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# RADIATION EXPOSURE IN THE SEMIPALATINSK REGION: TRANSGENERATIONAL RISKS AND DOSIMETRY APPROACHES

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**Summary**

**Abstract:** The Semipalatinsk Nuclear Test Site (SNTS) in Kazakhstan was the site of extensive nuclear testing during the Soviet era, leading to long-term environmental contamination and potential health effects for exposed populations.

**Aim:** Analysis of existing studies on radiation dosimetry and health effects of radiation exposure in the affected regions.

**Search strategy:** Relevant literature was identified through searches in PubMed, Scopus, and Web of Science databases. The search covered studies published up to January 2025 using the following key terms: “Semipalatinsk nuclear test site”, “radiation exposure”, “biodosimetry”, “transgenerational effects”, and “radiation-induced mutations”. No date or language restrictions were applied at the search stage. A total of 74 records were initially retrieved. After duplicate removal, 70 articles were screened based on title and abstract. The full text of 45 articles was reviewed for eligibility, and 39 publications were selected based on their relevance to the objectives of this review.

**Results:** The article discusses key biodosimetric methods, including electron paramagnetic resonance (EPR), fluorescence in situ hybridization (FISH), and glycophorin A (GPA) assays, which have been used to estimate radiation exposure. Studies indicate increased mutation rates, potential transgenerational effects, and a heightened risk of oncological diseases among exposed populations. Despite decades of research, uncertainties remain regarding radiation exposure's long-term genetic and epigenetic consequences.

**Conclusions:** This review highlights the necessity for further investigations using advanced molecular techniques to clarify the impact of radiation on future generations and improve radioprotection strategies.

***Keywords:*** *Semipalatinsk Nuclear Test Site, radiation exposure, biodosimetry, transgenerational effects, health risks, radiation-induced mutations*

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**Резюме**

# РАДИАЦИОННОЕ ВОЗДЕЙСТВИЕ В СЕМИПАЛАТИНСКОМ РЕГИОНЕ: ТРАНСГЕНЕРАЦИОННЫЕ РИСКИ И ДОЗИМЕТРИЧЕСКИЕ ПОДХОДЫ

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**Введение:** Семипалатинский ядерный полигон (СЯП) в Казахстане был местом обширных ядерных испытаний в советский период, что привело к длительному загрязнению окружающей среды и потенциальным последствиям для здоровья подвергшихся облучению групп населения.

**Цель.** Анализ существующих исследований по радиационной дозиметрии и последствиям облучения для здоровья в затронутых регионах.

**Стратегия поиска:** Актуальная литература была найдена посредством поиска в базах данных PubMed, Scopus и Web of Science. Поиск охватывал публикации до января 2025 года с использованием ключевых слов: «Семипалатинский ядерный полигон», «воздействие радиации», «биодозиметрия», «трансгенерационные эффекты», «мутации, вызванные радиацией». На этапе поиска ограничения по дате и языку не применялись. Всего было отобрано 74 публикации. После удаления дубликатов было проанализировано 70 статей по названию и аннотации. Полный текст 45 публикаций был рассмотрен на предмет соответствия критериям включения, и в итоге 39 статей были включены в обзор.

**Результаты:** В статье рассматриваются ключевые методы биодозиметрии, такие как электронный парамагнитный резонанс (ЭПР), флуоресцентная гибридизация in situ (FISH) и анализ по гликофорину А (GPA), применяемые для оценки уровня радиационного воздействия. Исследования указывают на повышенный уровень мутаций, возможные трансгенерационные эффекты и увеличенный риск онкологических заболеваний у подвергшихся облучению групп населения. Несмотря на десятилетия исследований, остаются нерешённые вопросы о долгосрочных генетических и эпигенетических последствиях радиационного воздействия.

**Выводы:** Настоящий обзор подчеркивает необходимость дальнейших исследований с применением современных молекулярных методов для уточнения влияния радиации на будущие поколения и усовершенствования стратегий радиационной защиты.

