Experimentations at post accidental levels of 137Cs in rats

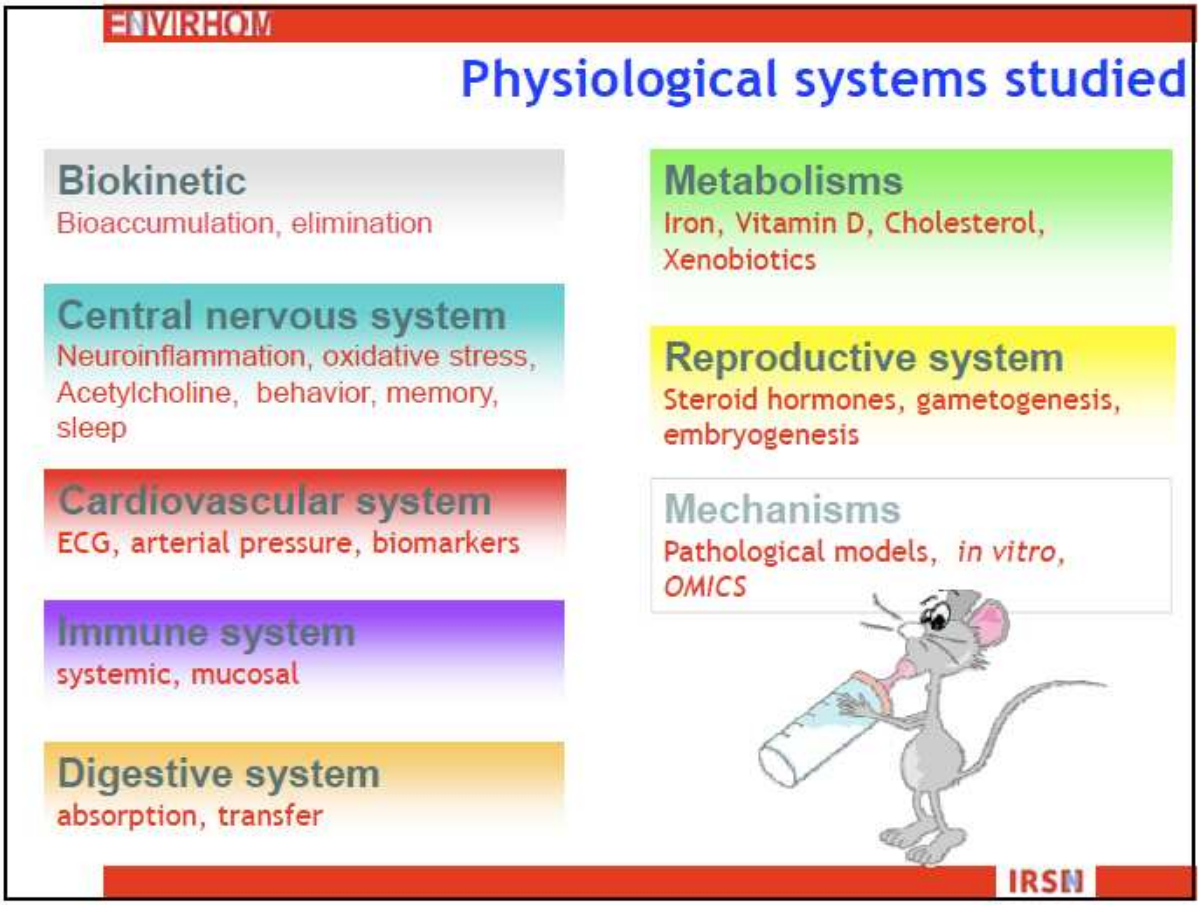

Table 1. Levels of radionuclides, after contamination with U (40 mg·L^{-1}) or ^{137}Cs (6500 Bq·L^{-1}) over a 1-month period, in the carcass, kidneys, thalamus, and cerebellum.

