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INCREASED REPRODUCTIVE HEALTH RISKS AFTER CHERNOBYL ACROSS EUROPE

WPŁYW KATASTROFY W CZARNOBYLU NA ZDROWIE NOWORODKÓW

Abstract: To investigate possible reproductive health risks after Chernobyl in Europe, we carried out time trend analyses and spatial-temporal analyses of pertinent reproductive health indicators based on logistic regression. Long-term dose dependent impacts of radioactive fallout after Chernobyl on stillbirths, birth defects, and the human sex odds at birth have been found. For example, from nearly all published data concerning Down's syndrome, long term increases after Chernobyl may be seen. Significant ecological relative risks for stillbirths and birth defects are in the range of 1.005 to 1.020 per kBq/m^2 ^{137}Cs. A relative risk coefficient of 1.010 per kBq/m^2 ^{137}Cs translates to a preliminary relative risk coefficient of 1.60 per mSv/a. Furthermore, there are striking jumps or broken sticks in the secular human birth sex odds trends in 1987 in practically all central and eastern European countries. No jumps or less pronounced jumps in the sex odds trends are visible in less exposed western European countries and in the USA. German district by district data imply a sex odds ratio of 1.015 per mSv/a.

Keywords: analytical ecological study, congenital malformation, environmental health, environmetrics, exposure-response relation, low-level ionizing radiation, male proportion, radiation epidemiology, radiation-induced genetic effects, sex ratio, spatial-temporal logistic regression

Like persistent anthropogenic chemicals in the environment [1-4], man-made ionizing radiation also poses an important ongoing environmental and human risk [5]. The disaster at the Nuclear Power Plant in Chernobyl in April 1986 resulted in the exposure of a large number of people to ionizing radiation that varied substantially, creating a new situation for epidemiology. The accidental event prompted numerous studies on the genetic effects of low dose ionizing radiation in man. Our main intention was to synoptically investigate whether there have been any changes in the prevalence of detrimental reproductive effects across Europe after Chernobyl. Those effects include possible spatial-temporal trend disturbances of births defects (eg Down's syndrome, cleft lip and palate, malformations of the heart), neonatal mortality, stillbirth, and the human sex odds (sex ratio) at birth. We aim to demonstrate lasting genetic or reproductive detrimental health effects after Chernobyl in moderately and highly affected European countries.

Our results are of principal importance for the etiologic understanding of radiation-induced genetic effects. Also, we are able to estimate the order of magnitude of the hereditary risks. Our risk estimates are in contrast to the assessment of ionizing radiation by international bodies (UNSCEAR, 2001 Report, Annex, p. 82). While UNSCEAR propagates genetic doubling doses in the range of a few Sieverts, we show in our paper that those doubling doses are more likely in the range of a few milli-Sieverts. Thus, it is in the same order of magnitude as the well known doubling dose for childhood leukemia after prenatal exposure.

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Methods

Many studies of possible Chernobyl health effects have been aimed at the detection of differences of pregnancy-outcome measurements between regions or time periods. These studies may generally be divided into two categories:

1. Marked geographical variations in contamination provide an opportunity to compare radiation-related outcome measures between human populations residing in different regions. Problems with regional comparisons of infant mortality data were discussed by Landau. Important characteristics (environmental conditions, social class, etc.) are rarely identical between regions. Therefore, the results should be adjusted to achieve comparability.
2. Another approach is to investigate changes in the frequencies of pertinent outcome variables over time. In the case of temporal comparisons, special care must be taken to avoid possible alterations in variable definition. However, if the population characteristics of interest are relatively stable over time, and if the time periods considered are not too large, problems with this approach seem less pronounced in contrast to regional comparisons. In this case, a combination of the regional and temporal comparison seems to be the most informative method.

The main idea behind a spatial-temporal approach is to model a data set that contains regional and temporal information simultaneously by adjusting the regression model for region-specific trend functions. The great advantage of this spatial-temporal method is that by considering partial trends of regional units, those regional units are, so to speak, compared with themselves, as the target variable describing the interesting characteristic varies from year to year or from month to month. Information on several regional units is then combined in a complete spatial-temporal model, giving rise to tests of local or global change-points in time as well as spatial trends in the outcome variable with regionally determined radioactive contamination or radiation doses.

The official European and German birth data and the fallout data were processed with Microsoft Excel 2002. For statistical analyses, we used R, MATHEMATICA 5.0 and mostly SAS 9.1.

Stillbirth in Europe at the national level

The Chernobyl accident has contaminated Eastern Europe more heavily than Western Europe. If there was an effect of the radioactive contamination on stillbirth proportions one would expect to find it more pronounced in Eastern Europe as compared with Western Europe. We therefore studied long-term time trends in European stillbirth proportions. Linear logistic regression was applied to model the time trends in stillbirth proportions. Dummy variables were used to account for effects that can be associated with certain years or locations. A synoptic logistic regression model is suggested for the western, central, and eastern parts of Europe. There is a marked differential effect in the long-term stillbirth time trends between Western Europe (Belgium, France, Great Britain, Iceland, Ireland, Luxembourg, Portugal, Spain), Central Europe (Austria, Denmark, Germany, Italy, Norway, Switzerland), and Eastern Europe represented by four countries (Greece, Hungary, Poland, Sweden). In contrast to the western and central European trends, the eastern European trend exhibits an absolute increase of the stillbirth proportion in 1986 as compared with 1985 and an apparent upward shift of the whole trend line from 1986 on.

