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Is exposure to ionising radiation associated with childhood cardiac arrhythmia in the Russian territories contaminated by the Chernobyl fallout? A cross-sectional population-based study

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ABSTRACT

Objective To investigate childhood cardiac arrhythmia and chronic exposure to caesium-137 (^{137}Cs) resulting from the Chernobyl accident.

Design Prospective cross-sectional study using exposed/unexposed design conducted in the Bryansk region from May 2009 to May 2013 on children selected on the basis of ^{137}Cs soil deposition: control territories ([^{137}Cs]<37 kBq per square metre, where children were considered as unexposed) and contaminated territories ([^{137}Cs]>555 kBq per square metre, where children were considered as exposed).

Setting Russian territories affected by the Chernobyl fallout (Bryansk region).

Participants This cross-sectional study included 18 152 children aged 2–18 years and living in the Bryansk region (Russia).

Main outcome measures All children received three medical examinations (ECG, echocardiography and ^{137}Cs whole-body activity measurement) and some of them were given with a 24-hour Holter monitoring and blood tests.

Results Cardiac arrhythmia was diagnosed in 1172 children living in contaminated territories and 1354 children living in control territories. The crude prevalence estimated to 13.3% in contaminated territories was significantly lower than in control territories with 15.2% over the period 2009–2013 (P<0.001). Considering ^{137}Cs whole-body burden as exposure, cardiac arrhythmia was found in 449 contaminated children and 2077 uncontaminated children, corresponding to an estimated crude prevalence of 14.5% and 14.2%, respectively, which does not differ significantly (P=0.74). Also, we investigated the association between territory, exposure to ^{137}Cs and cardiac arrhythmia: the adjusted OR was not significant (0.90 with 95% CI 0.81 to 1.00; P=0.06) for the territory. For ^{137}Cs whole-body burden, the ORs close to 1 did not reach statistical significance (P for trend=0.97).

Conclusion This study does not observe an association between cardiac arrhythmia and ^{137}Cs deposition levels in the Bryansk region exposed to Chernobyl fallout. The suspected increase of cardiac arrhythmia in children exposed to Chernobyl fallout is not confirmed.

Strengths and limitations of this study

- ► This study includes a large number of participants and a nice participation rate (91%). There is very little missing data (<1%).
- ► Conditions were met to show an effect if it would exist: the minimal detectable OR was estimated to be 1.2.
- ► Comprehensive information on potential previous homes of children included in the study was not available. In particular, we do not know if they were born in a contaminated territory or not.
- ► Some factors that may play a role in the occurrence of a cardiac arrhythmia have not been considered, such as hypertension, genetic factors and consumption of tobacco, alcohol or drugs.
- ► ECGs and echocardiography examinations were performed only once on each child.

INTRODUCTION

On 26 April 1986, the worst industrial accident that released worldwide man-made environmental ionising radiation occurred at the Reactor Number 4 of the Chernobyl nuclear power plant in the former Soviet Union. The radioactive fallout that spread mainly over northern Ukraine, southwestern Russia and Belarus as a result of the tragedy reached a total of about 13.10^{18} Becquerel (Bq). It heavily exposed a large population of about 5 million individuals at the time of the accident, including around 1.2 million children and adolescents, to a mixture of

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radionuclides among which iodine-131 and caesium-137 (^{137}Cs) are the most significant for the dose received by the affected people.[1 2] Apart from Chernobyl cohorts, the health effects of acute and protracted exposures to environmental radiation as a result of a nuclear event have been and are being widely studied, mainly in the Japanese survivors of the Hiroshima and Nagasaki bombings, and since March 2011 in the population exposed to the releases from the Fukushima Dai-chi nuclear power plant. Depending on the type of radiation exposure, dose rate and study population, short-term and long-term health risks of nuclear power plant accidents may include acute radiation syndrome, elevated rate of leukaemia and solid cancers, cataracts, circulatory diseases and increase in childhood thyroid cancers.[1–10] Besides these widely recognised radiation-induced pathologies, some authors claimed that exposed children may also exhibit various symptoms including chronic gastrointestinal pathology, gallbladder inflammation, chronic periodontitis, asthenia, apathy, tonsil hypertrophy, recurrent respiratory infections, endocrine disorders and cardiovascular symptoms, such as unstable blood pressure, sinus arrhythmia, repolarisation and conduction abnormalities.[11–14] However, these observations are still questionable as they are not based on significant statistical evidence and the causal link with an exposure to ionising radiation has not been demonstrated so far. Because the related publications have led to a recurrent debate and in the absence of well-designed studies, the Institut de Radioprotection et de Sûreté Nucléaire decided in 2005, together with the Russian Bryansk Diagnostic Center, to launch a research programme named 'EPICE' (acronym for 'Evaluation of Pathologies potentially Induced by CaEsium') aiming to explore the non-cancer effects exhibited in children living in Russian territories contaminated by the Chernobyl fallout versus control territories. This article presents the design and results of the first study that has been carried out in a group of about 18 000 Russian children to determine whether they suffer from cardiac arrhythmia and, if so, to confirm or refute the possible association with a chronic exposure to ^{137}Cs, the major radionuclide to which the local population is still being exposed significantly more than 30 years after the Chernobyl catastrophe.