	Remaining carcass*	Kidneys	Thalamus	Cerebellum
U group (µg·g of tissue^{-1})	0.14±0.13	0.10±0.02	0.062±0.048	0.022±0.020
^{137}Cs group (Bq·g of tissue^{-1})	4.65±0.34	—	—	—

Note: Data are expressed as means ± SD (n = 5 for each group of rats).
*Remaining carcass = whole body – (kidneys + brain) for U-contaminated rats. Remaining carcass = whole body – brain for Cs-contaminated rats.

Chronic contamination of rats with 137 cesium radionuclide: impact on the cardiovascular system.

(Gueguen *et al.*, 2008)

Abstract

Cardiovascular system impairment has been observed in children and in liquidators exposed to the Chernobyl nuclear power plant accident. No experimental studies of animals have

analyzed whether these disorders might be attributed to chronic ingestion of low levels of cesium 137 ((137)Cs). Biochemical, physiological, and molecular markers of the cardiovascular system were analyzed in rats exposed through drinking water to (137)Cs at a dose of 500 Bq kg(-1) (6500 Bq l(-1)). Plasma concentrations of CK and CK-MB were higher (+52%, $P < 0.05$) in contaminated rats. No histological alteration of the heart was observed, but gene expression was modified in the atria. Specifically, levels of ACE (angiotensin converting enzyme) and BNP (brain natriuretic peptide) gene expression increased significantly ($P < 0.05$). ECG analysis did not disclose any arrhythmia except ST- and RT-segment shortening (-9% and -11%, respectively, $P < 0.05$) in rats exposed to (137)Cs. Mean blood pressure decreased (-10%, $P < 0.05$), and its circadian rhythm disappeared. Overall, chronic contamination by an extreme environmental dose of (137)Cs for 3 months did not result in cardiac morphological changes, but the cardiovascular system impairments we observed could develop into more significant changes in sensitive animals or after longer contamination.

Effects of chronic 137Cs ingestion on barrier properties of jejunal epithelium in rats.

(Dublineau *et al.*, 2007)

Abstract

Environmental contamination by 137Cs is of particular public health interest because of the various sources of fallout originating from nuclear weapons, radiological source disruptions, and the Chernobyl disaster. This dispersion may lead to a chronic ecosystem contamination and subsequent ingestion of contaminated foodstuffs. The aim of this study was to thus determine the impact of a chronic ingestion of low-dose 137Cs on small intestine functions in rats. The animals received 150 Bq per day in drinking water over 3 mo. At these environmental doses, 137Cs contamination did not modify the crypt and villus architecture. In addition, epithelial integrity was maintained following the chronic ingestion of 137Cs, as demonstrated by histological analyses (no breakdown of the surface mucosa) and electrical transepithelial parameters (no change in potential difference and tissue conductance). Furthermore, cesium contamination seemed to induce contradictory effects on the apoptosis pathway, with an increase in the gene expression of Fas/FasL and a decrease in the apoptotic cell number present in intestinal mucosa. No marked inflammation was observed following chronic ingestion of 137Cs, as indicated by neutrophil infiltration and gene expression of cytokines and chemokines. Results indicated no imbalance in the Th1/Th2 response induced by cesium at low doses. Finally, evaluation of the functionality of the jejunal epithelium in rats contaminated chronically with 137Cs did not demonstrate changes in the maximal response to carbachol, nor in the cholinergic sensitivity of rat jejunal epithelium. In conclusion, this study shows that chronic ingestion of 137Cs over 3 mo at postaccidental doses exerts few biological effects on the epithelium of rat jejunum with regard to morphology, inflammation status, apoptosis/proliferation processes, and secretory functions.

Distribution of 137Cs in rat tissues after various schedules of chronic ingestion.

