Scientific and Citizen Forum on the Genetic Effects of Ionizing Radiation

Abstracts of the presentations and short biographies of the presenters

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Saturday 29th November 2014 - Geneva

8.30 am Welcome

9.00 am Introduction to the Forum

9.10 am ***Dr Inge Schmitz-Feuerhake***

9.55 am ***Dr Yuri Dubrova***

11.00 am ***Dr Wladimir Wertelecki***

11.45 am ***Dr Keith Baverstock***

2.00 pm ***Dr Timothy Mousseau***

2.45 pm ***Chiyo Nohara***

4.00 pm Question and Answer Session

5.50 pm Conclusion

Ruth Stégassy, presenter of the programme "Terre à Terre" on Radio France Culture, will moderate this forum.

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Abstract

Presentation of : *Inge Schmitz-Feuerhake*, German Society of Radiation Protection, Member (retired), University of Bremen, Germany

Title : Immediate and delayed genetic effects of ionizing radiation through irradiation and contamination

The International Commission on Radiological Protection (ICRP) and other international committees claim that hereditary diseases after low dose exposures to ionising radiation are virtually negligible. These organizations only take into account disorders due to dominant mutations in the first generation and they refer exclusively to Japanese atomic bomb survivors in whom significant effects have been missed. They ignore the results of a great number of scientific studies in human populations and their progeny which show hereditary diseases after occupational or diagnostic exposures and especially exposure to Chernobyl fallout. In the introduction, I will refer to the genetic effects which are to be expected based on our general knowledge about biological effects of radiation in living cells and in laboratory animals. I will then report on early deaths,

malformations, Down´s syndrome and other congenital anomalies which have been observed in humans after exposure of parents. According to current knowledge, there is no threshold below which heritable damage due to exposure to ionizing radiation does not occur. It has been clearly shown, however, that official risk estimates of the genetic effects of radiation are much too low.

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Dr Inge Schmitz-Feuerhake was a professor in experimental physics at the University of Bremen (Germany) from 1973 and until her retirement in 2000. Her research has assessed the biological effects of ionizing radiation at low dosage levels, as well as the diagnostic use of nuclear radiation. Her work made a major contribution to the development of biological dosimetry methods in which changes to the chromosomes in white blood cells are measured with extreme precision, by making it possible to count the concerned white blood cells under the microscope. She wrote of her scientific findings in comprehensible language, so that they can be understood by colleagues from related disciplines and interested laypeople. Dr Schmitz-Feuerhake became known in Germany since 1990 for examining the rise of the number of children suffering leukemia in the surroundings of the Krümmel Nuclear Power Plant. In 2003 she received the Nuclear-Free Future Award for her lifetime achievement. She is also chairman of the European Committee on Radiation Risk, and vice president of Gesellschaft für Strahlenschutz e.V. (German Society for Radiation Protection).

Abstract

Presentation of : *Dr Yuri E. Dubrova*, Department of Genetics, University of Leicester, United Kingdom

Title : Summary of past and present studies on the genetic effects of ionising radiation, including an overview of recent technological advances in this area, and of transgenerational effects of parental exposure to mutagens

Experimental evidence for radiation-induced mutation in the human germ line still remains highly controversial, which is mainly attributed to the low sensitivity of traditional approaches for mutation detection in humans. We have developed a new system for monitoring radiation-induced mutation in the human germline. This technique employs highly unstable minisatellite loci and because of the very high rate of spontaneous mutation altering allele length (repeat copy number) provides a system capable of detecting induced mutations in relatively small population samples. The results of recent studies have shown that tandem repeat minisatellite loci provide a highly efficient system for monitoring radiation-induced mutation in humans.
Using this technique, germline mutation has been studied among families from rural areas of Ukraine (Kiev and Zhitomir regions) and Belarus (Mogilev region), which were heavily contaminated by radionuclides after the Chernobyl accident [1-3]. A statistically significant 1.6-fold increase in mutation rate was found in the germline of exposed fathers, whereas the maternal germline mutation rate in the exposed families did not increase. In the Belarus cohort, the mutation rate was significantly higher in families with higher parental radiation dose estimated for chronic external and internal exposure to caesium-137, consistent with radiation induction of germline mutation. These data suggest that the elevated minisatellite mutation rate can be attributed to post-Chernobyl radioactive exposure. Similar results were obtained by analysing the pattern of minisatellite mutation induction in the cohort of irradiated families exposed to radioactive fallout from the above ground atomic bomb tests in the former USSR [4] or to discharges of radioactive