METHODS

Study design

This cross-sectional study using exposed/unexposed design was approved and validated by the Ethics Committee of the Russia's National Hematology Center in Moscow. It was conducted in the region of Bryansk from May 2009 to May 2013 on children aged 2–18 years. This study primarily intended to compare populations living in the least contaminated territories with those living in the most heavily contaminated territories. Children were selected on the basis of ^{137}Cs soil deposition: according to two international entities, contaminated areas are defined *as those with ^{137}Cs deposition levels >37 kBq per square metre*.[15 16] Therefore, we have considered in our study control territories as territories with [^{137}Cs]<1 Ci (Curie) per square kilometre or 37 kBq per square metre (where children were considered as unexposed) and, contaminated territories as territories with [^{137}Cs]>15 Ci per square kilometre or 555 kBq per square metre (where children were considered as exposed). The flow chart presented in figure 1 illustrates the inclusion of the subjects.

With regards to the control territories, the nine *raions* (a *raion* is a type of administrative unit of several post-Soviet states; the Bryansk region named 'Bryansk *oblast*' is divided into 27 *raions*) totally unpolluted with ^{137}Cs were selected. Four were excluded due to the presence of polluting chemical plants and substantial differences especially related to diet. To reach the targeted number of participants, a sixth *raion* was selected randomly among 14 *raions* comprising control territories and territories with ^{137}Cs soil deposition between 37 and 75 kBq per square metre. Children of this sixth *raion* came from unpolluted areas. Therefore, six *raions* (Zhukovsky, Kletnjansky, Dubrovsky, Rognedinsky, Zhiryatinsky and Bryansky) were found to be eligible for inclusion in the study. As of contaminated territories, the five *raions* were selected except one because of substantial population relocations (Novozybkovsky, Gordeevsky, Zlynkovsky and Krasnogorsky). Among eligible children 1794 did not accept to be surveyed because of various specific reasons (religious grounds, sport competition, fear of not being accepted in sport clubs or military institutions, refusal to undress, recent similar medical examination and ongoing medical care). Finally, out of 18 152 children examined, 455 children were excluded from the analysis because either they were suffering from a disease other than cardiac arrhythmia or from another disease leading to cardiac arrhythmia. Thus, the study included a total of 17 697 children.

Procedures

Data were collected by a Russian health professional team (interviewers, ultrasound practitioners, nurses, cardiologists and dosimetrists) who were on the field to meet children at schools where medical examinations were conducted. An informed consent was obtained from children or their parents. The participation in this study consisted first in completing a questionnaire and then undergoing several medical explorations.

Questionnaire

Each study participant was assigned with a personal number notified in an administrative and medical questionnaire bringing together all necessary information (administrative, demographic and anthropometric data; anamnesis targeted on cardiovascular area; results of whole-body ^{137}Cs activity, ECG, echocardiography and, when performed, a 24-hour Holter monitoring and blood tests; and conclusions of the cardiologist).

