**
- **SR OF CONTROL GP 2 (DE- DE) =   1034**
- **SR OF ALL JAPANESE KIDS   =   1055**
- **SR IN MAJOR COUNTRIES   = 1050 -   1065**

Fig 17.10 *Reanalysis of the sex ratio studies*

SR of the two control groups– DE-DE and NIC-NIC - are 1034 and 1089 respectively. It is strange that the scientists at ABCC/RERF did not pay any attention to this difference between the two control groups. Because of this gross difference between the 'control' groups, I have considered all children born to Japanese nationals in Japan as the reference group. There were 19,427,142 births in Japan during 1950-55; their SR was 1055 [11]. (Japanese SR increased to 1,066 during 1970-74 and decreased to 1,057 during 1990-94 [12]. Incidentally, during the second half of the 20th century all major countries with reliable birth statistics had SR in the range of 1050-1065 [13]) In this discussion Japanese SR is considered as the reference; ratios lower and higher than it will be deemed as female excess and male excess respectively. The male excess cohort would have experienced loss of

female zygotes due to dominant lethal mutations in the sperms and the female-excess cohort would have experienced loss of male zygotes due to recessive lethal mutation in the ova. The numbers of boys and girls 'missing' from the cohorts are given in columns (i) and (j) respectively. (If these 'missing' girls and boys were added to the cohort, their SR would be 1055). The estimated percentage of zygotes that could have been lost due to lethal mutation on X chromosome is given in column (m). To estimate this, the boys/girls born and 'missing' has been used as the denominator.

Results

Five exposure groups had excess of females and four have excess of males in comparison with the Japanese SR. In the female excess cohorts, the mothers were proximally exposed in three, were distally exposed in one and were NIC in one cohort. At the same time, the fathers were proximally exposed in one group, NIC in one and distally exposed in three groups. In the four male excess groups, the fathers were proximally exposed in two and NIC in the other two cohorts. The mothers were distally exposed in two and NIC in two groups. The percentage male in total births in the study during 1948-53 is 51.82 as against the reference percentage of 51.34 in Japan and the difference between them is statistically significant (df=1, p= 6.36, chi sq =0.012). Within the groups, the proportion of male in offspring of NIC-NIC couples is 52.12 and this difference is also highly significant. (df=1, p= 8.54, chi sq = 0.0034). An estimated 230 male zygotes and 869 female zygotes were lost from the female excess and male excess cohorts respectively. These represent 2.5% of the male zygotes and 3.3% of the female zygotes conceived during 1948-53.

The main findings of this reanalysis are:

- There has been an arbitrary, sex selective addition of data in the paper published in 1981. This has masked the effect on SR reported earlier.

- SR of both the internal and external control groups differs from the reference SR.

- There is a significant increase in SR in the total sample of the Phase I.

- SR of all the nine cohorts is different from the Japanese SR. The highest aberration (male excess) is found in the children of NIC fathers. The offspring of distally exposed mothers have a lower SR (Fig 11, 12).

THE MAIN FINDINGS OF THIS REANALYSIS

- **Arbitrary, sex selective addition of data in the 1981 paper masked the effect on SR.**

- **SR of both internal and external control groups differs from the reference SR.**

- **The highest male excess is in children of NIC fathers.**
- **The distally exposed mothers have a lower SR.**
- **Significant increase in SR in total sample of Phase I.**
- **SR of all the nine cohorts is different from the Japanese SR.**

Fig 17.11 The main results of reanalysis of the data

MALE DEFICIT - EXPOSED MOTHERS   MALE EXCESS - EXPOSED FATHERS
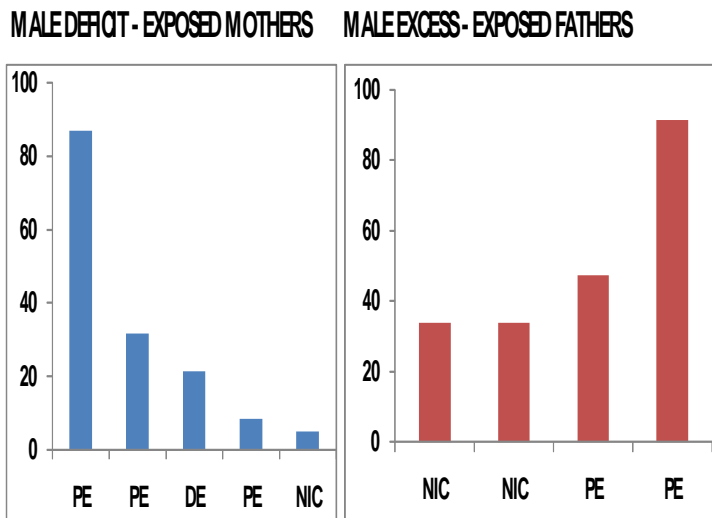
Fig 17.12 Deficit/ excess of males per 1000 females 1948-53

Discussion

In three out of the five female excess cohorts, mothers were proximally exposed and in two out of the four male-excess cohorts fathers were proximally exposed to instantaneous radiation from gamma rays and neutrons. The female excess could have been due to loss of male zygotes carrying a maternal X chromosome with recessive lethal mutation. Likewise, the male excess may be due to dominant lethal

mutation in the paternal X chromosome. These five experiences are pro-genetic theory. In the other two female excess cohorts, mothers were distally exposed in one and NIC in the other. Likewise, in the other two male-excess groups, the fathers were NIC. These aberrations could have been due to the inclusion of persons exposed to residual radiation from fall-out and NAP in the distally exposed and NIC groups. If this factor is taken into consideration, the changes in SR in all the nine cohorts in this analysis could be considered as radiation-induced and are pro-genetic theory.

Other Human studies on SR

The publication of preliminary results by ABCC in 1952 caused a flood of reports on radiation and birth SR by several scholars. Results of 18 series of post-irradiation births (9 father exposed and 9 mother exposed) are availabe [14]. This includes two series in which the parents were in utero ATB in the target cities. The sample sizes in all the individual series, except that of the US and Japanese radiologists are too small. All the authors used another small, unexposed group for comparison and some of which were different from the national SR. For instance, SR of all births in US during the fifties was 1050, SR of radiologist's children's was 1,057 and SR of the children of physicians in other specialties was 1,125. There appears to be something wrong with the data of physicians who were not radiologists. In this review, the SR in their respective countries during the period of study is used as the reference. The offspring SR in two out of nine series of paternal exposure -Czech miners and French patients- is lower and is contra-theory. SR of US radiologists' children does not differ from the national SR. In the remaining six series, there is an increase in male birth. The difference is statistically significant in the case of Japanese radiologists (chi sq 12.59, p= 0.003). If all the offspring of exposed fathers are brought together, the proportion of male is 52.38% and this is significantly different from the estimated mean proportion of 51.35% (chi sq 5.11, p = 0.0238). In the case of maternal exposure, all groups other than the Japanese in utero series show male deficit and are hence pro-theory. If all data of the children born to exposed mothers are combined, the difference is significant (chi sq 6.29, p= 0.0121) (Fig 13).
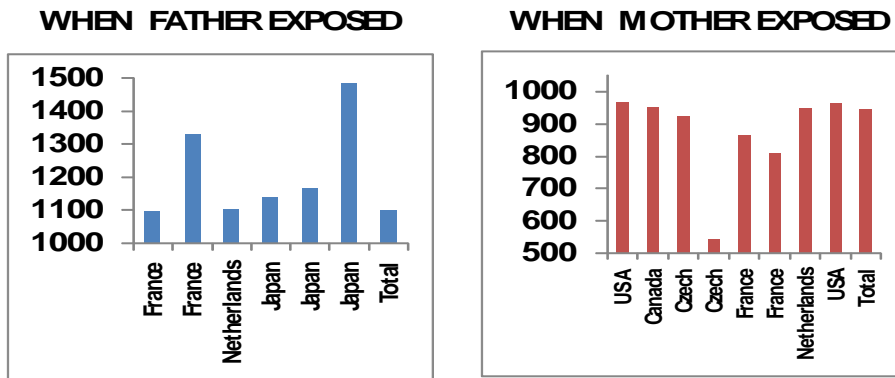
Fig 17.13 *Sex ratio after therapeutic radiation studies*

The Effects of Chronic Exposure

Most of the bomb survivors and the subjects of studies listed in table 3 received acute radiation either from the bombs or from the clinics. In the case of GE-3 study, there was a gap of about 20 to 80 months between the exposure and the conception. The target of exposure in this case is spermatogonial (stem) cells. In a situation of chronic exposure, besides the stem cells, the cells undergoing division are also exposed. Results of three studies of birth sex ratio of children born to parents exposed to chronic low dose radiation are summarized below.