waste into the river Techa [5]. The results of our studies provide the first experimental evidence that the mutation rate in human populations is increased by ionising radiation and show that minisatellite loci represent a powerful tool for monitoring germline mutation in humans. The advantages and shortcomings of this system and new experimental approaches for monitoring radiation-induced mutation in the human germline will be discussed.
The phenomenon of radiation-induced transgenerational instability defined as an increased rate of mutation observed in the non-exposed offspring of irradiated parents will also be presented. The results of recent animal and human studies will be compared and the potential contribution of transgenerational effects to the genetic risk of human exposure to ionising radiation will be discussed.

References

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5. Dubrova YE, Ploshchanskaya OG, Kozionova OS, Akleyev AV. 2006. Minisatellite germline mutation rate in the Techa River population. Mutat. Res., 602, 74-82.

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Dr Yuri E. Dubrova professor of genetics at the University of Leicester (UK), was born in Kiev (Ukraine). He obtained a BSc degree in Biology at Kiev State University and a PhD in Genetics Vavilov Institute of General Genetics in Moscow, where he undertook a number of research projects in population genetics. In 1994 he moved to the Department of Genetics, University of Leicester, to study the genetic effects of exposure to ionising radiation and chemical mutagens in mammals. Professor Yuri Dubrova's research interests focus on the analysis of germline mutation induction in humans and mice following exposure to ionising radiation, chemical mutagens and some anticancer drugs. His recent research has also involved transgenerational genomic instability manifesting in the offspring of exposed parents. He is the author of more than 110 peer-reviewed publications in his field.

Abstract

Presentation of : Dr Wladimir Wertelecki, Formerly of the Department of Medical Genetics and Birth Defects, University of South Alabama, USA
President of the Board of the OMNI-Net Ukraine Child Development Programmes

Title : Abnormal levels of incorporated ionizing radiation among pregnant women and high rates of malformations in infants in Ukraine

We report population-based rates of congenital anomalies in the Rivne province of Ukraine. The rates are significantly higher in the northern half of Rivne, a region called Polissia (P) which is polluted by Chornobyl ionizing radiation (IR). P is a region of forested wet-lands also called Prypiat Marshlands. Compared to other soils, those in P release 137Caesium (137Cs) to the food chain, more readily. Congenital anomalies (CA) with elevated rates noted in P are blastopathies which arise before the implantation of fertilized eggs. The blastopathies noted are conjoined twins, sacral teratomas (embryonal tumors of the lower spine), neural tube defects (anencephaly and spina bifida among others), and microcephaly-microphthalmia (reduced head size and/or reduced ocular globes). These blastopathies are prevalent among females and their population-based elevated rates are persistent and are among the highest reported in Europe.

In Ukraine, virtually all measurements of IR emanating from soil, inhaled or ingested are extrapolated from measurements of 137Cs. However, there are many other radionuclides that also are sources of IR. For instance we find 90Sr in potato plants grown in P and releases from atomic nuclear plants such as those in Kuznetsovsk and near Ostroh county may also add to the total levels of IR exposures. It is reasonable to conclude that IR impacts on the unborn are greater than calculated from extrapolations solely based on 137Cs measurements. The average 137Cs incorporated by 3,865 pregnant women from P was 40.4 and among those from non-P was 11.3 becquerels per kilogram of body weight respectively. The levels of incorporation of 137Cs have risen significantly over time.