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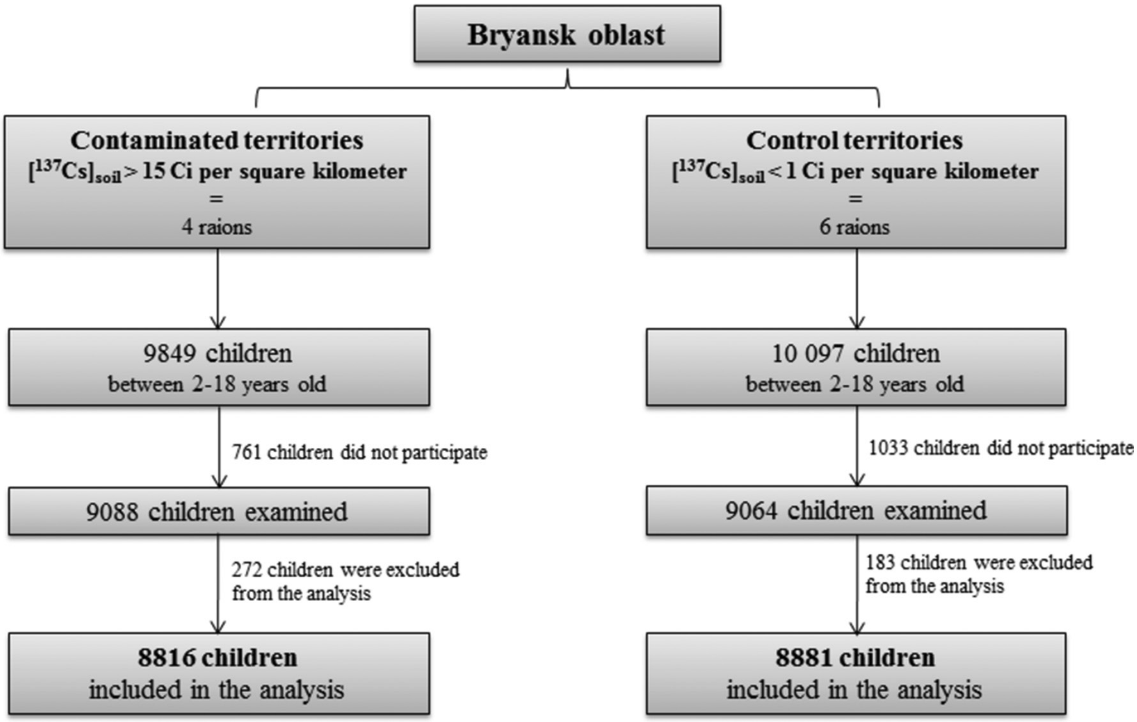

Figure 1 Flow chart of inclusion criteria. ^{137}Cs, 137-caesium.

Medical examination

After assessing their weight and height, all children were subjected to a direct measurement of whole-body ^{137}Cs activity performed with a radiometer-spectrometer RSU-01 'Signal-M'. The ^{137}Cs background activity was systematically assessed and subtracted from activity measured in children. The detection limit (DL) was evaluated to be around 1200 Bq for a 10 min counting time depending essentially on the background activity. Then, children underwent an ECG. The recorder was the CardioSoft V.6.5 resting ECG (GE Medical Systems Information Technologies). ECG was performed at rest for about 10 min and tracings were available for all children in the database. An echocardiography was also carried out using an ultrasound diagnostic scanner MyLab 30 CV (ESAOTE) with a phased array probe. For each echocardiography performed, among collected data we investigated more closely the following parameters: left ventricular diameter at end-systole, left ventricular diameter at end-diastole, left ventricle ejection fraction, left ventricular posterior wall thickness at end-diastole, left ventricle velocity, interventricular septum thickness at end-diastole, right ventricular diameter at end-diastole, mitral inflow velocity, left atrial diameter, aortic diameter, tricuspid peak velocity, trunk diameter of the pulmonary artery and pulmonary artery velocity; a later publication is being prepared to further explore these data. Only ultrasound images of pathological cases have been recorded into the database. For some randomly selected children, a 24-hour Holter monitoring was recorded with a CardioDay (Getemed Medizin). Blood tests to assess enzymatic (transaminases, Alkaline phosphatase (ALP), Lactate dehydrogenase (LDH), Gamma-glutamyltransferase (GGT), Creatine kinase (CK)), biochemical (Sodium (Na), Potassium (K), Calcium (Ca), Phosphorus (P), albumin), inflammatory (C-reactive protein (CRP)), renal (urea, creatinine), thyroid (Thyroid-stimulating hormone (TSH), Free thyroxine (FT4)) and cardiac (troponin T, Creatine kinase-MB (CK-MB)) profiles were performed. For blood assays, biologists employed a 9180 electrolyte analyser (Roche Diagnostics), an automated Enzyme immuno-assay (EIA) and chemistry analyser ChemWell (Awareness Technology), a biochemical analyser SYNCHRON CX4-CE (Beckman Coulter), a LIANA luminometer (Immunotech S.A.S.) and the Roche TROP T sensitive rapid assay.

Medical diagnosis of cardiac arrhythmia

The diagnoses of cardiac arrhythmia (including cardiac conduction and cardiac rhythm disorders)[17] have been registered according to WHO's International Classification of Diseases Tenth Revision (2010).[18] Pathologies/syndromes identified in the course of the study belong to the following categories: atrioventricular and left bundle-branch block (I44.0; I44.1; I44.2; I44.4; I44.5); other conduction disorders (I45.0; I45.1; I45.2; I45.4; I45.5; I45.6; I45.8); paroxysmal tachycardia (I47.1); other cardiac arrhythmias (I49.1; I49.3; I49.4; I49.5; I49.8); and abnormalities of heart beat (R00.0; R00.1).