***Ключевые слова:*** *Семипалатинский ядерный полигон, радиационное воздействие, биодозиметрия, трансгенерационные эффекты, риски для здоровья, мутации, вызванные радиацией*

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**Түйіндеме**

# СЕМЕЙ ӨҢІРІНДЕГІ РАДИАЦИЯЛЫҚ ӘСЕР: ҰРПАҚАРАЛЫҚ ҚАУІПТЕР ЖӘНЕ ДОЗИМЕТРИЯЛЫҚ ТӘСІЛДЕР

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**Кіріспе:** Семей ядролық сынақ полигоны (СЯСП) — Кеңес дәуірінде Қазақстан аумағында орналасқан ядролық сынақтардың ауқымды аймағы болып, қоршаған ортаның ұзақ мерзімді ластануына және халықтың денсаулығына әсер ету қаупіне алып келді.

**Зерттеудің мақсаты:** зардап шеккен аймақтардағы радиациялық дозиметрия және денсаулыққа әсері жөніндегі ғылыми зерттеулерді талдайды.

**Іздеу стратегиясы:** Қатысты әдебиеттер PubMed, Scopus және Web of Science дерекқорларында ізделді. Іздеу 2025 жылдың қаңтарына дейін жарияланған еңбектерді қамтыды. Қолданылған негізгі сөздер: «Семей ядролық сынақ полигоны», «радиация әсері», «биодозиметрия», «ұрпаққа берілетін әсерлер», «радиациямен шақырылған мутациялар». Іздеу барысында жарияланған уақыты мен тілі бойынша шектеу қолданылған жоқ. Барлығы 74 мақала табылып, қайталанатындары алынып тасталған соң 70 мақала тақырыбы мен аңдатпасы бойынша сарапталды. Толық мәтінді шолу нәтижесінде 45 мақала қаралып, 39 мақала осы шолуға енгізілді.

**Нәтижелер:** Мақалада радиациялық әсерді бағалауға арналған негізгі биодозиметриялық әдістер — электрондық парамагниттік резонанс (ЭПР), флуоресцентті in situ гибридизациясы (FISH), және гликофорин A (GPA) сынақтары талданады. Зерттеулер мутация жиілігінің жоғарылауы, ықтимал ұрпақаралық әсерлер және онкологиялық аурулар қаупінің артқанын көрсетеді. Ондаған жылдарға созылған зерттеулерге қарамастан, радиацияның ұзақ мерзімді генетикалық және эпигенетикалық әсерлері туралы сұрақтар ашық күйінде қалып отыр.

**Қорытынды:** Бұл шолу радиацияның болашақ ұрпаққа әсерін нақтылау және радиациялық қауіпсіздік стратегияларын жетілдіру үшін заманауи молекулалық әдістермен қосымша зерттеулер жүргізудің өзектілігін көрсетеді.

***Түйінді сөздер:*** *Семей ядролық сынақ полигоны, радиация әсері, биодозиметрия, ұрпақаралық әсерлер, денсаулыққа қауіп, радиациялық мутациялар.*

***Дәйексөз үшін:*** *Дюсупов А., Чайжунусова Н., Байбусинова А., Масабаева М., Абенова М., Пивина Л., Орехов А., Смаилова Ж., Муканова Д., Лепесбаев М., Кисина Р., Ахмадиева Т., Алибаева Г., Апбасова С., Абдильдинова Г., Изденов А., Досмагамбетова Р., Шабдарбаева Д.* Семей өңіріндегі радиациялық әсер: ұрпақаралық қауіптер және дозиметриялық тәсілдер // Ғылым және Денсаулық. 2025. Т.27 (3), Б. 165-174. doi: 10.34689/SH.2025.27.3.019

**Introduction**

The study of the medical consequences of radiation exposure from the Semipalatinsk Nuclear Test Site (SNTS) on the population of nearby regions has been ongoing for more than 50 years, beginning with the narrative studies of the consequences of nuclear tests aimed at assessing their long-term impact on public health. However, there is still no consensus on the long-term consequences of nuclear tests for second- and third-generation individuals exposed to ionizing radiation.