(Tourlonias *et al.*, 2010)

Abstract

The aim of this work was to compare the distribution of 137Cs in organisms after chronic ingestion following different schedules. Rats were contaminated through drinking water containing 6,500 Bq L(-1) of 137Cs, starting either at birth, at weaning, or upon reaching adult age (13 wk). Animals were then sacrificed after different durations of ingestion. 137Cs content of organs and excreta were determined by gamma counting. A slight decrease in 137Cs elimination through urine was observed according to the age of animals. All organs tested showed similar 137Cs content, with the exception of striated muscles and the thyroid at certain ages, which showed the highest accumulation of 137Cs. The lowest 137Cs concentration was found in the blood, which acts as a transfer compartment after absorption in the intestine. Substructures of the central nervous system showed a homogeneous level of 137Cs accumulation, except for the olfactive bulbs. In these structures, an increased concentration of 137Cs was observed, suggesting a possible direct route of intake through the nasal epithelium. Overall, these results are in agreement with current models for the biokinetics of 137Cs. However, these results also suggest that the thyroid should be taken into account in future models of 137Cs biokinetics.

Vitamin D metabolism impairment in the rat's offspring following maternal exposure to 137cesium.

(Tissandie *et al.*, 2009)

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Abstract

Previous works clearly showed that chronic contamination by 137cesium alters vitamin D metabolism. Since children are known to be a high-risk group for vitamin D metabolism disorders, effects of 137Cs on vitamin D biosynthetic pathway were investigated in newborn rats. The experiments were performed in 21-day-old male offspring of dams exposed to 137Cs in their drinking water at a dose of 6,500 Bq/l (150 Bq/rat/day) during the lactation period. Significant modifications of blood calcium (-7%, $P < 0.05$), phosphate (+80%, $P < 0.01$) and osteocalcin (-25%, $P < 0.05$) levels were observed in contaminated offspring, associated with an increase of blood vitamin D3 (+25%, $P < 0.01$). Besides, decreased expression levels of cyp2r1 and cyp27b1 (-26 and -39%, respectively, $P < 0.01$) were measured in liver and kidney suggesting a physiological adaptation in response to the rise in vitamin D level. Expressions of vdr, ecac1, cabp-d28k, ecac2 and cabp-9k involved in renal and intestinal calcium transport were unaffected. Altogether, these data show that early exposure to post-accidental doses of 137Cs induces the alteration of vitamin D metabolism, associated with a dysregulation of mineral homeostasis.

Chronic contamination with 137cesium in rat: effect on liver cholesterol metabolism.

(Souidi *et al.*, 2006)

Abstract

After the Chernobyl nuclear accident, epidemiological studies on human populations living in 137Cs-contaminated areas revealed the increase frequencies of thyroid cancer and evoked the apparition of cardiovascular diseases, hormonal effect, liver alteration, and lipid disorder. Actually, it raises a problem of public safety for the populations living on these territories that are exposed to low levels of 137Cs during a long period through food. Then it is necessary to study potential effect of this chronic contamination. To mimic this situation, the authors investigate the potential biological effects of chronic exposure to 137Cs at a postaccidental dose (150 Bq/rat/day) on hepatic metabolism of cholesterol in rat. Plasma lipid level, gene expression and activity were analyzed. It was observed that in 137Cs-exposed rats, gene expression of low-density lipoprotein receptor (LDLr), apolipoprotein B (apoB), and liver X receptor alpha (LXRalpha) are increased (95%, $p < .05$; 34%, $p < .05$; 20%, $p < 0.05$, respectively), whereas transporter adenosine triphosphate-binding cassette transporter G5 (ABCG5) is decreased (42%, $p < .05$). In addition, cytochrome P450 27A1 (CYP27A1) activity is increased (34%, $p < .05$) in contaminated rat liver. In conclusion, the results suggest that 137Cs contamination at low-level induces molecular modifications of the liver cholesterol metabolism without leading to a dysregulation of its homeostasis. These results suggest that chronic long term exposure at low-level of 137Cs may evolve to lipid disorder.

Chronic contamination with 137Cesium affects Vitamin D3 metabolism in rats.