Statistical analyses

The characteristics of the study population were described by number (percentages) for categorical variables and by mean (min–max) and median for continuous variable ('caesium burden': ^{137}Cs whole-body burden). Age at diagnosis was categorised into tertiles based on the

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distribution among healthy children (<10, 10–13, ≥14 years). Body mass index (BMI) was calculated as weight (kg) divided by squared height (m) and was categorised according to age and sex as recommended by WHO (underweight, normal weight, overweight, obesity).[19] As of ionising radiation exposure variables, two were considered: 'territory' (control, contaminated); 'caesium burden', which was categorised into quartiles based on the distribution among healthy children with a positive whole-body contamination (not detectable;]DL–35[; [35-50[; [50-70[;≥70 Bq/kg). The associations between territory or caesium burden and cardiac arrhythmia risk were analysed using a non-conditional logistic regression.[20] In multivariate analysis, all ORs with 95% CIs were adjusted for variables having a P value<0.25 on univariate analysis. Tests for interaction were performed to assess whether territory or caesium burden association with the presence of cardiac arrhythmia risk were modified by parameters such as BMI, drug intake with cardiac arrhythmia as side effects, caesium burden or territory. A generalised linear model was used to determine the contribution of each variable to the caesium burden.

Sensitivity analysis on children with cardiac arrhythmia who underwent blood test was conducted using χ^2 test. Other sensitivity analyses were undertaken on children with cardiac conduction disorders only, children with cardiac rhythm disorders only or all children diagnosed with also sinus arrhythmia. Statistical tests were two-sided and P values<0.05 were considered statistically significant. Tests for trend were performed by considering categorical variables as continuous variables using the Wald χ^2 statistic. All data were analysed with the use of SAS software V.9.2 (SAS Institute).

Patient involvement

No patients were involved in setting the research question or the outcome measures, nor they were involved in developing plans for design or implementation of the study. No patients were asked to advise on interpretation or writing up of results. The authors plan to disseminate the results of the research to study participants through public meetings as soon as the article is published.

RESULTS

The study included 8816 exposed and 8881 unexposed children. Table 1 shows all characteristics of participants.

Males and females were almost equally represented, and distribution of children by age category was quite similar. All children underwent three medical examinations (ECG, echocardiography and ^{137}Cs whole-body activity measurement) and a 24-hour Holter monitoring was performed in 15.6% and 27.2% of exposed and unexposed children, respectively. It is understood that for children who were given both an ECG and a 24-hour Holter monitoring the final diagnosis has considered systematically the results of the Holter as a more sensitive examination compared with the ECG. Thereby, cardiac arrhythmia was diagnosed in 1172 exposed and 1354 unexposed children. The crude prevalence estimated to be 13.3% in contaminated territories was significantly lower than in control territories with 15.2% over the period 2009–2013 (P<0.001). The prevalence ratio was 0.87 (95% CI 0.84 to 0.90). Considering caesium burden as exposure (data not shown), cardiac arrhythmia was found in 449 contaminated children and 2077 uncontaminated children, corresponding to an estimated crude prevalence of 14.5% and 14.2%, respectively, which does not differ significantly (P=0.74) and resulting in a prevalence ratio of 1.02 (95% CI 0.97 to 1.07).

The distribution of caesium burden was described by a log-normal shape; 21.4% of children living in contaminated territories had a detectable ^{137}Cs whole-body contamination compared with 13.6% of children living in control territories (table 1). The distribution of children living in contaminated territories rose with increasing ^{137}Cs whole-body contamination in contrast with children living in control territories for whom the trend was reversed. Indeed, 4.5% and 4.8% of those children had a ^{137}Cs whole-body contamination <35 Bq/kg, while with ^{137}Cs whole-body contamination exceeding 70 Bq/kg the gap was widening (7.1% and 2.1%, respectively). The calculation of the committed effective dose in the 3105 children with a detectable caesium burden showed that only 24 patients were >1 mSv (with a maximum dose of 5.77 mSv per year).

As of their lifestyle, characteristics were similar in both exposed and unexposed children: nearly two-thirds of children lived in urban area and dietary habits seemed to be similar except for consumption of forest products (mushrooms, berries, meat), which decreased in exposed children (62.2%) compared with unexposed children (80.7%). In both territories, the distribution of children according to BMI categories was balanced. The number of children with a high BMI (overweight and obesity combined) represented 23.5% and 23.9% in contaminated and control areas, respectively. When the participants were questioned about drug intake, it happens that a limited number of children took drugs, 1.2% and 2.9% in the contaminated and control territories, respectively. Among the identified drugs, more than three-quarters were vasoconstrictors, antibiotics, antihistaminics and bronchodilators.