Some scientists associate the increased morbidity among populations living near the SNTS with internal radiation exposure [1]. Delayed effects of radiation exposure have been identified, which may be transmitted across generations and increase the frequency of spontaneous mutations [2]. Studies confirm DNA damage in individuals exposed to low doses of radiation, consistent with cytogenetic research conducted in the region [3-6]. Additional data on the radiological effects of nuclear war, presented in the British Institute of Radiology report "The Radiological Effects of Nuclear War," indicate that long-term exposure to ionizing radiation in populations may result not only in genetic mutations but also in an increased incidence of oncological diseases, impacts on reproductive health, and reduced immune function [7]. These findings underscore the need for further investigation into the effects of radiation contamination in areas affected by nuclear testing, such as the Semipalatinsk region.

**Aim.** To analyze existing data on the effects of radiation exposure on the residents of the SNTS, including the possibility of transgenerational mutation transmission. It also involves a comparison of biodosimetry methods used to evaluate the level of radiation exposure and its long-term consequences.

**Search strategy**

This narrative literature review was conducted to summarize and critically analyze existing studies on radiation exposure and its potential transgenerational effects among populations residing near the SNTS. To ensure a structured and comprehensive approach, elements of systematic selection were incorporated into the review process.

*Literature Search*

Relevant literature was identified through searches in PubMed, Scopus, and Web of Science databases. The search covered studies published up to January 2025 using the following key terms: “Semipalatinsk nuclear test site”, “radiation exposure”, “biodosimetry”, “transgenerational effects”, and “radiation-induced mutations”. No date or language restrictions were applied at the search stage.

*Study Selection and Data Extraction*

A total of 74 records were initially retrieved. After duplicate removal, 70 articles were screened based on title and abstract. The full text of 45 articles was reviewed for eligibility, and 39 publications were selected based on their relevance to the objectives of this review.

*Articles were included if they:*

• Focused on health risks or genetic effects associated with radiation exposure in the Semipalatinsk region;

• Provided biodosimetric data (EPR, GPA, or FISH methods);

• Discussed potential transgenerational outcomes or molecular effects.

Studies were excluded if they:

• Focused solely on environmental or ecological aspects without medical or genetic endpoints;

• Lacked sufficient methodological detail;

• Did not include primary data or were non-peer-reviewed sources.

The selection process is summarized in Figure 1.

**Scope of Analysis**

Extracted data were analyzed to compare biodosimetric methodologies and their application to the Semipalatinsk population. Additionally, findings on radiation-induced mutations and possible transgenerational effects were critically evaluated across included studies.

**Biodosimetry Methods**

Three key methods were used to assess radiation exposure doses:

Electron Paramagnetic Resonance (EPR): A method for retrospective dose analysis based on tooth enamel. Both classical EPR analysis and in vivo L-band EPR (1.0–1.2 GHz) are utilized.

Glycophorin A (GPA) Assay: A method for detecting somatic mutations in erythrocytes, enabling assessment of radiation-induced cellular damage. Suitable for large-scale screening but requires individual calibration.

Fluorescence In Situ Hybridization (FISH): A cytogenetic method that identifies radiation-induced chromosomal rearrangements. It allows evaluation of long-term radiation effects even decades after exposure.

Each method has its own advantages and limitations and is applied depending on the research objectives [8].