In a retrospective cohort study of 260,060 singleton births between 1950 and 1989 to mothers resident in Cumbria, north west England, Dickinson et al observed that the SR among children of men employed at any time at Sellafield plutonium processing plant was 1.094 (95% CI: 1060, 1.128), significantly higher than that among other Cumbrian children, 1055 (95% CI: 1.046, 1.063). SR of children whose fathers were estimated to have received more than 10 mSv of radiation in the 90 days preceding conception was even higher at 1396 (95% CI: 1.127, 1.729) [15] (Fig 14)

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EXCESS MALES PER 1000 FEMALES
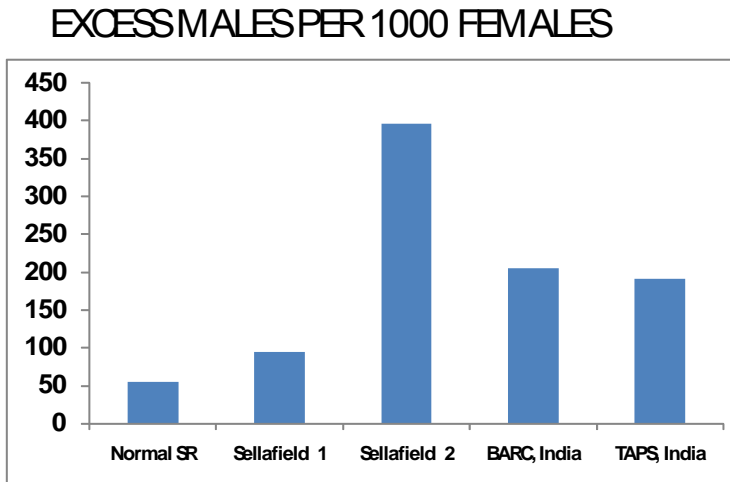
Sellafield 1 = All Workers (1950-1989)

Sellafield 2 =90 days B4 conception

BARC, India = 1960-1984
TAPS, India = 1970-1994

Fig 17.14 *Sellafield workers study*

Scherb and Voigt conducted the largest sex ratio study of 25 million births during 1984 to 1992 in eight European countries (Czech Republic, Denmark, Finland, Hungary, Norway, Poland, and Sweden and Germany). They found a uniform downward trend of the male birth proportion from 1982 to 1986 and a sudden increase in 1987 with an odds ratio of 1.0047 (1.0013–1.0081, p = 0.0061). The authors attribute the shift in 1987 to the radiation exposure from the 1986 accident at the Chernobyl nuclear reactor [16].

A study of 31,569 children born to the workers of the Bhabha Atomic Research Centre (BARC) and the Tarapur Atomic Power Station (TAPS) during the years 1956-1994, also shows significantly higher proportion of male, which cannot be explained by any other factor. In BARC, SR of 1960-1984 cohort was 1205. When compared with the reference SR of 1060, there is a significant excess of male in BARC (df=1, Chi sq =68.93, p=0.00000) and TAPS (df=1, chi sq=10, p=0.00165) [17].

Manipulated data and an untested theory

The proposal for the genetic study in the bombed cities was made by James V Neel, a US naval officer, who served with ABCC. He and his colleague William Schull of the Department of Human Genetics, University of Michigan Medical School, were co-authors in all the papers dealing with SR. In spite of their 'negative' findings, these authors believe that "genetic damage did occur because of the radiation exposure." [18]. Ernest Sternglass quotes from a lecture by Neel in 1963: "in view of the vast body of data regarding the mutagenic effects of radiation, it can scarcely be doubted that the survivors of Hiroshima and Nagasaki sustained genetic damage. The question is not `Is there damage?' but rather `Can the damage be detected?'" [19].

Change in SR was the first demonstrated effect of radiation induced mutations. Since Herman Mueller's historic experiment in 1927, the effect has been repeated in several test systems. Now we have a fairly large series of human data also from bomb survivors, radiation workers, down-winders and people exposed to the Chernobyl fallout. Commenting on the sex ratio study of Sellafield workers, WH James, an expert on birth sex ratio says: "as far as I know, ionizing radiation is the only reproductive hazard which causes men to sire an excess of sons" [20]. At the same time, Neel and co-authors from RERF propose a new hypothesis on sex-linked lethal mutation, based on the observation that one of the X chromosomes in the somatic cells of the mammalian female is inactivated – a process known as Lyonization. They argue that since one X chromosome in the somatic cells of the female is inactivated, "it became clear that sex-linked mutations induced in males were unlikely to have a dominant lethal effect in females" [21]. This implies that a female zygote would have a normal and complete life, even with only one X chromosome. RERF website also claims that "given these developments, most human geneticists no longer accept the simple, early arguments, and contend that prediction of the effects of lethal mutations on the frequency of male births is not possible" [22].

Lyonization or methylation of one of the two X chromosomes in the female has been known for over three decades. However, lyonization does not involve complete silencing of all the genes. According to Carrel and Huntington, about 25% of the genes on the 'lyonized' X chromosome, most of them in the pseudo-autosomal region (PAR), are not inactivated [23]. In other words, the second X chromosome or at least its un-silenced genes are necessary for the normal growth

and development of the female. Some girls are born with one X chromosome only (45XO), a condition known as Turner syndrome. They are severely handicapped and are infertile. About 98% of the 45XO zygotes are lost before term. Birth incidence of 45 XO is 4/10,000 births. For all practical purposes, 45 XO can be considered as the product of a dominant X-linked lethal mutation. This reanalysis shows that 869 girls were missing from the four male-excess cohorts with a total birth of 52,616. There could have been 21 45XO girls in the above cohorts. These and the missing girls might have inherited a lethally mutated X chromosome.

The Universe and the Samples

In an epidemiological study, there are samples that are representative of the universe. When the samples for GE-3 studies were assembled, the two control groups – NIC and DE represented not only the victims, but also of the aggressor. The soldiers who were marched to occupy the conquered lands, the scientists who were to assess the impacts of the new weapons and the doctors and other social workers who went there to heal the wounds were NIC. Likewise, there were 'distally exposed' people in USA also. Twenty one days before the bombing of Hiroshima, the Gadget, the first atom bomb in the trinity test series with an estimated yield of 21 KT was exploded in New Mexico. The fall-out plume was not tracked; there is no documentation about the distally exposed cohorts there. The workers, down-winders and down-streamers of the Hanford pile and other facilities have been living with the fission products five years before the explosions. All these people were also 'distally' exposed. In short, there was a conflict of interest in all the health studies conducted in the bombed cities. I had personal and group interactions with the members of F1 generation in Hiroshima and Nagasaki during the 1990's. They were not interested to discuss the genetic effects of ionizing radiation. This is understandable. People do not want to be told of a permanent and irreversible change in their genome. So, in the bomb cities, the epidemiologists and their subjects had a vested interest in not seeing the genetic effects. Today, sixty four years after the bombings, the universe of the ABCC-RERF studies consist of all of us on the planet. Nuclear weapon tests, accidents at Chernobyl, Three Mile Island and Sellafield and routine releases from nuclear power plants have released a million times more radionuclides into the environment.