A comprehensive analysis of prenatal exposures to alcohol, another potent cause of CA, did not reveal P vs. non-P differences.

The observations in Rivne emerge from descriptive epidemiological investigations seeking to detect associations to guide prospective cause-effect investigations. The concurrence of elevated population-based rates of blastopathies and higher incorporated levels of 137Cs in pregnant women reflects an association but does not constitute proof of causation. The observations in Rivne are sufficiently compelling to justify prospective investigations of specific cause - specific effect research projects. In the context of the circumstances emerging in Japan following the Fukushima Daiichi disaster, it is also our view that concurrent, parallel, homologous studies of populations in Rivne and Japan will accelerate and broaden the understanding of IR impacts on human embryos.

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Dr Wladimir Wertelecki is President of the Board of the OMNI-Net Ukraine Child Development Programmes, a group that has done extensive studies into congenital malformations in the Polissia region in Rivne, Ukraine. Polissia is one of the most affected regions by the Chornobyl disaster. He is adjunct Professor at the Dysmorphology Division of the University of California in San Diego and at the Graduate Program in Biomedical Anthropology of the New York State University in Binghamton. Dr Wertelecki was born in Poland and is fluent in languages of regions impacted by the 1986 Chornobyl disaster.

Largely educated in Switzerland and Argentina, where he obtained his medical degree from the University of Buenos Aires, he trained in Pediatrics at the Saint Louis Children's Hospital of the Washington University and in Clinical Genetics at the Boston Children's Hospital of the Harvard School of Medicine. Dr Wertelecki was Chair of the Department of Medical Genetics and Birth Defects, University of South Alabama, from 1974 to 2010. His major areas of interest include medical genetics, human handicaps, and pediatrics. He has organized many conferences dealing with genetics and birth defects, as well as public health and other issues. He is the recipient of numerous awards and the author of more than 250 articles and abstracts.

Abstract

Presentation of : *Dr Keith Baverstock*, Department of Environmental Sciences, University of Eastern Finland, Finland

Title : The role and potential consequences of genomic instability induced by environmental stressors

The approach taken in this presentation is based on SYSTEM BIOLOGY concepts. A SYSTEM is any collections of objects that interact with one another to produce some specific outcome and can be conveniently thought of as being isolated from their surroundings (environment).
A CELL in a human is a system constituted of interacting molecules that produces properties called its PHENOTYPE. The ENVIRONMENT of the cell is the ORGANISM (human being).

The ORGANISM also has a phenotype comprised of the cellular phenotypes. The ENVIRONMENT of the organism is the ECOSYSTEM in which the organism evolved.

The three systems, cell, organism and ecosystem, INTERACT with one another so that a change in any one system can cause changes (usually not predictable) in the others and this is particularly true of changes that influence the cellular phenotype. In such complex systems EVERYTHING DEPENDS ON EVERYTHING ELSE.

The cell as a system contains MATERIAL THINGS (molecules like DNA peptides and proteins) and PROCESSES (interactions between the molecules). Conventional molecular biology tends to concentrate on the molecules (MOLECULAR BIOLOGY) largely ignoring the latter. It is dominated by MATERIALISM. In the approach described here PROCESSES are the more central. This approach is HOLISTIC. Holistic approaches are in general not regarded as “scientific” by many biologists because if everything depends on everything else the traditional experimental approaches (called REDUCTIONISTIC) are difficult if not impossible to apply.

Biological systems are governed by physics. The default physics, as taught in schools, is NEWTONIAN PHYSICS, but it is not relevant to biological systems: it is primarily the physics of MATERIAL based systems and not of PROCESS based systems. The appropriate physics is the physics of COMPLEX DISSIPATIVE (energy or nutrient consuming) SYSTEMS. All that it is necessary to understand is that this kind of physics supports uniquely biological features that are underpinned by PROCESSES.