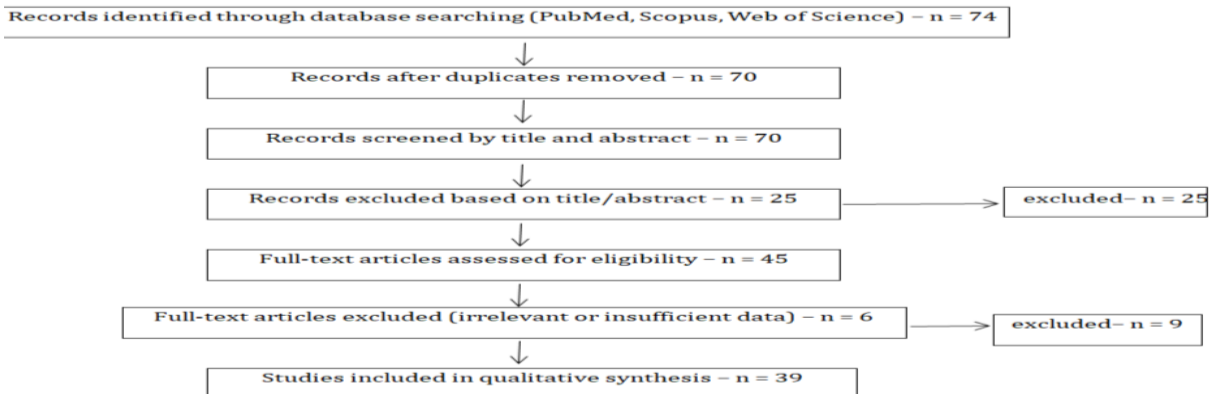


**Figure 1. PRISMA flow diagram showing the selection process of studies included in the narrative review.**

**Results**

Assessment of radiation exposure doses is a critical component of radiation biology and epidemiology. This section presents the key biodosimetry methods (Figure 1). Each biodosimetry method has its own characteristics and limitations when studying the long-term effects of radiation.

Radiobiological studies of populations living near the SNTS have identified statistically significant genetic and cellular changes in individuals exposed to chronic low-dose and acute radiation [9,10,11]. In this context, comparing biodosimetry methods and their applicability for assessing the consequences of radiation exposure in residents of nearby regions is crucial (Table 1).

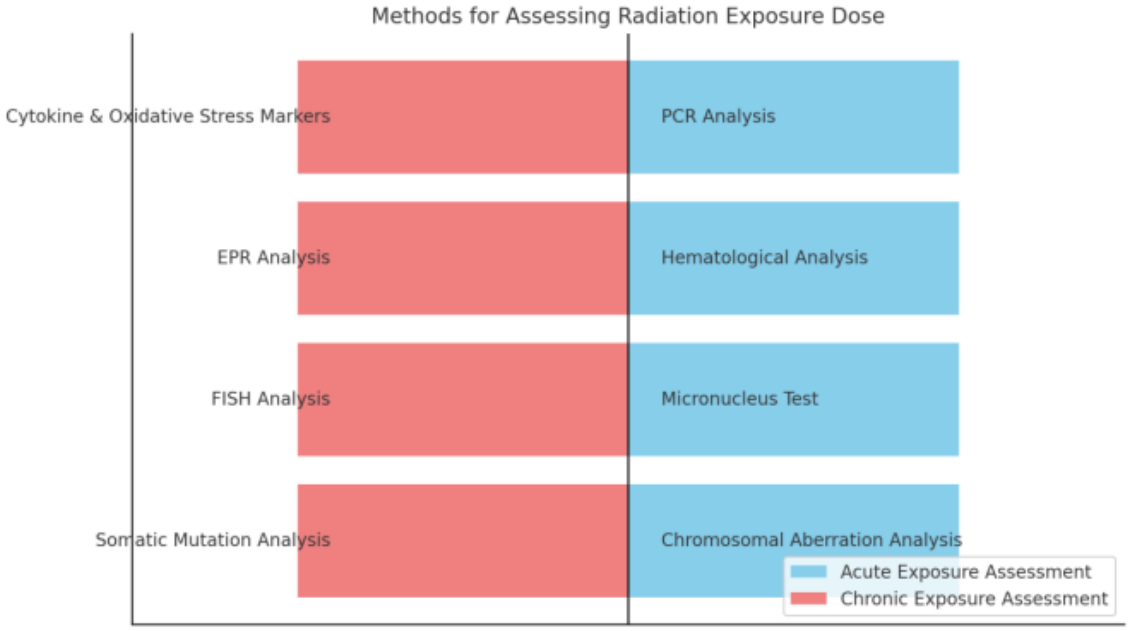


**Figure 2. Key methods for assessing radiation exposure doses.**

*Table 1.*

**Comparison of biodosimetry methods for radiation exposure at the SNTS.**

| Method | Applicability in the context of the SNTS | Limitations |
|---|---|---|
| EPR | Determination of accumulated dose, particularly in cases of acute exposure | Requires tooth extraction; not suitable for mass screening |
| GPA | Detection of somatic mutations in exposed groups | Sensitive to individual factors; requires calibration |
| FISH | Assessment of long-term genetic damage | Requires precise dosimetric correlation, but is the most informative |

The EPR method revealed accumulated radiation doses in residents of the region exposed to prolonged radionuclide exposure. EPR-based studies indicated average cumulative radiation doses ranging from 150 to 250 mSv, which is comparable to the levels observed in Chernobyl liquidators [12]. Ionizing radiation induces the formation of stable radicals in dental enamel in proportion to the dose received, making EPR an effective tool for retrospective biodosimetry, especially in cases of radiological emergencies [13–15]. However, the method requires the isolation of tooth enamel and is therefore unsuitable for mass screening. Recent technological advances have enabled in vivo EPR analysis in the L-band range (1.0–1.2 GHz), expanding its potential for rapid screening applications [15–17].