Conclusion

Incidentally, ABCC-RERF studies have almost all the features of a prospective epidemiological study and have large number of exposed persons of both sexes. RERF's negative 'findings' dampened the interest of a generation of workers in radiation genetics. The reports of RERF, the biggest health research facility on earth, are considered as the final word by the radiation standard setting agencies like the Biological Effects of Ionizing Radiation (BEIR) committee of the US National Academy of Sciences and UNSCEAR. Even after the intense exposure to ionizing radiations for three generations from making and testing of bombs and operation of nuclear power plants, the United Nations' Scientific Committee on Effects of Atomic Radiation (UNSCEAR) claims "no radiation-induced genetic diseases have so far been demonstrated in human populations exposed to ionizing radiation."[24]. So powerful is the influence of RERF that even researchers who report strong positive association like Dickinson and co-authors think that the "studies of the possible association between parental preconceptional irradiation and an altered sex ratio do not yet satisfy the Bradford Hill criteria for inferring a causal relationship [25]. All because, the final word has been pronounced by RERF. A proper reanalysis of all the genetic studies conducted by ABCC and RERF will undoubtedly reveal the true impact of radiation on the gene and our ignorance about us.

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Underestimation of genetic and somatic effects of ionizing radiation among the A-bomb survivors in Hiroshima-Nagasaki

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Introduction

In August 1945 two fission devices exploded in the morning skies of Hiroshima and Nagasaki with the 'brightness of a thousand Suns' and explosive energy equivalent to 36,000 tons of TNT.1.These generated heat blast and ionizing radiations (IR). The sources of IR were gamma rays (photons), neutrons, neutron activation products (NAP), fission products (FP), and micro/nanoparticles of unfissioned 235uranium (235U) and 239plutonium (239Pu). The photons and neutrons caused prompt exposure within seconds in an area with radius of about 2,500 meters of the hypocenters (OTH). Radioactive particles like NAP, FP and other radioactive particles contaminated the soil and water bodies and the food web. Besides the external radiation, these were also sources of chronic internal radiation through inhalation and ingestion. NAPs are radioactive species like 14carbon and 3tritium formed when neutrons interact with the nuclei of stable atoms of nitrogen and hydrogen. Out of 50 kg of enriched uranium in the core of Hiroshima bomb, only 855 grams were fissioned. Out of an estimated 15 kg of Pu in the Nagasaki bomb 1.2 kg was fissioned. Fission products are nanoparticles with radioactive half lives ranging from seconds to millions of years. FP yields were 4.35x1024 atoms in Hiroshima and 6.09x1024 atoms in Nagasaki. The estimated yields of NAP were about half that of the FP. Within an hour of detonation, part of the bomb debris containing radioactive particles fell in the outskirts of the cities and the rest was lofted to the stratosphere. These particles were found in the ice core drilled from the Arctic ice caps as well as in the samples of soil, sediment, and tree rings from fall out areas in Japan. Hiroshima-Nagasaki events have been billed as the first major global circulation experiment.2 (Please see supplementary table 1 for the physics of the bombs)

Residual Radioactivity near the hypocentres and in the fallout areas

The Atomic Bomb Casualty Commission (ABCC) was constituted in 1945 to study the impacts of the bombs. ABCC conducted studies of radiation effects till 1975. The Radiation Effects Research Foundation (RERF), set up with financial support from the governments of USA and Japan took over the assets and programmes of ABCC. Measurements of residual external radiation near the hypocentres and the fallout areas were done by Japanese and US scientists within days of the events. In the dosimetry report published by ABCC 14 years after the study, the authors lament about the ordinary people's ignorance of residual radiation.[3] The FP fallout areas were Koi Takasu, 3 km west of Hiroshima and Nishiyama, 2.8 km east of Nagasaki. Studies of concentration of plutonium, cesium, and strontium in soil, sediment and tree rings from the hypocentres and fall-out areas sampled during 1980s bear signatures of the devices. The concentration $^{239/240}$Pu at 2.8 km was 1800 Becquerel per square meter (Bq/m^2), thirty times higher than the total Pu fall-out in Japan from all nuclear weapon tests during 1945-64. Concentration of ^{137}cesium was 5260 Bq/m^2, seven times higher than the deposition at Washington County that received the highest fallout from all weapon tests at Nevada, USA. (Supplementary table 2 for contamination details)

Dose Groups in epidemiological studies

In the epidemiological studies, the survivors who were within 2,500 meters OTH at the time of bomb (ATB) were considered as the exposed group. Distance from hypocentres, shielding by structures, and history of symptoms of acute radiation were the criteria for dose-grouping. There were two control groups in the studies, i.e. (i) Not In City (NIC) ATB consisting of subjects who were beyond 10,000 meters OTH and (ii) the Distally Exposed group consisting of residents who were between 3,000 -10,000 meters OTH ATB. DS02, the newest bomb dosimetry adopted in 2002 assigns a dose of 5 milliSievert (mSv) to the distally exposed (Control) and 10 mSv and above to the proximally exposed subjects. Eighty percent of the NIC group consisted of immigrants from other prefectures and overseas dominions who came to the cities when rebuilding activities started a couple of months after the events. The rest of the NIC were residents who were temporarily away from the cities ATB and had returned to the cities as early as they could. They participated in search and rescue operations near the hypocentres and were exposed to residual radiation. Many of them experienced acute radiation syndromes. People

who entered the cities within 14 days of the explosions were treated as bomb survivors under the Atomic Bomb Survivors Medical Treatment Law (ABSMTL) 1957[4]. These people and the residents under the fallout cloud in the distally exposed cohort were exposed to internal and external radiations.

In response to ABSTML, ABCC split the NIC group as NIC Early Entrants (EE) and NIC Late Entrants (LE). NIC EE consisted of subjects who entered the cities within 30 days of the bombings. In spite of this bifurcation, the combined NIC group is still considered as the control group in all the genetic studies and some of the somatic studies being conducted by RERF. The labels 'early entrants' and 'late entrants' cannot be found in any report of RERF. This paper is a review of genetic and somatic effects of the bombs. On the genetic effects, two papers of the SR study published in 1965 and 1981 are compared and reanalyzed. The reappraisal of somatic effects is based on the 1973 LSS report authored by Moriyuma and Kato which provided separate mortality data for NIC EE and LE for the first and the last time.

PART I - SEX RATIO – ABERRATIONS IN THE CONTROL GROUPS

Radiation-induced dominant lethal mutation in male X chromosome and recessive lethal mutation in female X chromosome will lead to deficit of girls and boys respectively in the progenies conceived after the exposure. This was demonstrated experimentally by HJ Muller in fruit flies in 1927.[5] In 1965 Schull et.al summarized the results of 16 studies of 13,511children conceived after exposures.[6] In eight of these, the mothers and in the remaining eight the fathers were exposed at the workplaces or in the clinics. When compared with the national birth SR, the findings in 14 studies were pro genetic theory. In recent times, change in SR has been observed in children of workers of the plutonium processing plant at Sellafield[7] and in Chernobyl- contaminated Europe[8]. In view of the increasing threat to the genome from environmental mutagens, Davis et al suggested that birth SR be treated as a sentinel health indicator.[9]

ABCC study of 70,212 children born during 1948-53, showed a male deficit in exposed mothers' offspring (p <0.05) and female deficit in exposed fathers' offspring.[10] Since these findings were pro-genetic theory, the second phase SR study was conducted during 1954-62. The report of the extended study of 140,252 children born during 1948-62 was published in 1965.[6] The last report of this study published in 1981 after a revision in dosimetry concluded that the results of 1948-53 and 1954-62 were opposite in direction and the positive effects reported earlier was fortuitous and irrelevant for the radiation debate.[11,12]

Comparison of the reports published in 1965 and 1981, (given in supplementary table 3) reveals sex selective changes in database in the 1981 report. During 1948-53, there were 70,212 births (SR =1,078) in 1965 report and 70,082 births (SR = 1075) in 1981 report. 103 boys and 27 girls were missing in the 1981 report. Total birth and SR during Phase II were 70,330 (SR= 1,071) in 1965 report and 72,902 (SR=1,100) in 1981 report. In the 1981 report, 1819 boys and 753 girls were added to the database. Boys were added in all cohorts except the NIC-NIC. Total children in the database for both phases according to 1965 report were 140,542 and SR was 1,074. The number increased to 142,984 and SR increased to 1,088 in 1981 report. Since the number given in two subsequent reviews authored by Neel and Schull in 199113 and Nakamura in 200614 is 140,542, it seems that the 1981 data was incorrect. The data error and the conclusions of 1981 report have not been corrected so far.