One of the features underpinned by complex dissipative system physics is that of the ATTRACTOR. An attractor is a quasi-stable state, meaning that it is STABLE under some circumstances but not others. Newtonian physics does not support the concept of the attractor. As an example consider a long room with two light bulbs, one at each end that can be switched on and off independently, and a fly. When one bulb is lighted the fly will be invariably found at that end of the room. That is a quasi-stable state of the room/lightbulb/fly system. If that light is switched off and the other switched on the fly will move to the other end of the room: that is a second quasi-stable state of the system. If both bulbs are either switched on or switched off, the fly could be anywhere and that is an unstable state of the system. The lighted bulb is an attractor for the fly.

In the presentation I have used another familiar system, the rider/bicycle system. A bicycle with a rider is able to adopt an upright position, which is not possible for the bicycle on its own. The rider can shift his/her weight to the right or the left and steer the front wheel with the handlebars to the left and the right. These four, so-called dimensions of the system, enable a quasi-stable (attractor) state of the system. If the rider loses control of one or more of these dimensions, stability will be lost and the rider will fall off the bicycle - the system is destroyed. The attractor in a human cell has several thousand dimensions and many attractor states, so loss of one attractor does not necessarily mean the destruction (death) of the cell.

The properties of the cell, its phenotype, are represented by an attractor state. This quasi-stability in a cell from a stably replicating species can be disrupted by exposure to agents that damage DNA which may result either in cell death or in the adoption of another quasi stable state (phenotype) which is still capable of replication. However, the replication may be unstable and the cell is said to be GENOMICALLY UNSTABLE.

Cells then are capable of switching irreversibly and randomly between different phenotypes, only one of which can replicate the true system of the species, others will lead to abnormalities. If the cells in question are what we call GERM CELLS, sperm or eggs, abnormalities will appear in all the cells of an organism derived from such a phenotype. Furthermore, the abnormalities can be passed on to future generations.

So far, GENOMIC INSTABILITY has been observed in cells in culture and in nonhuman organisms ranging from worms to rats. Understanding the nature of genomic instability has not proved possible within the conventional framework of biology, namely genetics. What is presented here is a major reformulation of the way biology works. It has been published in a major peer-reviewed journal and therefore subject to intensive scrutiny. Its status is that of a hypothesis which needs to be further tested. However, the concepts used are more soundly based in physics than those used in conventional biology and the hypothesis has considerable explanatory power. It is therefore, reasonable to try to formulate the long-term consequences of genomic instability.

These are, over several generations, a progressive decline in the healthiness and well-being of affected individuals, including the bringing forward of diseases normally of late-onset and the occurrence of malformations. It may be 10 generations (300 years) before the full impact of genomic instability induced today is abundantly clear.

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Dr Keith Baverstock is currently a docent in the Faculty of Natural and Environmental Sciences of the University of Kuopio, Finland, where he lectures and researches on the effects of ionising radiation. Dr Baverstock, a graduate of London University, led the Radiation Protection Programme at the World Health Organisation's Regional Office for Europe from 1991 to 2003. From 1998 to 2002 he set-up a dedicated project office in Helsinki for nuclear emergencies and public health and in 2002 he transferred to the WHO's European Centre for Environment and Health located in Bonn where he was the Regional Advisor for Radiation and Public Health. The WHO's radiation programme was instrumental in bringing to world attention the increase in thyroid cancer in Belarus, now attributed to the Chernobyl accident.
In 2001 he was a member of a UN mission charged with making a situation analysis on the Chernobyl affected regions of Belarus, Russia and Ukraine. The mission report "The human consequences of the Chernobyl accident: a strategy for recovery" was published by the UN in 2002. From November 2003 to April 2005 he served on the UK Committee for Radioactive Waste Management (CoRWM). Currently he is a partner in the European commission funded ARCH project the objective of which is to develop a strategic research agenda for the health effects of the Chernobyl accident. His current research interests are in the dynamical aspects of the process by which ionising radiation and other environmental agents cause genomic instability and cancer, the effects on human health of low doses of ionising radiation and the psychosocial aspects of exposure to ionising radiation.