(Tissandie *et al.*, 2006)

Abstract

Twenty years after Chernobyl disaster, many people are still chronically exposed to low dose of (137)Cs, mainly through the food consumption. A large variety of diseases have been described in highly exposed people with (137)Cs, which include bone disorders. The aim of this work was to investigate the biological effects of a chronic exposure to (137)Cs on Vitamin D(3) metabolism, a hormone essential in bone homeostasis. Rats were exposed to (137)Cs in their drinking water for 3 months at a dose of 6500 Bq/l (approximately 150 Bq/rat/day), a similar concentration ingested by the population living in contaminated territories in the former USSR countries. Cytochromes P450 enzymes involved in Vitamin D(3) metabolism, related nuclear receptors and Vitamin D(3) target genes were assessed by real time PCR in liver, kidney and brain. Vitamin D, PTH, calcium and phosphate levels were measured in plasma. An increase in the expression level of cyp2r1 (40%, $p<0.05$) was observed in the liver of (137)Cs-exposed rats. However a significant decrease of Vitamin D (1,25(OH)D(3)) plasma level (53%, $p=0.02$) was observed. In brain, cyp2r1 mRNA level was decreased by 20% ($p<0.05$), while the expression level of cyp27b1 is increased (35%, $p<0.05$) after (137)Cs contamination. In conclusion, this study showed for the first time that chronic exposure with post-accidental doses of (137)Cs affects Vitamin D(3) active form level and induces molecular modifications of CYPs enzymes involved its metabolism in liver and brain, without leading to mineral homeostasis disorders.

Effect of U and 137Cs chronic contamination on dopamine and serotonin metabolism in the central nervous system of the rat.

(Houpert *et al.*, 2004)

Abstract

Following the Chernobyl accident, the most significant problem for the population of the former Soviet Union for the next 50-70 years will be chronic internal contamination by radionuclides. One of the few experiments carried out in this field reported that neurotransmitter metabolism in the central nervous system of the rat was disturbed after feeding with oats contaminated by 137Cs for 1 month. The present study assessed the effect of chronic contamination by depleted U or 137Cs on the metabolism of two neurotransmitters in cerebral areas of rats. Dopamine and serotonin were chosen because their metabolism has been shown to be disturbed after external irradiation, even at moderate doses. Dopamine, serotonin, and some of their catabolites were measured by high-pressure liquid chromatography coupled with an electrochemical detector in five cerebral structures of rats contaminated over a 1-month period by drinking water (40 mg U.L -1 or 6500 Bq 137Cs.L -1). In the striatum, hippocampus, cerebral cortex, thalamus, and cerebellum, the dopamine, serotonin, and catabolite levels were not significantly different between the control rats and rats contaminated by U or 137Cs. These results are not in accordance with those previously described.

Evaluation of the effect of chronic exposure to 137Cesium on sleep-wake cycle in rats.

(Lestaevel *et al.*, 2006)

Abstract

Since the Chernobyl accident, the most significant problem for the population living in the contaminated areas is chronic exposure by ingestion of radionuclides, notably (137)Cs, a radioactive isotope of cesium. It can be found in the whole body, including the central nervous system. The present study aimed to assess the effect of (137)Cs on the central nervous system and notably on open-field activity and the electroencephalographic pattern. Rats were exposed up to 90 days to drinking water contaminated with (137)Cs at a dosage of 400 Bq kg(-1), which is similar to that ingested by the population living in contaminated territories. At this level of exposure, no significant effect was observed on open-field activity. On the other hand, at 30 days exposure, (137)Cs decreased the number of episodes of wakefulness and slow wave sleep and increased the mean duration of these stages. At 90 days exposure, the power of 0.5-4 Hz band of (137)Cs-exposed rats was increased in comparison with controls. These electrophysiological changes may be due to a regional (137)Cs accumulation in the brain stem. In conclusion, the neurocognitive effects of (137)Cs need further evaluation and central disorders of population living in contaminated territories must be considered.