Moreover, on a single country basis, a surprisingly consistent picture evolves of significantly increased stillbirth rates after Chernobyl of ca 5% in Poland, ca 10% in parts of Germany and Sweden, ca 20% in Denmark and Finland, and up to ca 30% in Iceland and Hungary. Lower and higher contaminated regions show weaker or stronger effects, respectively [6-9].

Stillbirth in Bavaria and in the former GDR (Germany) at the district level

For all districts of Bavaria and the former GDR, including West Berlin, we computed the district-specific mean ^{137}Cs fallout. A synoptic spatial-temporal analysis at the district level, employing logistic regression, was performed for Bavaria + GDR + West Berlin (combined). The analysis is based on 4,265,510 live births and 19,877 stillbirths from 1980 to 1993 in a total of 3,324 district years. This analysis, adjusted for district-specific intercepts and linear-time trend parameters, yields significant gender-specific relative risks (RR) per kBq/m^2 ^{137}Cs for stillbirths [7, 10]:

Male: RR = 1.0073, 95%-CL = [1.0034, 1.0113], p = 0.000245

Female: RR = 1.0048, 95%-CL = [1.0004, 1.0091], p = 0.031092

Total: RR = 1.0061, 95%-CL = [1.0032, 1.0089], p = 0.000026

Based on environmental measurements at the district level in Bavaria, a conversion coefficient from kBq/m^2 Cs to mSv/a of 0.0143 (95%-CL = [0.0124, 0.0162]) was derived. (This is in good agreement with a theoretical value of 0.0123 used in ECOSYS by the former GSF) Applying the conversion coefficient of 0.0143, the above relative risks per kBq/m^2 ^{137}Cs translate to preliminary relative risks per mSv/a:

Male: RR = 1.41, 95%-CL = [1.17, 1.69], p = 0.000245

Female: RR = 1.25, 95%-CL = [1.02, 1.53], p = 0.031092

Total: RR = 1.33, 95%-CL = [1.16, 1.51], p = 0.000026

Perinatal mortality in Germany

We also studied perinatal mortality in Germany. Our main intention was to investigate whether perinatal mortality, as reflected in official records, was increased in 1987 as a possible effect of the Chernobyl accident. We disclosed that, in Germany as a whole, there was a significantly elevated perinatal mortality proportion in 1987 as compared with the secular trend function. To investigate the impact of statistical models on results, we applied three standard regression techniques. The increase, relative to the logistic trend function, is 4.8% (p = 0.0046) of the expected perinatal death proportion for 1987. The observed significant increase in 1987 is essentially independent of the statistical model used. Even more pronounced levels of 8.2% (p = 0. 0458) and 8.5% (p = 0.0702) have been found in the higher contaminated areas of the former German Democratic Republic (GDR), including West Berlin, and of Bavaria, respectively [10, 11].

Cleft lip and cleft palate birth rate in Bavaria and the former GDR

Cleft lip and palates (CLP) occur with a frequency of between 1 and 2 cases in 1000 live births and thus belong to the most frequent congenital anomalies. In the former German Democratic Republic (GDR), records covering 1967-1989 for CLP newborns show a 9.4%

increase of the prevalence of CLP from 1987 to 1989, possibly due to Chernobyl [12]. In Bavaria, all congenital malformations in children's hospitals have been recorded from 1984 to 1991. Among these data, 1324 cases with CLP were found. A spatial-temporal analysis aimed at uncovering a possible association of the CLP occurrence with the Chernobyl fallout on a district level, as well as a synoptic analysis of the GDR and Bavarian data were carried out. In Bavaria, from October 1986 to December 1990, the CLP frequency increased by 9.5% ($p = 0.10$) relative to the trend as computed from the remaining years. The association of CLP rates with fallout on a district level is reflected by a significant relative risk (RR) per kBq/m^2 of RR=1.008 ($p = 0.03$). A synoptic analysis of the Bavarian data and the GDR data restricted to the overlapping time window from 1984 to 1989 discloses a simultaneous significant jump of the CLP prevalence by 8.6% ($p = 0.02$) after 1986. The presumption of a long-term increase of CLP after exposure to Chernobyl fallout is corroborated by the analysis of the Bavarian congenital malformation data [13].