Abstract

Presentation of : *Dr Timothy Mousseau*, Professor of Biological Sciences, University of South Carolina, USA - with Anders P. Møller

Title : Biological consequences of radiation in the environment for individuals, populations and ecosystems : lessons from Chernobyl and Fukushima

Recent empirical studies and literature surveys provide strong evidence for significant biological consequences of low dose-rate radiation such as that found in Chernobyl and Fukushima affected regions, as well as naturally radioactive regions of the world. These effects are observed at all levels of biological organization from the DNA to ecosystems and in many cases suggest that the Chernobyl and Fukushima radiological disasters have resulted in significant injuries to individuals and populations and have serious implications for ecosystem functioning. Most of these studies have been actively ignored by United Nations organizations (e.g. IAEA and UNSCEAR) because they were not conducted specifically with nuclear regulatory ends in mind. However, it is evident that a greater effort must be made to consider the implications of these recent findings not only for the plants and animals of these regions, but also the human populations in the surrounding areas.

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Dr Timothy Mousseau has been a member of the faculty of the Department of Biological Sciences at the University of South Carolina since 1991. He received his doctoral degree in 1988 from McGill University and completed a NSERC (Canada) postdoctoral fellowship in Population Biology at the University of California, Davis. At USC Dr Mousseau and his students have worked on a wide diversity of organisms, from bacteria to beetles to birds, and his primary areas of research interest include the genetic basis of adaptation in natural populations. Since 1999, Professor Mousseau and his collaborators have explored the ecological, genetic and evolutionary consequences of low-dose radiation in populations of plants, animals and people inhabiting the Chernobyl region of Ukraine and Belarus. He recently initiated a second research program in Fukushima, Japan. His research suggests that many species of plants and animals experience increased mutational loads as a result of exposure to radionuclides stemming from the Chernobyl disaster. In some species (e.g. The barn swallow, Hirundo rustica), this mutational load has had dramatic consequences for reproduction and survival. Dr. Mousseau's current research is aimed at accurately assessing doses received by animals living in the wild and elucidating the causes of variation among different species in their apparent sensitivity to radionuclide exposure.

Abstract

Presentation of : *Chiyo Nohara*, University of Okinawa, Japan

Title : The biological impacts of the Fukushima nuclear accident on the pale grass blue butterfly

The collapse of the Fuku Dai-ichi Nuclear Power Plant caused a massive release of radioactive materials to the environment. A prompt and reliable system for evaluating the biological impacts of this accident on animals has not been available. Here we show that the accident caused

physiological and genetic damage to the pale grass blue Zizeeria maha, a common lycaenid butterfly in Japan. We collected the first voltine adults in the Fukushima area in May 2011, some of which showed relatively mild abnormalities. The F1 offspring from the first voltine females showed more severe abnormalities, which were inherited by the F2 generation. Adult butterflies collected in September 2011 showed more severe abnormalities than those collected in May. Similar abnormalities were experimentally reproduced in individuals from a non contaminated area by external and internal low dose exposures. We conclude that artificial radionuclides from the Fukushima Nuclear Power Plant caused physiological and genetic damage to this species.

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Chiyo Nohara is a member of a team from the BCPH Unit of Molecular Physiology, Department of Chemistry, Biology and Marine Science, Faculty of Science at the University of the Ryukus in Okinawa (Japan) which has evaluated the effects of the Fukushima nuclear accident on the pale grass blue butterfly Zizeeria maha, the most common butterfly in Japan.
Their findings imply transgenerational accumulation of genetic damage. Before moving to Okinawa Ms Nohara was lecturer on government auditing and later associate professor in business administration at Aichi Toho University, 1993-2005; associate professor in business administration at Aichi University, 2005-2009; former member of the Evaluation Committee for Incorporated Administrative Agencies at the Ministry of Land, Infrastructure, Transport and Tourism; former member of the Public Sector Evaluation Committee of Nagoya city, Tokai city and Mie prefecture.Mie.