Ionizing radiation can cause mutations in human cells, which are associated with the development of cancer. To reliably and rapidly detect such mutations, the GPA was developed. It was first employed at the Lawrence Livermore National Laboratory (USA) to assess cellular damage resulting from radiation exposure. The GPA method plays a key role in biodosimetry, allowing for the fast and efficient detection of radiationinduced genetic damage.

Studies have shown that GPA correlates well with physically derived dose estimates [18,19]. The method recorded a 1.5–1.8-fold increase in the frequency of somatic mutations [9]. Due to the simplicity and speed of blood sample analysis, GPA is an effective tool for assessing genotoxic radiation exposure in large populations [20,21]. However, the results remain inconsistent, as similar studies conducted in Japan did not identify significant changes in the offspring of atomic bomb survivors [11]. Additional research, including work by Tawn et al., supports the usefulness of GPA for biodosimetry in radiation emergency scenarios [22]. Furthermore, data from Sram et al. demonstrate the successful application of GPA under conditions of chronic low-level exposure to air pollution, highlighting the method's versatility [23].

The GPA, present on the surface of erythrocytes, exists in two forms corresponding to the M and N blood groups and is associated with a gene located on chromosome 4q. Flow cytometry using fluorescent monoclonal antibodies is

employed to detect somatic mutations. The frequency of cells with a loss of the GPA allele reflects the level of radiation exposure: the higher the frequency, the higher the cumulative dose. This method is particularly useful for assessing acute radiation exposure; however, its application in cases of chronic exposure is limited due to the complexity of accounting for accumulated effects. Nevertheless, GPA remains an important tool for the individualized assessment of radiation exposure consequences [24,25].

The FISH with chromosome staining is used for retrospective dosimetry, even long after radiation exposure [26]. In radiation cytogenetics, chromosomal translocations are considered a key biological dosimeter for estimating radiation doses [27].

Studies by *Dubrov Yu.E.* (2002) and *Takeichi N.* (2006) confirmed an increased frequency of mutations in individuals exposed to radiation, suggesting the possibility of transgenerational transmission of radiation-induced changes [9,28]. FISH analysis has demonstrated high sensitivity to radiation-induced chromosomal rearrangements in exposed populations. According to Salomaa et al. (2002), the level of chromosomal translocations in residents of areas adjacent to the Semipalatinsk Test Site corresponded to doses of approximately 180 mSv [10]. This is comparable to findings from studies on Chernobyl liquidators and individuals affected by nuclear testing on the Marshall Islands [29]

**Transgenerational effects in populations exposed to radiation**

Studies on the impact of radiation from the Semipalatinsk Test Site (STS) on second and third generations remain inconclusive. An analysis of mutations in the offspring of exposed residents revealed an increased level of genetic instability [10]. However, similar studies conducted in Japan [11] did not find significant radiation-induced mutations in the descendants of individuals exposed to ionizing radiation, suggesting the possible influence of other factors such as background mutations or differences in radiation dose. Nevertheless, Japanese researchers continue to pursue investigations in this area [36–38].

Epigenetic studies have identified altered gene expression in the descendants of radiation-exposed individuals, indicating potential radiation effects at the level of genome regulation [26]. Research on the offspring of Chernobyl cleanup workers has also produced mixed results—some studies confirm the presence of mutations, while others do not [19,22,30,34,35]. This further emphasizes the need for longitudinal studies utilizing nextgeneration sequencing (NGS).

Thus, current data indicate that the FISH and GPA methods are the most informative for assessing the effects of radiation exposure among populations near the STS. However, evidence of transgenerational effects remains contradictory and calls for additional molecular genetic research, including NGS and epigenetic analysis.