Molecular modifications of cholesterol metabolism in the liver and the brain after chronic contamination with cesium 137.

(Racine *et al.*, 2009)

Abstract

Twenty years after Chernobyl accident, the daily ingestion of foodstuff grown on contaminated grounds remains the main source for internal exposure to ionizing radiations, and primarily to cesium 137 ((137)Cs). Though the effects of a long-term internal contamination with radionuclides are poorly documented, several non-cancerous pathologies have been described in this population. However, lipid metabolism was never investigated after chronic internal contamination although disturbances were observed in externally-exposed people. In this regard, we assessed the effects of a chronic ingestion of (137)Cs on hepatic and cerebral cholesterol metabolism. To mimic a chronically-exposed population, rats were given (137)Cs-supplemented water at a post-accidental dose (150 Bq/rat/day) during 9 months. The plasma profile, and brain and liver cholesterol concentrations were unchanged. A decrease of ACAT 2, Apo E, and LXR<alpha>mRNA levels was recorded in the liver. In the brain, a decrease of CYP27A1 and ACAT 1 gene expression was observed. These results clearly show that cholesterol metabolism is not disrupted by a chronic ingestion of (137)Cs, although several molecular alterations are observed. This work would be interestingly completed by studying the influence of (137)Cs in models likely more sensitive to contaminants, such as the fetus or individuals susceptible to a lipidic disease.

Hepatic cholesterol metabolism following a chronic ingestion of cesium-137 starting at fetal stage in rats.

(Racine *et al.*, 2010)

Abstract

The Chernobyl accident released many radionuclides in the environment. Some are still contaminating the ground and thus the people through dietary intake. The long-term sanitary consequences of this disaster are still unclear and several biological systems remain to be investigated. Cholesterol metabolism is of particular interest, with regard to the link established between atherosclerosis and exposure to high-dose ionizing radiations. This study assesses the effect of cesium-137 on cholesterol metabolism in rats, after a chronic exposure since fetal life. To achieve this, rat dams were contaminated with cesium-137-supplemented water from two weeks before mating until the weaning of the pups. Thereafter, the weaned rats were given direct access to the contaminated drinking water until the age of 9 months. After the sacrifice, cholesterol metabolism was investigated in the liver at gene expression and protein level. The cholesterolemia was preserved, as well as the cholesterol concentration in the liver. At molecular level, the gene expressions of ACAT 2 (a cholesterol storage enzyme), of Apolipoprotein A-I and of RXR (a nuclear receptor involved in cholesterol metabolism) were significantly decreased. In addition, the enzymatic activity of CYP27A1, which catabolizes cholesterol, was increased. The results indicate that the rats seem to adapt

to the cesium-137 contamination and display modifications of hepatic cholesterol metabolism only at molecular level and within physiological range.

In vivo effects of chronic contamination with 137 cesium on testicular and adrenal steroidogenesis.

(Grignard *et al.*, 2008)

Abstract

More than 20 years after Chernobyl nuclear power plant explosion, radionuclides are still mainly bound to the organic soil layers. The radiation exposure is dominated by the external exposure to gamma-radiation following the decay of (137)Cs and by soil-to-plant-to-human transfer of (137)Cs into the food chain. Because of this persistence of contamination with (137)Cs, questions regarding public health for people living in contaminated areas were raised. We investigated the biological effects of chronic exposure to (137)Cs on testicular and adrenal steroidogenesis metabolisms in rat. Animals were exposed to radionuclide in their drinking water for 9 months at a dose of 6,500 Bq/l (610 Bq/kg/day). Cesium contamination decreases the level of circulating 17beta-estradiol, and increases corticosterone level. In testis, several nuclear receptors messenger expression is disrupted; levels of mRNA encoding Liver X receptor alpha (LXRalpha) and LXRbeta are increased, whereas farnesoid X receptor mRNA presents a lower level. Adrenal metabolism presents a paradoxical decrease in cyp11a1 gene expression. In conclusion, our results show for the first time molecular and hormonal modifications in testicular and adrenal steroidogenic metabolism, induced by chronic contamination with low doses of (137)Cs.