In univariate analysis, the risk of cardiac arrhythmia was significantly decreased with sex, drug intake, BMI and territory variables (table 2). However, children >14 years had a 2.3-fold increase of cardiac arrhythmia risk compared with younger children (<10 years). For caesium burden, children with contamination <35 Bq/kg presented a significant higher risk of cardiac arrhythmia than children with no detectable contamination (OR 1.37; 95% CI 1.15 to 1.65).

The adjusted OR was no longer significant (0.90 with 95% CI 0.81 to 1.00; P=0.06) for the territory. Similarly,

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Table 1 Description of the study population

Characteristics	Contaminated territories (exposed population) n=8816	(%)*	Control territories (unexposed population) n=8881	(%)*
Sex				
Male	4436	(50.3)	4534	(51.1)
Female	4380	(49.7)	4347	(48.9)
Age (years)				
<10	3412	(38.7)	3057	(34.4)
10–13	2598	(29.5)	3109	(35.0)
≥14	2806	(31.8)	2715	(30.6)
Type of medical examination				
ECG Echocardiography Caesium-137 whole-body activity	8816	(100)	8881	(100)
Holter†	1377	(1536)	2418	(27.2)
Health condition				
Healthy	7644	(86.7)	7527	(84.8)
With cardiac arrhythmia (including cardiac conduction disorders)	1172	(13.3)	1354	(15.2)
Drug intake possibly responsible for cardiac arrhythmia				
No	3933	(44.6)	8335	(93.9)
Yes	108	(1.2)	257	(2.9)
Unknown	4775	(54.2)	289	(3.3)
Body mass index (WHO classification)				
Underweight	179	(2.0)	204	(2.3)
Normal weight	6565	(74.5)	6550	(73.8)
Overweight	1219	(13.8)	1218	(13.7)
Obesity	853	(9.7)	909	(10.2)
Place of residence				
Rural area	2833	(32.1)	3165	(35.6)
Urban area	5983	(67.9)	5716	(64.4)
Caesium burden (Bq/kg)				
Not detectable	6925	(78.6)	7667	(86.3)
]DL–35[	394	(4.5)	425	(4.8)
[35–50[	454	(5.1)	349	(3.9)
[50–70[	413	(4.7)	250	(2.8)
70 and more	630	(7.1)	190	(2.1)
Mean‡(min–max)	73.8 (14.3–2137.5)		47.3 (13.2–143.1)	
Median‡	53.8		41.8	
Dietary habits				
Shop (clean food)	8128	(92.2)	7676	(86.4)
Personal farm (milk, meat, vegetables)	6448	(73.1)	6722	(75.7)
Forest (mushrooms, berries, meat)	5486	(62.2)	7171	(80.7)
Local reservoirs, rivers (fish, crayfish)	3862	(43.8)	4237	(47.7)

*The percentages may not sum to 100 because of rounding.
†Data were missing for 37 children.
‡Only among children with detectable caesium burden.

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Table 2 Univariate analysis of associated factors related to cardiac arrhythmia

Associated factors	OR	(95% CI)	P values
Sex			
Male	1	–	
Female	**0.66**	(0.61 to 0.72)	<0.01
Age (years)			
<10	1	–	
10–13	0.97	(0.87 to 1.09)	
≥14	**2.27**	(2.06 to 2.51)	<0.01*
Drug intake possibly responsible for cardiac arrhythmia			
No	1	–	
Yes	0.79	(0.58 to 1.09)	0.16
Unknown	**0.89**	(0.81 to 0.98)	0.02
Body mass index (WHO classification)			
Underweight	1	–	
Normal weight	0.88	(0.67 to 1.15)	
Overweight	**0.71**	(0.53 to 0.95)	
Obesity	**0.62**	(0.45 to 0.84)	<0.01*
Territory			
Control	1	–	
Contaminated	**0.85**	(0.78 to 0.93)	<0.01
Caesium burden (Bq/kg)			
Not detectable	1	–	
]DL–35[	**1.37**	(1.15 to 1.65)	
[35–50[	0.98	(0.80 to 1.20)	
[50–70[	0.89	(0.70 to 1.12)	
70 and more	0.84	(0.68 to 1.04)	0.17*

The ORs indicated in bold are statistically significant.
*P values for trend.