Reanalysis of 1948-53 SR data

Since the change in database and its impact on SR is modest for 1948-53, I have reanalyzed this data as published in 1981. In RERF report, there were five dose groups – NIC, <5mSv (Distally Exposed) and three proximally exposed groups with dose ranging from 10 mSv to 2000 mSv. More than 75% of the children were born to the 'unexposed' parents in four parental groups and there are fewer than 50 children in many of the remaining 21 groups. Since the chance of being born as a boy or a girl is almost 50-50, large number of birth is required for detecting any real deviation in SR. The data under consideration do not permit disaggregation into 25 cells. To reduce the number of cells, I have compressed the dose groups into three as – NIC, Distally Exposed and Proximally Exposed. (Table 1). SR and proportion male (male birth/total birth) are given in columns (f) and (g). Estimated number of lost zygotes that resulted in the deviant SR is given in columns (h) and (i).

Results

SR of the total sample is 1975, as against the background SR of 1955. This difference is statistically significant. (p= 0.0117). Of the nine groups in this analysis, five are male-deficit and four are female deficit. The group in which both the parents were proximally exposed (row 1) had the lowest SR of 968. Offspring of proximally exposed fathers and NIC mothers registered the highest SR of 1146. Though these are wide off the background sex ratio, they are not statistically significant. Nearly half the children in the study were parented by NIC-NIC couple (row 7). Their SR was 1089 and this significantly different from the background SR. (p= 0.0034).

DISCUSSION

Genetic effects

The number of children born to people exposed to the prompt radiation (proximally exposed group) was small. Hence, the SR study did not reveal any significant difference. The total sample in the study exhibits a statistically significant male excess in comparison with the Japanese national SR. This is mainly due to the male excess in the two comparison groups (rows 6 and 7) in which fathers were NIC. Of these two groups, offspring SR of NIC-NIC (row 7) couples is statistically significant. In the absence of any other competing hypothesis, it is likely that the high maleness in this group and also the other group (distally exposed mother and NIC father at row 6) is due to the exposure of some fathers to residual radiations. There is however, no visible impact of exposure on the offspring of NIC mothers. This may be because of the fewer number of females among the NIC Early Entrants and also due to the sexual division of labour prevalent in Japan during the Second World War.

This is the first attempt to assess the risk of IR induced somatic and genetic effects in the bomb survivors in one analysis. Within eight years of exposure, control groups in the genetic study exhibited mutation-induced loss of pregnancies. They also started dying earlier, which became statistically visible within 27 years post bombing. These findings from two different studies are complementary to each other. In the absence of any other known risk factor, these excesses can be attributed to exposure to residual radiations.

Assuming that the changes in SR are due to X-linked lethality, 230 male and 869 female zygotes (0.6% and 2.6% of the total boys and girls in the study) were lost from the cohort. Out of 20,252 identified genes in the human genome, 5.6% are located on the X chromosome.[18] Since there are lethal genes on autosomes also, the total zygotic losses would have been much higher. Likewise, the exposure could have caused detrimental mutations as well, which may be visible after a reanalysis of other endpoints in GE3 study with a realistic dosimetry. Since the NIC and the distally exposed cohorts serve as the control groups in all other genetic studies conducted by RERF, this reanalysis has implications for all of them.

Row No	Exposure Status of		Male	Female	S R	Proportion Male	Missing Boys	Missing Girls	Chi Sq	p
	Mother	Father								
(a)	(b)	(c)	(d)	(e)	(f)	(g)	(h) *	(i) *	(j)	(k)
				1948-53						
1	Proximal	Proximal	762	787	968	49.19	68		2.86	0.0909
2	Proximal	NIC	2959	2891	1024	50.58	91		1.35	0.2456
3	Distal	Distal	2816	2724	1034	50.83	58		0.58	0.4479
4	Proximal	Distal	582	556	1047	51.14	5		0.02	0.8938
5	NIC	Distal	1736	1653	1050	51.22	8		0.02	0.8934
6	Distal	NIC	7747	7115	1089	52.13		228	3.69	0.0546
7	NIC	NIC	17785	16332	1089	52.13		526	8.54	0.0034
8	Distal	Proximal	884	802	1102	52.43		36	0.80	0.3697
9	NIC	Proximal	1042	909	1146	53.41		79	3.34	0.0675
10	Total		36313	33769	1075	51.82	230	869	6.36	0.0117
11	Japan	1950-55	9973545	9453597	1055	51.34				

Source: RERF TR 8-71 (Ref 11);

Distal = Distally exposed (Estimated dose < 5 mSv); Proximal = Proximally exposed 10mSv+; NIC =Not in city at the time of the bomb

Table 1 *Sex ratio changes and the missing zygotes. Children of Hiroshima-Nagasaki by parental dose and sex 1948-53*

Table 2. Life Span Study- Persons, person years, deaths till 1972 and relative risks by cause of deaths and dose groups

dose	Persons	Person-	Observed Death		SolidTumours				Other Diseases			
Group	in 1950	Years	till 1972		Per	Rela-	Chi	*p*	Per	Rela-	Chi	*P*
Rad (R)		till 1972	Solid	Other	1000	tive	Square		1000	tive	Square	
			Tumor	Diseases	pyrs	Risk			pyrs	Risk		
(b)	(c)	(d)	(e)	(f)	(g)	(h)	(i)	(j)	(k)	(l)	(m)	(n)
NIC LE	21915	418612	757	3114	1.8				7.4			
NIC EE	4608	85846	210	752	2.4	100	14.8	0.0001	8.8	100	15.91	0.00006
0 R	34642	685040	1434	5955	2.1	86	10.5	0.0010	8.7	99	49.18	0.00000
1 -9 R	20492	407022	798	3432	2.0	80	2.5	0.1100	8.4	96	25.34	0.00000
10-49 R	14407	285593	630	2507	2.2	90	13.4	0.0002	8.8	100	37.67	0.00000
50-99 R	3896	77206	183	693	2.4	97	10.5	0.0010	9.0	102	19.69	0.00000
>100 rads	5676	113294	262	907	2.3	95	3.2	0.0700	8.0	91	3.39	0.65
Total	105636	2072613	4274	17360	2.1	84			8.4	96		

* Relative risks estimated using the mortality data of NIC LE; Other diseases include non-malignant diseases and leukemias.

NIC LE = Not in city, late entrants. NIC EE = not in city early entrants.
Source: Table 1 p 20. Table 2 p22, Table 5.1 p43 and Table 8.1 p64 of ABCC Life span study Technical Report No 15-73

Somatic Effects

In the case of mortality study, during 1950-72, there were 1,358 deaths attributable to radiation. In the latest LSS report for 1950-97, 440 or 8% of the total cancer death and 275 or less than 1% of the total non-cancer deaths was attributed to the bombs. This is about ten times lower than the risk estimated from our reanalysis. In 1975 RERF stopped publication of the mortality statistics of NIC. According to Preston et al "this group has routinely been excluded from LSS mortality and cancer incidence analyses because of concerns about the comparability of their mortality rates to those for the rest of the cohort."[19] These concerns have not been made public so far. NIC is the control group is all the genetic studies of RERF. They have been used as the control group in recent LSS reports like the incidence of cancer in people exposed in childhood or in-utero[20] and in the study of incidence of cancer in LSS during 1958-98. Preston et al say: "in contrast to the first LSS cancer incidence report in 1994, the so-called NIC group was included in the new analyses because the addition of about 25,000 cohort members considerably improves the precision of the descriptions of baseline cancer risk patterns."[21] The distally exposed group had 35,545 members (in 1950) and 918,200 person-years till 1997. The reason for reinventing the NIC may be more than an improvement in the precision of baseline risk. Incidence of cancer per 100,000 person-years in dose groups NIC, <5 mSv and 5- 100 mSv was 587, 610, and 604 respectively.