Down's syndrome in Belarus and in West Berlin

Trisomy 21 is a major cause of human prenatal and postnatal morbidity and mortality. It can be diagnosed unequivocally and thus offers important prerequisites for epidemiological studies. Nonetheless, even despite decades of research, apart from maternal age, germ line mosaicism and altered levels of recombination, no single exogenous or endogenous factor leading to trisomy 21 has been identified unambiguously. Most cases result from maternal meiotic nondisjunction, which happens around conception. Maternal age distribution and selective abortion after prenatal diagnosis have the strongest influence on its frequency. If these variables remain constant, then any sudden increase in frequency must be due either to chance or to an environmental factor. Based on time trend analyses allowing for jumps, significant and abrupt increases of trisomy 21 were observed in January 1987 in West-Berlin and in Belarus. In both areas, ascertainment of all (pre- and) postnatally diagnosed cases of trisomy 21 between 1982 and 1992 can be considered complete. In both cases, the most relevant exposure, explaining the January 1987 peak, was the inhalation of iodine-131 (physical half-live about 8 days) due to the Chernobyl reactor accident, exactly nine months earlier. In addition, a long-term effect was also observed in several European countries: Bavaria in Germany, Hungary, the Lothian Region of Scotland, North West England, and Sweden. This is explained by the total long-term exposure, especially due to ^{137}Cs. These coherent observations, which also fulfill the Bradford Hill criteria, prove that the increase in trisomy 21 was not a chance event but is causally related to low dose irradiation. Thus, maternal meiosis is an error prone process that is highly sensitive to the effect of exogenous factors, particularly around conception. This conclusion has not only practical consequences for genetic counseling under the aspect of risk avoidance and primary prevention but also theoretical implications concerning the physiology of the meiotic process [14-19].

Sex odds in Europe

To investigate trends in the sex odds before and after the Chernobyl accident, gender-specific annual birth statistics were obtained from the Czech Republic, Denmark, Finland, Germany, Hungary, Norway, Poland, and Sweden between 1982 and 1992. For parts of Germany, annual birth statistics and fallout measurements after Chernobyl are available at

the district level. Trend models allowing for discontinuities of the male birth proportions are suggested. Superimposed on a downward trend in male proportions there was a jump in 1987 with a sex odds ratio of 1.0047 (95%-confidence interval: 1.0013÷1.0081, p = 0.0061). A positive association of the male proportion in Germany between 1986 and 1991 with radioactive exposure at the district level is reflected by a sex odds ratio of 1.0145 per mSv/a (1.0021÷1.0271, p = 0.0218). Consequently, a long-term chronic impact of radioactive fallout on the human secondary sex ratio across Europe has been found [20, 21].

Conclusion

The effects of ionizing radiation at doses below 10 mSv are little understood. Recent epidemiologic evidence, including our observations on radiation-induced genetic effects after Chernobyl, suggests that there is harm at doses below 1 mSv or, alternatively, that the established dose concept is invalid altogether. Moreover, the disclosed persistently disturbed human sex odds at birth after Chernobyl allows the estimation of the order of magnitude of 1 million missing children from 1986 till to date across Europe. A recovery of the disturbed European sex odds is currently not foreseeable with the consequence that the number of missing children will still be increasing in many years to come. In conclusion, time trend analyses and spatial-temporal analyses of official German and European birth statistics reveal certain disturbances of the sex ratio after the Chernobyl accident. These results add evidence to related more recent findings in the field of radiation epidemiology (see references) and cast doubt on the official assessment of the so-called 'low-level' ionizing radiation by pertinent national and international institutions. The effects we observed are probably a consequence of less than 0.5 additional mSv/a per individual in the overall mean in Europe. The legal limiting value of 1 mSv/a holding for the general population in many countries may be put in perspective.

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WPŁYW KATASTROFY W CZARNOBYLU NA ZDROWIE NOWORODKÓW

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Abstrakt: W celu zbadania wpływu katastrofy w Czarnobylu na zdrowie noworodków w Europie przeprowadzono analizę trendów w czasie i analizę przestrzenno-czasową podstawowych wskaźników zdrowia nowonarodzonych dzieci, wykorzystując regresję logistyczną. Stwierdzono, że długoterminowe działanie dawki radioaktywnego opadu po katastrofie w Czarnobylu ma wpływ na zwiększoną liczbę martwych urodzeń, wady wrodzone i płeć człowieka. Na podstawie przeglądu literatury dotyczącego zespołu Downa, można wnioskować, że po katastrofie w Czarnobylu nastąpi wzrost liczy osób z tym zespołem. Znaczne ekologiczne względne ryzyko wystąpienia martwych porodów i wad wrodzonych jest w zakresie od 1,005 do 1,020 kBq/m^2 ^{137}Cs. Względny współczynnik ryzyka 1,010 kBq/m^2 dla ^{137}Cs odpowiada przybliżonemu względnemu współczynnikowi ryzyka równemu 1,60 mSv/a. Ponadto stwierdzono dysproporcje w płci u dzieci urodzonych w 1987 roku w niemal wszystkich krajach Europy Środkowej i Wschodniej. Nie zaobserwowano takich tendencji w krajach Europy Zachodniej oraz w USA. Na podstawie danych z Niemiec podano, że współczynnik nierówności płci wynosi 1,015 na 1 mSv/a.

Słowa kluczowe: badania analityczno-ekologiczne, wady wrodzone, zdrowe środowisko, związek ekspozycja-odpowiedź, niski poziom promieniowania jonizującego, odsetek mężczyzn, epidemiologia radiacyjna, skutki genetyczne wywołane promieniowaniem, współczynnik płci, regresja logistyczna przestrzenno-czasowa