Table 3 Multivariate logistic regression model for associated factors in relation to cardiac arrhythmia

Associated factors	OR*	(95% CI)	P values
Territory			
Control	1	–	
Contaminated	0.90	(0.81 to 1.00)	0.06
Caesium burden (Bq/kg)			
Not detectable	1	–	
]DL–35[	1.07	(0.89 to 1.29)	
[35–50[	1.00	(0.81 to 1.23)	
[50–70[	1.04	(0.82 to 1.31)	
70 and more	0.96	(0.77 to 1.20)	0.97

For caesium burden, adjustment for sex, age, drug intake, body mass index and territory.
*For territory, adjustment for sex, age, drug intake, body mass index and caesium burden.

for caesium burden, the ORs close to 1 did not reach statistical significance (P values for trend=0.97) (table 3).

Thus, there was no evidence of any association between the presence of cardiac arrhythmia and territory or caesium burden.

When we paid attention to the caesium burden, the ranking in the explanation of the variance of this variable was first territory, age (particularly <10 years), ^{137}Cs whole-body activity measurement performed during autumn season and consumption of forest products, by order of importance (results not shown).

Furthermore, associations between the presence of cardiac arrhythmia and territory or caesium burden were not significantly different according to BMI, drug intake and territory or caesium burden (results not shown).

Finally, we investigated the risk of all diagnosed cases with sinus arrhythmia cases (considered as pathological in Russia), cardiac conduction disorders cases only and cardiac rhythm disorders only (table A in online supplementary appendix). All results were similar to those of cardiac arrhythmia cases (table 3) except for the relationship between cardiac conduction disorders and territory for which the OR was statistically significant (0.82; 95% CI 0.69 to 0.99; P=0.04), thereby suggesting that living in a contaminated territory would not increase the risk to develop a cardiac arrhythmia.

Another sensitivity analysis was performed for children with cardiac arrhythmia who had blood tests (n=1079). The results are shown in table B in online supplementary appendix.

Among measured blood parameters were included calcium, potassium, and TSH and FT4 for thyroid function, which are the major biological parameters whose variations are often observed in a context of a cardiac arrhythmia.[21 22] The proportion of children with hypocalcaemia was significantly higher in control territories compared with contaminated territories (P=0.001) and the inverse was observed for children with hyperkalaemia (P=0.004). However, when considering caesium burden as exposure, no significant differences were evidenced (P=0.18 for children with hyperkalaemia and P=0.98 for children with hypocalcaemia) (data not shown). With respect to other biological parameters investigated, the sensitivity analysis did not evidence differences between children living in control territories compared with contaminated territories. Similar observations were made when considering caesium burden as exposure (data not shown).

DISCUSSION

Health consequences of the Chernobyl accident in children internally exposed to ionising radiation

The ways that usually characterise human radiation exposure are total or partial body irradiation, external contamination (radioactive particle skin deposit) and internal contamination (inhalation, ingestion, wound). The latter

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route that implies incorporation inside the body of radioactive material, which is inhaled and/or ingested, is of particular importance when assessing the health consequences for exposed children. Thus, while the scientific community was expecting after the Chernobyl accident an increased incidence in childhood leukaemia as observed in the Hiroshima and Nagasaki survivors, an increase in the frequency of thyroid cancer in children was observed since 1990.[23] This observation was lately confirmed in a number of publications along the decades that followed the accident.[1 2 9 10] The childhood thyroid cancer epidemic is now widely recognised as a major consequence of the Chernobyl accident despite doubts that some experts expressed about the accuracy of diagnosis and because of the short period of latency.[1 2] Indeed, according to the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) 2008 report, 6848 cases of thyroid cancer were reported in the affected territories of Belarus, Ukraine and Russia between 1991 and 2005 in children under age 18 years in 1986.[2] Actually the risk of developing a thyroid cancer after childhood exposure is known since years as described in an updated pooled analysis recently published.[24] However at the time of the Chernobyl accident, radiation-induced thyroid cancer was recognised as a potential consequence of an external irradiation only, delivered mainly in the context of childhood cancer therapies. In the Chernobyl situation, children were exposed mostly because of the ingestion of food and milk contaminated with iodine-131, short-lived radioactive iodines and tellurium. The radioactive iodines were accumulated into the thyroid, which was often deficient in stable iodine, leading thus to the development of thyroid cancer in children, especially in those who were under age 4 years at the time of the accident.