Nanotoxicity of fission particles

Fission products are single atom particles with a diameter of less than one nanometer (nm= billionth of a meter). Nuclear weapon tests, accidents, and routine releases from nuclear facilities have released more than 10^{30} SAPs since 1940. The bio-kinetics and bio-activity of particles of this size are not well known. Because of their high surface area to mass ratio, nanoparticles generate reactive oxygen species that cause DNA mutation. In other words, the fission particles have both size-dependent and radiological toxicity. The ICRP model for deposition of particles for the respiratory tract is based on studies for particles above 100 nm (0.1 μm). Fission products and bomb debris in the size range of nucleation mode particles (~ 10 nm) can also move up the food chain more efficiently. "Micron-sized zooplankton and larger filter-feeding organisms make up the basis of aquatic food webs. Many filtering apparatuses of filter feeders do not selectively strain items from the water; rather they take all nano-sized materials"[22]. The same is true for the immune system

surveillance inside the body; the macrophages do not recognize fission products as foreign bodies.

The Ethical issue of withholding data

RERF researchers had found two serious health problems within a segment of their study population. The first was an abnormally high sex ratio in some of the cohorts, which was similar to the child sex ratio in India now, a topic that was discussed in the academic journals[23] and in the lay press. The second problem was the 'inconsistent' mortality pattern of NIC cohort. These findings were ignored as they were immaterial for their hypothesis. Leave alone chasing the etiology of these serious health problems, the authors did not even bother to state what the inconsistency was. If NIC members were dying earlier than normal, as life time participants in an epidemiological study, they have a right to know why. Can epidemiologists ignore serious health anomalies found in their subjects because they are unrelated to the hypothesis?

CONCLUSION

Exclusion of nano-sized fission products, unfissioned plutonium and uranium, and neutron activation products from the dosimetry, inclusion of people exposed to these in the control groups, endless dis-aggregation and mismanagement of data resulted in underestimation health risks of the survivors. The finding of significant aberration in SR of NIC offspring and higher mortality risks among NIC EE and distally exposed cohort are unequivocal evidences for the impact of exposure to residual radiations. ABCC-RERF studies have almost all the features of a prospective epidemiological study and have large number of exposed persons of both sexes, followed up for over six decades. The studies that were initiated in the middle of the last century are likely to continue for another three-four decades. The reports of RERF, the biggest and the oldest environmental health research facility on earth, are considered as the final word by the radiation standard setting agencies and independent analysts as well. These studies will reveal the true genetic and somatic impacts of ionizing radiation if the anomalies in dosimetry are corrected.

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On the Assessment of Adverse Consequences of Chernobyl APS Accident on Health of Population and Liquidators

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Since 1987 till the present time, at the Emanuel Institute of Biochemical Physics, Russian Academy of Sciences, studies on the effect of low-dose low-level irradiation on biophysical and biochemical parameters of the genetic and membrane apparatus of cells of organs of exposed animals are being carried out.

We investigated the structural parameters of the genome (by the method of DNA binding to nitrocellulose filters), structural parameters of nuclear, microsomal, mitochondrial, and plasmic (synaptic and erythrocyte) membranes (by the method of spin probes localized in various layers of membranes), the composition and oxidation degree of membrane lipids, and the functional activity of cells – the activity of enzymes, relationship between isozymic forms, and regulating properties. We investigated also the effect of low-level irradiation on the sensitivity of cells, biopolymers, and animals to subsequent action of various damaging factors, including high-dose irradiation. The animals were exposed to a source of ^{137} Cs γ-radiation at the dose-rates 41.6 x 10^{-3}, 4.16 x 10^{-3}, and 0.416 x 10^{-3} mGy. The doses were varied from 6 x 10^{-4} to 1.2 Gy.

As a result of the studies performed, the following conclusions were made:

1. Low radiation doses affect actively the metabolism of animals and man.
2. Over certain dose ranges, low-level irradiation is even more effective than acute high-level.
3. The dose–effect dependence of irradiation may be nonlinear, nonmonotonic, and polymodal in character.
4. Doses that cause the extreme effects depend on the irradiation dose-rate (intensity); they are lower at a lower intensity.
5. . Low-dose irradiation causes changes (mainly, enhancement) in the sensitivity to the action of other damaging factors. [1,2]

We explain the nonlinear and nonmonotonic dose–effect dependence that we obtained in our experiments with low-dose low-level irradiation by changes in the relationship between damages and reparation of the damages. With this kind of low-level irradiation, the reparative systems either are not initiated (induced), or function inadequately, or are initiated with a delay, i.e., when the exposed object has already received radiation damages.

Recently, the absence of reparation at low irradiation doses was verified ont the cell level, [3] and the complex character of the dose dependence was confirmed [4]. Previously, we published a similar scheme of dependence of damages on irradiation dose, which was different for different dose ranges. According to the scheme, the quantitative characteristics were similar for the doses that differed by several orders of magnitude; in a certain dose range, the effect may have an opposite sign.

The results obtained and supported by numerous experiments are important because the above dose dependences made it possible to come to conclusion about a radiogenic or non-radiogenic character of changes observed in an irradiated organism. The indisputable conclusion that if the effect increases with the dose it is evidence for its radiogenic nature is by no means in favor of an opposite statement, i.e., that the absence of a direct dose–effect dependence but its nonmonotonic character is evidence for the absence of a relation of the effect to irradiation.

In autumn 2005, there were published the UNSCEAR Report and materials of the IAEA, WHO, and the UNDP Commission on results of analysis of the Chernobyl APS accident consequences including its harmful effects on health of population and liquidators. The data reported are in contradiction with the conclusions of many Russian scientists and other International organizations such as the American National BEIR Committee (on biological effects of Ionizing radiation) [5]. The controversy stems mainly from the underestimation and misunderstanding of the effects of low irradiation doses, reluctance to apply other criteria to assess the consequences, and conviction (groundless) that low doses cause either no damages or such minor damages that they may be neglected and disregarded.

Neither IAEA nor WHO while defining the irradiation risks took into account the phenomena associated with the action of low irradiation doses and increase the risks; these are the programmed death of cells (apoptosis), 'bystander effect', and radiation-induced instability of the genome, which. in turn, results in enhancement of the sensitivity of organisms to the action of other damaging factors and more serious forms of development of diseases of other than the radiation

genesis. The BEIR-7 reports on sources of errors made while analyzing the state of health of irradiated contingents of people and on the danger of low-level ionizing radiation for health. In the Report, the conclusion made previously that there are no safe levels of radiation, i.e., even very low doses may cause cancer, has been confirmed.

Low-level radiation causes also other health disorders such cardiac diseases and insults, hepatites, mental diseases, and others.

The factor of dose effectivenes and dose-rate for low doses was decreased from 2 to 1.5, which means that the anticipated amount of harmful effects of low doses on health is higher than it was considered earlier (see BEIR-7 Report, 2005).

Similar recommendations for assessment of low-dose risks were made by Russian scientists, who published five monographs on the effects of low doses of radiation on health.

We will emphasize some of the commentaries on the IAEA, WHO, and UNDP reports.

1. No consideration was given to changes in the morbidity rates, which, according to the experts, are related to the accident as a social (not only radiation) risk factor, i.e., stress caused by the accident, necessity of leaving for other regions, changes in the living conditions, radiophobia (fear of radiation), etc. The IAEA and WHO disregard these diseases as a result of the accident.