Comparison of the effects of enriched uranium and 137-cesium on the behaviour of rats after chronic exposure.

(Houpert *et al.*, 2007)

Abstract

PURPOSE: A radionuclide that accumulates in the central nervous system is likely to exert both a chemical and a radiological effect. The present study aimed at assessing the behavioral effect of two radionuclides previously shown to accumulate in the central nervous system after chronic exposure--uranium and cesium.
MATERIALS AND METHODS: Rats were exposed for 9 months to drinking water contaminated with either enriched uranium at a dosage of 40 mg U x l(-1) or 137-cesium at a dosage of 6500 Bq x l(-1), which correspond to the highest concentrations measured in some wells in the south of Finland (uranium) or in the milk in Belarus in the year following the Chernobyl accident (137-cesium).
RESULTS: At this level of exposure, 137-cesium had no effect on the locomotor activity measured in an open-field, on immobility time in a forced swimming test, on spontaneous alternation in a Y-maze and on novel object exploration in an object recognition test. Enriched uranium exposure specifically reduced the spontaneous alternation measured in the Y-maze after 3 and 9 months exposure although it did not affect the other parameters.

CONCLUSION: Enriched uranium exposure altered the spatial working memory capacities and this effect was correlated with previously described accumulation of uranium in the hippocampus which is one of the cerebral areas involved in this memory system.

Comparison of Prussian blue and apple-pectin efficacy on ^{137}Cs decorporation in rats

(Le *et al.*, 2006)

Abstract

Cesium-137 (^{137}Cs) is one of the most important nuclear fission elements that contaminated the environment after the explosion of the Chernobyl nuclear power plant in Ukraine (1986). The aim of the study was to compare the efficacy of two chelating agent, Prussian blue and apple-pectin on ^{137}cesium decorporation in rats. Rats were intravenously injected with a solution of ^{137}cesium (5 kBq per rat). Chelating agents, Prussian blue or apple-pectin were given immediately after Cs contamination and during 11 days by addition of each chelating agent in drinking water at a concentration corresponding to 400 mg kg^{-1} day^{-1}. Efficiency was evaluated 11 days after contamination (at the end of treatment) through their ability to promote Cs excretion and to reduce the radionuclide accumulation in some retention compartments (blood, liver, kidneys, spleen, skeleton and in the remaining carcass). In these conditions after treatment with Prussian blue a fivefold increase in fecal excretion of Cs was observed and was associated with a reduction in the radionuclide retention in the main organs measured. In contrast, no significant differences were observed between untreated rats and rats treated with apple-pectin. These observations were discussed in terms of ability of pectins to bind Cs and compared to recently published results obtained after treatment of Cs-contaminated children with this chelate.

Microsatellite mutations in the offspring of irradiated parents 19 years after the Cesium-137 accident.

(da Cruz *et al.*, 2008)

Abstract

In September of 1987, a radiotherapy unit containing 50.9 TBq of Cs(137)Cl was removed from an abandoned radiotherapy clinic. This unit was subsequently disassembled leading to the most serious radiological accident yet to occur in the Western hemisphere. This event provides an opportunity to assess the genetic effects of ionizing radiation. We surveyed genetic variation of 12 microsatellite loci in 10 families of exposed individuals and their offspring and also in non-exposed families from the same area of Goias state. We found an increase in the number of new alleles in the offspring of the exposed individuals. The mutation rate was found to be higher in the exposed families compared to the control group. These results indicated that exposure to ionizing radiation can be detected in offspring of exposed individuals and also suggest that the elevated microsatellite mutation rate can be attributed to radioactive exposure.

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