Rationale of this study

To date, thyroid cancer is the only disease undoubtedly attributable to ionising radiation in exposed Chernobyl children. However, arguing that children have been and are still exposed to ^{137}Cs because of the consumption of foodstuffs such as mushrooms and berries locally produced and contaminated as a result of a transfer of radionuclides from the soil, some authors attribute to radiation exposure a number of other illnesses exhibited in children living in contaminated territories, such as various infections, gastric symptoms or cardiovascular diseases, among cardiac arrhythmias that are frequently mentioned.[14] These authors state that such diseases would be caused by a chronic incorporation and heterogeneous accumulation of radioactive caesium inside the body, particularly into the myocardium.[11–14] However, there is no indication of an accumulation into the myocardium in a publication presenting an update of the biokinetic models for radiocaesium and its progeny as these radionuclides are known to be distributed mainly in the skeletal muscles.[25] Because it was not possible to verify the scientific data put forward by these authors, we decided to launch the EPICE programme, recognising that it was not possible for us to address questions that several non-governmental organisations raised about cardiac arrhythmias exhibited in exposed children resulting from a chronic incorporation of ^{137}Cs.

To solve the question about a homogenous versus heterogeneous distribution of caesium into the body, we performed previously to this study some direct measurements of ^{137}Cs activity in a group of 49 Russian children living in the Bryansk contaminated territories and suffering from cardiac arrhythmia, gastric symptoms and lens opacities. This work did not evidence an accumulation of ^{137}Cs in the heart region compared with the neck region (including the thyroid), the abdominal region and skeletal muscles. Therefore, our results supported the hypothesis that ^{137}Cs was homogeneously distributed inside the body of enrolled children (data not shown).

Study design

Cross-sectional studies do not permit the reconstruction of a time sequence between exposure and observed disease. The objective of the present study was to compare the prevalence of a disease between two geographical areas. Indeed, it would have been of added value to consider time trends in the frequency of arrhythmia among children after the Chernobyl accident. However, a cross-sectional design is not suitable for spatiotemporal approaches.

One of the other classical potential biases of this type of study is the lack of control of population migration that is the capacity to know whether people in each area have moved since birth. In our study, comprehensive information on potential previous homes of children was not available. In particular, we do not know if they were born in a contaminated territory or not. However, it should be noted that these populations with limited financial resources were likely not geographically mobile, notably because of financial compensations which represented a strong argument that was very carefully considered by the families when deciding on to move or not to move to an unexposed area.

In our protocol, the control group has been defined as children living in territories with [^{137}Cs]<37 kBq per square metre in the Bryansk oblast. We decided not to consider territories far away from the contamination to avoid too large differences in terms of socioeconomic living conditions, which are quite specific to the oblast of Bryansk compared with other Russian regions.

Comparison with other studies

Two large studies addressing the prevalence of cardiac conduction disturbances in children have been published in the early 21st century. A first survey performed by questionnaire, electrocardiography, phonocardiography and physical examination was conducted in Taipei, Taiwan, between 1999 and 2001 in a population of 432 166 elementary and high school students aged from 6 to 20 years. In this study, the authors, after excluding students with congenital heart disease, assessed a prevalence of 0.75%.[26]

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A second analysis of disturbances of cardiac rhythm by using ECG performed as part of a cardiac screening test was carried out in Chiba City, Japan, between 1996 and 2001 in a population of 152 322 children. In this study, the prevalence of disturbances of cardiac rhythm was 1.25% in elementary school students aged from 5 to 6 years and 2.32% in junior high school students aged from 12 to 13 years.[27] To our understanding, the two studies mentioned above were performed in children not exposed to artificial sources of ionising radiation in a context of a large-scale screening.

Another study explored arrhythmia in infants in the UK (Northern Region of England).[28] Nevertheless, this paper was dealing with incidence and so that conclusions of this study cannot be directly compared with our results since the present study considered the prevalence of childhood arrhythmia.

To our knowledge, our study is the largest one having explored cardiovascular functions among children in a context of internal radiation contamination. The results of our work show a crude prevalence of cardiac arrhythmia significantly lower in children living in contaminated versus control territories (13.3% vs 15.2%). Compared with the studies performed in Taipei and Chiba, the assessed prevalence seems much higher. However, we do think that outcomes of our study are not comparable to those of the two Asian studies. Thus, the number of children included in our study is much smaller; the examinations on which we based our diagnosis of cardiac diseases are more comprehensive (ECG, echocardiography, Holter); and the two studies mentioned above were performed in Asian children living in very different socioeconomic conditions compared with our group of Caucasian children who lived in much more unfavourable conditions.