2. No consideration was given to those oncological diseases, for which no usual dose–effect dependences were determined and can be explained in terms of conventional models, although the radiogenic nature of diseases caused by low irradiation doses should be determined by using specific biomarkers, in accordance with requirements of molecular epidemiology, but not on the basis of dose dependences.

3. No consideration was given to other somatic non-oncological diseases, although, according to L. Preston [6], the radiation component is an important one for a great number of such diseases. Ivanov et al. [7] showed that cerebrovascular diseases of liquidators are of the radiogenic nature. One should not deny the possibility of increasing these diseases as a result of the accident. For example, the number of radiation-induced non-cancer thyroid diseases of children should be taken into account while summing-up the results of irradiation effects on health of people. The IAEA and WHO do not take them into account.

4. Neither IAEA nor WHO consider the high level of invalidity of liquidators. About 57% of liquidators were acknowledged invalids; for 95% of them, the invalidity is caused by the ChAPS accident.

5. At present, the problem of premature aging of liquidators is under wide discussion; there exists a great difference between the biological and passport age for them. The phenomenon is not taken into account as relevant to deterioration of health.

6. The IAEA and WHO consider only thyroid cancers as adverse effects on health of children irradiated after the Chernobyl accident. However, the deterioration of the children health associated with occurrence of more than one chronic diseases is not taken into account. The deterioration of health of children of liquidators is not taken into account too.

One more source of errors in assessment of consequences of the accident is a choice of control groups. Usually, to determine the relation of a disease to irradiation, two kinds of control are used: (a) the internal control, i.e., people of the same age and living under the same conditions as those under study but who received considerably lower irradiation doses than the cohort of people under study and (b) the external control, for which average values are considered that were recorded for the population of Russia and other regions. Each of the above approaches has advantages and drawbacks. However, it should be noted that if a dose–effect curve has no threshold but is appreciably nonlinear and has an extremum point in the range of low doses, the choice of the internal control may lead to a false decrease in the relative risk of morbidity for the cohort under study and make an illusion of a favorable effect of irradiation.

Note that the IAEA and WHO do not deny categorically the radiogenic nature of a great number of somatic diseases but do not consider them as a consequence of the ChAPS accident except for the statement that there is no enough statistical reliability of the results obtained.

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Perinatal mortality in contaminated regions of Ukraine after the Chernobyl accident

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Abstract

Perinatal mortality rates in the Ukrainian regions most affected by the Chernobyl fallout - Zhitomir oblast, Kiev oblast and the city of Kiev (study region) - show a rise and fall during the 1990's relative to the rest of Ukraine (control region). A biological model, which was previously applied to perinatal mortality data from Belarus, 1985-1998, and to perinatal mortality in Germany following the atmospheric nuclear weapon tests, interprets the observed increase as a late effect from incorporated strontium-90. The observed effect translates to 1048 excess perinatal deaths in the study region until 2004.

Introduction

In 1987 the year following the Chernobyl accident, a short-term increase of perinatal mortality rates was found in Germany. This increase was shown to correlate with incorporated radioactive caesium [1] which has a short biological half-life of only some months. After the atmospheric weapons tests in the 1960's, a deviation from the long-term trend of perinatal mortality was observed in West Germany with the maximum incidence in 1970, seven years after the peak fallout in 1963. This increase was interpreted as a late effect of incorporated strontium [2]. In the regions of Belarus and Ukraine near the Chernobyl site, strontium soil depositions exceeding 1 Ci/km² (37 kBq/m²) were detected outside the 30 km exclusion zone. A late effect of strontium on perinatal mortality rates could therefore be expected in the regions neighbouring the Chernobyl reactor. Actually, a rise of perinatal mortality rates in the Gomel region (*oblast*) relative to the rest of Belarus was found in the 1990's which could be associated with incorporated strontium [3]. In the present study, the

perinatal mortality rates in the three most contaminated Ukrainian regions Zhitomir oblast, Kiev oblast and Kiev city are compared with the rest of Ukraine.

Data and Methods

All data in this study are from the State Committee of Statistics of Ukraine and the Ministry of Public Health of Ukraine. Ukrainian data on maternal age distribution (needed to calculate the average strontium burden of pregnant women) were not available, so Belarus data from the Statistics Department of the Ministry of Health of Belarus were used instead.

Using the approach adopted in [3], the perinatal mortality rates in the two most contaminated Ukrainian oblasts and Kiev city are compared with the corresponding rates in the rest of Ukraine to ascertain possible effects of strontium in the 1990's. This approach has the advantage that no assumptions have to be made for the secular trend of the data. If the study and control regions differ in radiation contamination but are similar in socio-economic structure, other factors that might have a global influence on infant mortality in Ukraine should not influence the ratio of the perinatal mortality rates in the study and the control region.

Instead of the rate ratios, the odds ratios (OR) are used which are defined by

$$OR = p_1/(1-p_1) / (p_0/(1-p_0))$$

where p_1 and p_0 are the rates in the study region (1) and the control region (0). For p_1, $p_0 \ll 1$ the odds ratios approach the rate ratios.

For the data analysis the logarithms of the odds ratios are used. A population weighted non-linear regression model of the form

$$(1) \qquad \log(OR) = \beta_0 + \beta_1 \cdot t + \beta_2 \cdot Sr$$

is applied where parameter β_0 is the intercept, β_1 allows for a temporal trend of the odds ratios, parameters β_2 and β_3 estimate the effect of strontium concentration (Sr) in pregnant women.

The data are weighted with weights var (ln(OR)) which are defined by

$$var(\ln(OR)) = 1/(SB_1+NEO_1)+1/(LB_1-NEO_1)+1/(SB_0+NEO_0)+1/(LB_0-NEO_0),$$

where LB, SB and NEO are the numbers of live births, stillbirth and early neonatal deaths in the study (1) and the control (0) regions, respectively.

In addition to model (1), model (2) is applied which allows for a curvilinear shape of the dose response relationship.

(2) $\ln(OR) = \beta_0 + \beta_1 \cdot t + \beta_2 \cdot Sr^{\beta_3}$

Here parameter β_3 is the power of dose.

The following calculation of the development of strontium concentration in pregnant women is based on two simple model assumptions; (a) strontium incorporation occurs in 1986, the year of the Chernobyl accident, and (b) strontium is incorporated at age 14, the age of maximum bone growth [4]. A possible adverse effect of strontium on the newborn will only manifest several years later, at the time of birth. Then the average strontium concentration in a given year following 1986 is proportional to the percentage of pregnant women born in 1972. This percentage follows from the maternal age distribution. Since Ukrainian data on the maternal age distribution could not obtained we used data from Belarus. The data are grouped in 5 year strata. The shaded area in Figure 1 is the average maternal age distribution in Belarus for 1992-1996. To determine annual values, the data were approximated by the superposition of two lognormal distributions (solid line in Figure 1).

Also the strontium excretion from the body must be taken into account. According to the model used in ICRP Publication 67 [5], strontium excretion contains both a fast and a slow component. The strontium term Sr(t), which is proportional to the strontium concentration, thus has the following form:

$Sr(t) = F(t-1972) \cdot (A_1 \cdot \exp(-\ln(2) \cdot (t-1986)/T_1) + A_2 \cdot \exp(-\ln(2) \cdot (t-1986)/T_2))$

where F(t-1972) is the fraction of pregnant women in year t who were born in 1972. $T_1 = 2.4$ years and $T_2 = 13.7$ years are effective half-lives of strontium in the female body. The constants A_1, A_2 and the half-lives T_1, T_2 are determined from a regression of tabulated values given in [5]. A more detailed description of the model is given in [3].
The function nls() of the statistical package R is used for the data evaluation [6].