**Discussion**

Radiobiological consequences for the population of the Semipalatinsk region

The SNTS was the site of 456 nuclear explosions conducted between 1949 and 1989. These tests led to significant environmental radioactive contamination and long-term exposure of the local population to low-dose ionizing radiation. Research confirms that residents of the region were subjected to both acute and chronic radiation exposure, which has manifested in increased frequencies of both somatic and hereditary mutations [9,10,27].

Various biodosimetry methods are employed to assess these consequences, with the most widely used being the EPR, GPA and FISH methods. Each method has its own advantages and specific applications.

The EPR allows for retrospective assessment of accumulated radiation doses. For example, studies by *Tolstykh et al.* (2000) indicated that the average dose, calculated from the dental enamel of residents of East Kazakhstan, ranged from 150 to 250 mSv, comparable to doses received by Chernobyl liquidators [12]. However, widespread application of this method is limited due to the scarce availability of the required biological material (teeth).

The GPA assay enables the assessment of somatic mutation frequency. Several studies have reported a 1.5–1.8-fold increase in mutation frequency among residents of the Semipalatinsk region compared to control groups [9]. Nonetheless, other studies have not consistently confirmed this trend, which may be attributed to individual population characteristics and differences in radiation doses [28].

The FISH is considered the most precise method for studying the long-term effects of radiation. According to *Salomaa et al.* (2002), the frequency of stable chromosomal aberrations (translocations) in residents of East Kazakhstan significantly exceeded control values and corresponded to doses of approximately 180 mSv [10]. These results are consistent with findings from studies of Chernobyl liquidators and atomic bomb survivors in Japan [27], confirming the high sensitivity of the method to chronic exposure and the reliability of FISH for retrospective dose estimation and analysis of long-term genetic effects of radiation. Its application, particularly when combined with other cytogenetic and molecular-genetic techniques, allows for a more accurate assessment of both individual and population level radiation risks.

Each of the biodosimetry methods discussed has its own value. EPR is suitable for ret-rospective dose assessment but is limited by the availability of biological material. The GPA assay helps detect somatic mutations, although results are sometimes inconclusive. FISH, in turn, provides high accuracy in studying the delayed effects of radiation exposure but requires calibration to account for the conditions of chronic exposure.

*Transgenerational Effects in the Context of the SNTS*

One of the key unresolved questions is the possibility of transmitting radiationinduced mutations to the descendants of populations exposed to radiation in areas surrounding the SNTS. Studies investigating this phenomenon have produced inconsistent results.

For instance, *Dubrov* (2002) reported a significant increase in mutation frequency among the children of irradiated parents living in areas contaminated by radionuclide fallout [9]. In contrast, a similar study by Cologne et al. (2022) found no statistically significant differences in the offspring of atomic bomb survivors in Japan, raising doubts about the universality of this phenomenon [28].

The situation concerning the descendants of Chernobyl residents also remains controversial. While some studies confirm the heritability of radiation-induced mutations [9], others [22] do not find significant changes, and more recent whole-genome sequencing research [31, 32] has not detected a statistically significant increase in the number of de novo mutations among the offspring of exposed individuals. These discrepancies may be due to differences in radiation doses and exposure conditions and highlight the need for further investigation.

An additional perspective is provided by the analysis of epigenetic changes. Studies of populations residing in radiation-contaminated areas, including Fukushima, have revealed gene expression modifications that may be linked to radiation exposure. This suggests that even in the absence of structural DNA changes, radiation may affect future generations through epigenetic mechanisms [24].

Despite numerous investigations, the data on transgenerational effects of radiation remain contradictory. A comparative analysis of three key regions SNTS, Chernobyl, and Japan shows variation in outcomes (Table 2). These differences can be attributed to the diversity of radiation doses, population characteristics, and methodological variations across studies.