Very importantly, this study does not observe an association between cardiac arrhythmia and territory or caesium burden, and even shows a higher number of arrhythmic patients living in control territories, despite a higher caesium burden in children enrolled in contaminated versus control territories. We note that the number of 24-hour Holter monitoring was higher in control territories than in contaminated territories (2418 and 1377, respectively). Therefore, we cannot exclude that this difference in the frequency of Holter may be linked to a higher number of cardiac arrhythmia in control territories. However, the percentage of children diagnosed with a cardiac arrhythmia on the basis of both positive ECG and positive Holter is similar in contaminated territories and control territories (56% and 54%, respectively). In addition, other factors not related to radiation exposure (eg, lifestyle) may also affect the frequency of arrhythmia in control territories.

Focusing on the dose assessed in children measured with a detectable caesium burden, our study shows that only 24 among 3105 patients (0.8%) have received a radioactive dose above the annual exposure limit of 1 mSv recommended by the International Commission of Radiological Protection in a normal situation.[29] It seems to argue that the presence of an arrhythmia is related to neither the radioactive dose nor the contamination of the territory where children lived, which is not directly proportional to the ^{137}Cs whole burden. Moreover, for the same ingested amount of ^{137}Cs, some children will present a high body burden, while for others the radioactive caesium will not be detectable because of the interindividual variability in the behaviour of caesium in the body and weight differences from a child to another. Regarding the effect of the season on the measurement of whole-body ^{137}Cs burden, a thorough analysis shows that among the 449 children with both cardiac arrhythmia and whole-body ^{137}Cs activity above the DL, 259 live in the contaminated territories and 190 in the controlled territories. When looking at the season when the ^{137}Cs measurement was performed, the results show that the majority of children were measured during the autumn or winter, with a comparable result between contaminated territories (67%) and controlled territories (61%). This result is, after all, rather not surprising because mushrooms, berries and game (eg, wild boar meat) are highly eaten in Russian families mostly along fall and winter. These forest products are known to be the most heavily contaminated with ^{137}Cs in both contaminated and controlled territories. Finally we notice that the individuals with a detectable caesium burden and living in contaminated territories have been contaminated as a result of a long-lasting soil caesium contamination and not because they were exposed directly to the Chernobyl releases, notably radioactive iodines, as they were born several years after the accident.

CONCLUSION

The study presented in this article has been carried out in the largest group ever observed among children with cardiac arrhythmia in the Russian territories affected by the Chernobyl fallout. Our results show a higher prevalence of childhood cardiac arrhythmia over the period 2009–2013 in control versus contaminated territories in the Russian *oblast* of Bryansk where the study has been implemented. Also we do not observe an association between cardiac arrhythmia and ^{137}Cs deposition levels in the Bryansk region exposed to Chernobyl fallout. The suspected increase in the frequency of childhood cardiac arrhythmia that some scientists evoked in children exposed to chronic incorporation of ^{137}Cs is not confirmed. Therefore, it would not be recommended to implement a large-scale screening of cardiovascular diseases in children exposed to radioactive releases right after a nuclear accident comparable to the thyroid cancer screening that started just after the Fukushima accident.[30] However, these data may be useful for future comparative study of cardiac arrhythmia in children exposed to ionising radiation in other contexts, such as cancer radiation therapies. Also this study offered a unique opportunity to collect in a very large group of children an

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impressive amount of information related to the normal limits for the paediatric ECG and echocardiography that will certainly help to adjust the diagnostic criteria used so far by the paediatricians.[31] The publication of the results of this study will be followed by another article presenting the results of a large-scale screening of lens opacities in a similar group of children living in the same *oblast* of Bryansk. This ongoing study is being achieved and will hopefully provide some elements of answer to another question often raised when assessing the health consequences of childhood exposure to ionising radiation after a nuclear accident.

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Contributors PG and JRJ had the idea for the study. JRJ, GL, VD, AS, IK and AB contributed to the design, the conduct of the study and the recruitment of patients. VD, AS, IK, and AB contributed to the collection of clinical data. IK contributed to the design of the database and the entry of computer data. JRJ, GL and ID contributed to medical diagnoses consultation. JRJ and GL contributed to literature search and drafted the report. DF and J-PH contributed to the analysis of dosimetry data. JRJ, GL and EC contributed to statistical data analysis and interpretation. All authors critically reviewed the manuscript and approved the final version of the draft. The research was designed, conducted, analysed and interpreted by the authors entirely independently of the funding sources.

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Patient consent Parental/guardian consent obtained.

Ethics approval This study was approved and validated by the Ethics Committee of the Russia's National Hematology Center in Moscow. The study was conducted in accordance with the principles of the Declaration of Helsinki.

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