Results

The trends of perinatal mortality rates, 1985-2004, in the three most contaminated Ukrainian regions combined, i.e. Zhitomir oblast, Kiev oblast, Kiev city (study region), together with the rates in the rest of Ukraine (control region), are displayed in Figure 2. Perinatal mortality data for Kiev city were not available before 1985, and the definition of stillbirth was changed after 2004, so the time span for the data evaluation is 1985-2004. The time variable t is calendar year minus 1980, i.e., t=0 in 1980.
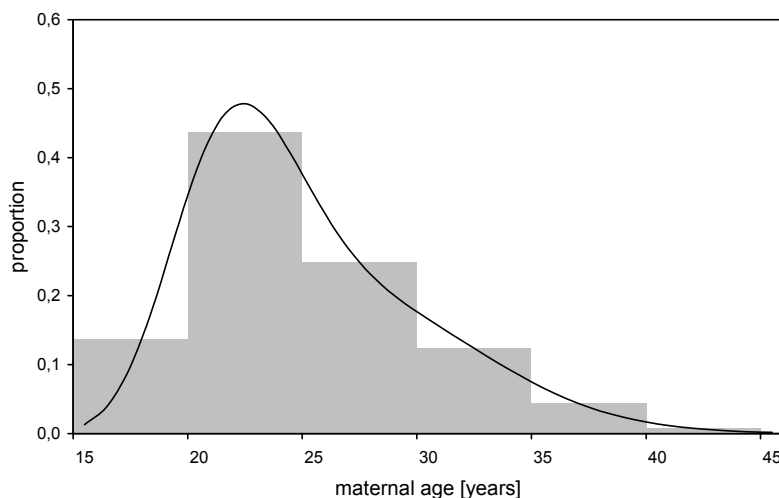
Fig. 19.1*: Maternal age distribution in Belarus, averaged over 1992-1996, and interpolation curve using two superimposed lognormal distributions*

The results of a regression of the odds ratios of perinatal mortality with a linear strontium term ($\beta_3=1$) are listed in Table 1. The residual sum of squares (SSE) is 31.4 with 17 degrees of freedom (df=17).

Table 19.1: Regression results with model (1)

parameter	meaning	estimate	SE	t-value	p-value
β_0	intercept	0.0732	0.0279	2.628	0.0176
β_1	temporal trend	-0.0078	0.0023	-3.456	0.0030
β_2	strontium effect	0.0564	0.0092	6.124	1.1E-05

The odds ratios show a significant time trend (p=0.003). The strontium term is highly significant (p < 0.0001).

A regression of the data using the full model (eq.1), which allows for a curvilinear dose response, leads to an appreciable reduction of the sum of squares (SSE=26.8, df=16); the F test yields p=0.119. The effect of the strontium term (parameters β_2 and β_3) on the goodness of fit is highly significant; the sums of squares are 100.6

(df=18) without and 26.8 (df=16) with the strontium term (F=22.0; p=3E-6; F test with 2 and 16 degrees of freedom). The parameter estimates are given in Table 2.

Table 2: *Regression results with model (2)*

| parameter	meaning	estimate	SE	t-value	p-value
β_0	intercept	0.0767	0.0265	2.891	0.0106
β_1	temporal trend	-0.0063	0.0023	-2.746	0.0144
β_2	strontium effect	0.0196	0.0199	0.984	0.3396
β_3	power of dose	1.8031	0.7660	2.354	0.0317

The best estimate of the power of dose is 1.80 ± 0.77. Figure 3 shows the trend of the odds ratios and the regression line.

Discussion

The present study finds a highly significant association of perinatal mortality rates in the most contaminated regions of Ukraine (Zhitomir oblast, Kiev oblast and Kiev city) with the calculated strontium burden of pregnant women. The increase translates to 1048 excess perinatal deaths. The peak deviation from the long-term trend is observed in 1993, 7 years after the Chernobyl accident. There is no appreciable increase in 1987, the first year after the Chernobyl accident, when the main effect from caesium is expected.

In West Germany, a similar deviation from the secular trend of perinatal mortality was found after the atmospheric nuclear weapons tests which peaked in 1970, seven years after the maximum fallout intensity. The same model as in the present analysis was applied, i.e., the excess perinatal mortality was interpreted as a late effect of incorporated strontium. The best estimate of the power of dose in the strontium term was 1.9 [2].

Our results contradict the negative findings reported in the WHO report published in 2005 [7]. *Inter alia*, the WHO report evaluated data of pregnancy outcome from Ukraine and the other countries of the former Soviet Union and stated that they were mostly of a descriptive nature and provided only percentage changes without specification of the time period and the actual numbers involved. So the WHO Expert Group concluded that it was not able to evaluate the evidence and draw conclusions
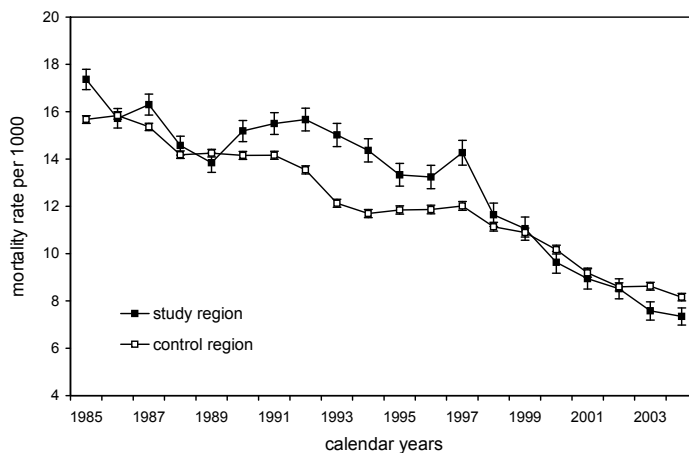
Fig. 19.2*: Trends of perinatal mortality rates in Zhitomir oblast, Kiev oblast and Kiev City combined (study region) and in the rest of Ukraine (control region).*
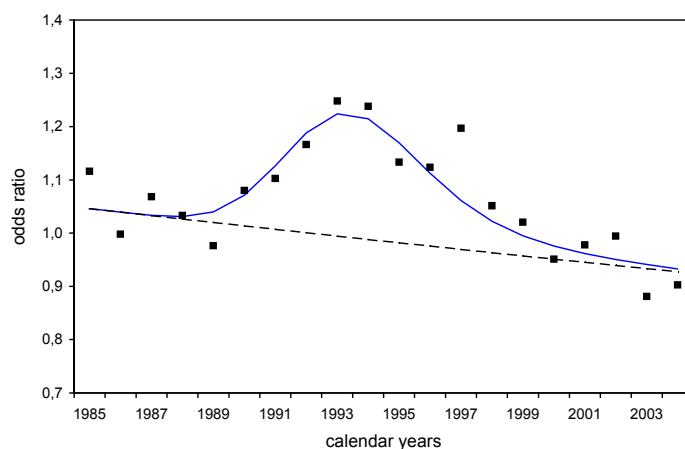
Fig. 19.3: *Odds ratios of perinatal mortality rates in Zhitomir oblast, Kiev oblast and Kiev city combined (study region) and in the rest of Ukraine (control region). The solid line is the regression result, the broken line is the expected undisturbed trend of the odds ratios.*

The WHO report does not deal with perinatal mortality but it contains data on infant mortality. The time trends of infant mortality in the contaminated Ukrainian oblasts of Zhitomir and Kiev and their most highly contaminated districts (5 each) are compared with the corresponding rates in Poltava oblast, a so-called "clean" area. In Poltava oblast, the rates exhibit a monotonously falling trend during 1981-2000, but in the highly contaminated Zhitomir and Kiev oblasts the rates in 1991-1995 were

higher than in 1986-1990 and in 1996-2000. The authors of the report state that no clear trend of infant mortality was found.

Our results challenge the concept of a dose threshold of around 100 mGy fetal dose of low-LET radiation for teratogenic effects [8] since the estimated individual foetal doses were only in the range of some mSv in the years following the Chernobyl accident.