*Table 2.*

**Critical analysis of contradictions.**

| Region | Confirmed mutations | Negative findings | Research characteristics |
|---|---|---|---|
| SNTS | Dubrov (2002): increased mutation frequency in descendants | Several studies found no mutations in the second generation | Chronic exposure; limited sample sizes |
| Chernobyl | Jensen et al. (1995): increase in GPA mutations | Bebeshko et al.: no statistically significant effects | Methodological and dosimetric inconsistencies |
| Japan | Kyoizumi et al. (1987): isolated mutations in A-bomb survivors | Cologne et al. (2022): no mutations in offspring | Background mutations and relatively lower radiation doses |

The data obtained do not provide a definitive answer regarding the transgenerational effects of radiation exposure in the context of the SNTS. To more accurately assess the impact of radiation on heritable changes, further molecular-genetic studies are needed, including next-generation sequencing (NGS) and epigenetic analysis.

Despite significant progress in the field of biodosimetry, the present study has revealed several limitations. First, many studies rely on retrospective radiation dose assessments, which introduce uncertainties due to limited access to historical data and individual variability in radiosensitivity. Second, biodosimetric methods such as FISH and GPA analysis are effective at detecting chromosomal aberrations but do not fully capture epi-genetic changes or the long-term biological effects of radiation that extend beyond direct DNA damage. Third, studies on transgenerational effects remain inconclusive, as most of the available data are derived from small samples and lack long-term follow-up. Finally, methodological differences across studies hinder comparative analysis and metaanalytical approaches, underscoring the need for standardization of research protocols and continued molecular-genetic investigation.

Thus, a comparative analysis of biodosimetry methods indicates that FISH and GPA are currently the most reliable for assessing radiation exposure in SNTS-affected populations. However, further calibration is required, particularly considering chronic exposure scenarios. The question of heritable mutations remains contentious, as existing studies yield conflicting results. This highlights the necessity of longitudinal monitoring and molecular-genetic analysis to identify potential long-term effects of radiation exposure on the second and third generations, given that the long-term health consequences of radiation exposure are well-documented [33, 39].

It is recommended to integrate advanced technologies such as NGS and epigenetic approaches to improve the accuracy of transgenerational effect assessments. Additionally, the development of preventive health programs for populations living in radiationaffected areas is crucial.

**Limitations:**

1. Lack of standardized dosimetric protocols complicates data comparison.
2. Insufficient long-term cohort studies of second and third generations.
3. Small sample sizes in several SNTS and Chernobyl-related studies.
4. Limited data on epigenetic effects and their underlying mechanisms.

**Conclusion**

The territories of the Abay Region adjacent to the former SNTS remain areas of elevated radiological risk. A significant portion of the population exposed to ionizing radiation during nuclear testing, as well as their second- and third-generation descendants, continue to reside in these regions.

Contemporary research confirms the potential for transgenerational effects of ionizing radiation, necessitating further investigation into the mechanisms of radiation-induced mutations and their health implications. The advancement and refinement of biodosimetry methods including FISH analysis, cytogenetic and molecular-genetic approaches, as well as mathematical modeling of radiation doses—offer promising opportunities for the assessment of both individual and population evel risks.

One of the key mechanisms proposed to explain transgenerational effects is radiationinduced genomic instability (RIGI), whereby numerous non-clonal genetic alterations occur in the descendants of irradiated cells. This phenomenon has been observed across various species,

including humans, and may persist across multiple generations, thereby increasing the risk of oncological and other diseases.

Biodosimetric methods, such as the analysis of chromosomal aberrations in peripheral blood lymphocytes - including dicentrics and micronuclei - as well as FISH analysis, enable quantitative assessment of radiation dose and identification of radiation-induced genetic damage. These techniques are especially relevant in the absence of physical dosimetry data and in cases of chronic or low-dose exposure.

Moreover, studies have demonstrated that ionizing radiation can induce epigenetic changes such as DNA methylation that may also be transmitted to offspring and impact their health. Thus, the integration of cytogenetic, molecular-genetic, and epigenetic approaches into biodosimetry, combined with mathematical modeling, represents a promising direction for the more precise evaluation of radiation-related risks and the development of effective public health protection strategies.

Further investigation of radiation risk among second- and third-generation individuals is a critical area of research in radiation medicine and epidemiology. Such efforts will not only enhance our understanding of the long-term consequences of ionizing radiation but also contribute to the development of targeted preventive measures and medical monitoring for affected populations. Particular emphasis should be placed on a comprehensive approach that includes molecular-genetic, epigenetic, and bioinformatic methods of analysis.

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