The results of this study should be interpreted with due caution since they are based on highly aggregated data. But as long as there is no other feasible way to study small radiation effects in large human populations the findings must not be dismissed on grounds of the inherent limitations of the ecological study design.

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Appendix: Perinatal mortality data in the study and control regions

year	study region			control region		
	live births	stillbirths	early neonatal deaths	live births	stillbirths	early neonatal deaths
1985	91285	906	695	580205	6029	3158
1986	90169	792	638	612236	6289	3508
1987	79919	762	553	601013	5980	3342
1988	89380	824	490	565296	5062	3027
1989	82572	718	435	525837	4707	2853
1990	75203	668	484	506796	4388	2847
1991	71079	593	518	488655	4152	2825
1992	66395	555	494	463995	3708	2625
1993	61915	488	449	433637	3014	2283
1994	58293	451	393	404959	2805	1963
1995	55738	432	317	381385	2545	2003
1996	53526	400	314	360159	2418	1883
1997	50968	404	329	340645	2158	1961
1998	47272	308	246	324694	1981	1657
1999	44664	273	224	299880	1807	1479
2000	45030	235	201	295066	1606	1411
2001	44381	229	170	287716	1372	1283
2002	47442	238	168	295804	1361	1194
2003	50961	234	154	306667	1501	1157
2004	55165	260	147	316929	1466	1131

ECRR - CERI
European Committee on Radiation Risk
Comité Européenne sur le Risque de l'Irradiation

The Lesvos Declaration

6th May 2009

A. Whereas, the International Commission on Radiological Protection (ICRP) has promulgated certain risk coefficients for ionizing radiation exposure,

B. Whereas, the ICRP radiation risk coefficients are used worldwide by federal and state governmental bodies to promulgate radiation protection laws and standards for exposure to workers and the general public from waste disposal, nuclear weapons, management of contaminated land and materials, naturally occurring and technologically enhanced radioactive materials (NORM and TENORM), nuclear power plant and all stages of the nuclear fuel cycle, compensation and rehabilitation schemes, etc,

C. Whereas, the Chernobyl accident has provided the most important and indispensable opportunity to discover the yields of serious ill health following exposure to fission products and has demonstrated the inadequacy of the current ICRP risk model, especially as applied to foetal and early childhood exposures to radiation,

D. Whereas, by common consent the ICRP risk model cannot validly be applied to post-accident exposures, nor to incorporated radioactive material resulting in internal exposure,

E. Whereas, the ICRP risk model was developed before the discovery of the DNA structure and the discovery that certain radionuclides have chemical affinities for DNA, so that the concept of absorbed dose as used by ICRP cannot account for the effects of exposure to these radionuclides,

F. Whereas, the ICRP has not taken into consideration new discoveries of non-targeted effects such as genomic instability and bystander or secondary effects with regard to understanding radiation risk and particularly the spectrum of consequent illnesses,

G. Whereas, the non-cancer effects of radiation exposure may make it impossible to accurately determine the levels of cancer consequent upon exposure, because of confounding causes of death,

H. Whereas, the ICRP considers the status of its reports to be purely advisory,

I. Whereas, there is an immediate, urgent and continuing requirement for appropriate regulation of existing situations involving radioactivity, to protect the human population and the biosphere,

We the undersigned, in our individual capacities

1. assert that the ICRP risk coefficients are out of date and that use of these coefficients leads to radiation risks being significantly underestimated,

2. assert that employing the ICRP risk model to predict the health effects of radiation leads to errors which are at minimum 10 fold while we are aware of studies relating to certain types of exposure that suggest that the error is even greater,

3. assert that the yield of non-cancer illnesses from radiation exposure, in particular damage to the cardio-vascular, immune, central nervous and reproductive systems, is significant but as yet unquantified,

4. urge the responsible authorities, as well as all of those responsible for causing radiation exposures, to rely no longer upon the existing ICRP model in determining radiation protection standards and managing risks,

5. urge the responsible authorities and all those responsible for causing exposures, to adopt a generally precautionary approach, and in the absence of another workable and sufficiently precautionary risk model, to apply without undue delay the provisional ECRR 2003 risk model, which more accurately bounds the risks reflected by current observations,

6. demand immediate research into the health effects of incorporated radionuclides, particularly by revisiting the many historical epidemiological studies of exposed populations, including re-

examination of the data from Japanese A-bomb survivors, Chernobyl and other affected territories and independent monitoring of incorporated radioactive substances in exposed populations,

7. consider it to be a human right for individuals to know the level of radiation to which they are exposed, and also to be correctly informed as to the potential consequences of that exposure,

8. are concerned by the escalating use of radiation for medical investigation and other general applications,

9. urge significant publicly funded research into medical techniques which do not involve radiation exposures to patients.

Statements contained herein reflect the opinions of the undersigned and are not meant to reflect the positions of any institution to which we are affiliated.

Professor Yuri Bandazhevski (Belarus)
Professor Carmel Mothershill (Canada)
Dr Christos Matsoukas (Greece)
Professor Chris Busby (UK)
Professor Rosa Goncharova (Belarus)
Professor Alexey Yablokov (Russia)
Professor Mikhail Malko (Belarus)
Professor Shoji Sawada (Japan)
Professor Daniil Gluzman (Ukraine)
Professor Angelina Nyagu (Ukraine)
Dr Hagen Scherb (Germany)
Professor Alexey Nesterenko (Belarus)
Professor Inge Schmitz-Feuerhake (Germany)
Dr Sebastian Pflugbeil (Germany)
Professor Michel Fernex (France)
Dr Alfred Koerblein (Germany)
Dr Marvin Resnikoff (United States)

Back Cover

For those who wish to know the health consequences of the Fukushima catastrophe, the answers are to be found within this volume and in the radiation risk model of the ECRR. The data presented at the 2009 Lesvos conference of the European Committee on Radiation Risk show the real world effects of living in areas contaminated with the dispersed contents of an exploded nuclear reactor. Twenty five years of studies of people living on the Chernobyl contaminated territories has been enough to quantify in detail the cancers, the heart disease, the loss of lifespan, the congenital illnesses, even the changes in sex ratio, in childhood intelligence and in mental health that follow the exposures to radioactive contamination from fission products, activation products and uranium fuel particles.

All of these are described in this volume in great detail, by the eminent scientists who have studied them. As Edmund Burke famously said, *Those who don't know history are doomed to repeat it* ; but the true history of the health effects of exposure to the radioactive substances released by both the Chernobyl and Fukushima catastrophes have been covered up by the power of the nuclear lobby. And the main instrument that has been used for this is the radiation risk model of the International Commission on Radiological Protection, the ICRP. But as far as scientific evidence goes, the simplistic ICRP risk model is now bankrupt. It is now clear to all, except governments who depend upon the ICRP model to justify their support of nuclear energy and nuclear weapons, that the model is unsafe. With terrifying prescience, the matter was raised in 2009, in a videotaped meeting between the Scientific Secretary of the ECRR Prof. Chris Busby and the just-retired Scientific Secretary of the ICRP, Dr Jack Valentin. In this meeting, and presented in this volume, Valentin states quite unequivocally, that the ICRP model cannot be used to assess the risk from a major accident at a nuclear power station. *It is not what it is for,* he said. Yet this is just exactly what it is being used for 7 months after the Fukushima catastrophe.

This is a political issue, an issue of democracy. It is also an issue for those involved, deciding whether to evacuate their children from the contaminated areas. Perfect political decisions require accurate information. For those decision-makers and members of the public who want to know what will happen to the people of Fukushima and wider areas of Japan, the information is here.

The cornerstone of Science Philosophy is the *Canon of Agreement*, which states that *the antecedent conditions of a phenomenon, when repeated, will produce the same phenomenon.* Let no one doubt that the Chernobyl experiment, repeated in Fukushima, will cause the same result, a result reported in these proceedings in all its terrifying clarity.