

## Heterogeneity of Wintering Animals as a Basis for Transgenerational Transmission of Radiation-Induced Effects in Rodents

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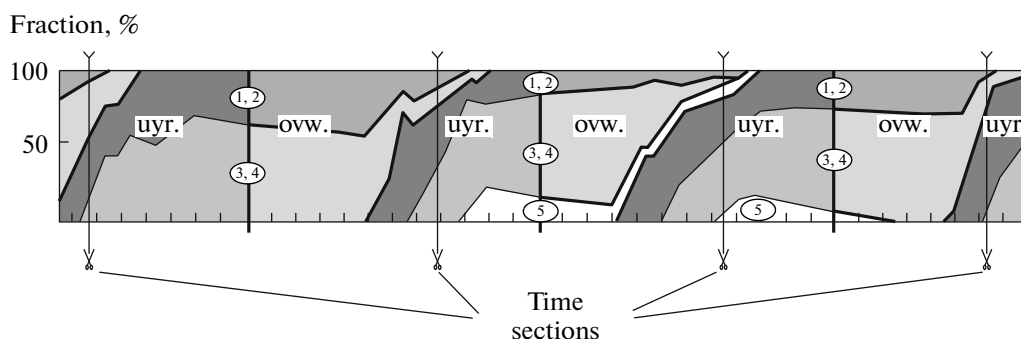
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This paper describes the results of a long-term (over 10 years) monitoring of the structural and functional composition of a population of a background rodent species—the pygmy wood mouse (*Sylvaemus uralensis* Pall.)—from the zone of Eastern Ural radioactive trace, formed as a result of the Kyshtym nuclear accident (Chelyabinsk oblast, Southern Urals in 1957. The goal of this work was to study the dynamics of fine age structure (an element of the demographic structure), that is the structure at the level of elementary intrapopulation units (cohort) of a supraorganismal level, providing for analysis of intrapopulation events in rodents in a radiation-affected biocenosis. It has been found that a group of overwintering mice displays a considerable diversity due to the annual presence of representatives of all generations born in the previous year, although the fractions of these animals vary in different years. The possibility of transmitting genetic information not only via successive generations, but also directly from the first generation of a year to the first generation of the next year (transgenerational transmission) has been demonstrated using the functional developmental approach [1]. This pertains to the remote radiation-induced genetic and epigenetic effects in animals inhabiting the zone of radiation pollution.

The problem set follows from the results of our earlier studies [1–3]. The functional developmental approach [1, 2], based on the dualism of ontogenetics, has been used to analyze the dynamics of major population parameters. The essence of this approach consists in using the functional integration of individuals in groups corresponding to two types of ontogeny as the main criterion for separating intrapopulation structural units. The functional state of animals

(related to the specificity of growth, development, and reproductive state) is the basic characteristic, as well as the synchronism of its changes with time. Each group consists of individuals that, as a rule, originate from several cohorts functionally integrated in reproduction of the population. The term cohort is widely used in the international [4] and Russian [5] literature. In rodents and other animals giving several litters in succession, a cohort is understood as regular mass offspring starting from the beginning of spring reproduction. We believe that cohorts can be reasonably regarded as elementary structural age units in population when analyzing the fine age structure. The functional developmental approach considerably simplifies separation of cohorts, especially with an available effective age marker. The age of wood mice has been determined according to the degree of grinding surface abrasion of the upper molars [6].

In this work, we have demonstrated that the group of overwintering *S. uralensis* individuals trapped in different years in the Eastern Ural Radiation Reserve is highly heterogeneous (figure). This group always contains individuals from the first cohorts of the previous year (the first generation, children of overwintering individuals), their proportion normally varying from 10 to 30% and reaching 100% under extreme conditions [1, 2]. The main part of the overwintering group consists of the individuals belonging to the third and fourth cohorts (children and grandchildren of the overwintering individuals of the previous year, the second generation). The fifth cohort is the smallest (mainly, great grandchildren of the overwintering individuals, the third generation) and is not present in the population every year. Note a high heterogeneity (the degree of which considerably varies from year to year) of individual cohorts in their origin, since the parents of any cohort often belong to different generations. In addition, the heterogeneity increases due to an “age cross” (pairing of individuals belonging to different



Fine age structure of a population of murine rodents with time sections for individual years: 1–5, cohorts; ovw, overwintering; and uyr, underyearlings.

age groups [2, 7]. It has been shown using time sections for different years (figure) that ten cohorts are concurrently present, including five cohorts of the individuals born in the previous year and five cohorts born in the current year. These results agree well the earlier published data [1, 2], which demonstrate a high heterogeneity of the origin in the group of overwintering individuals using a larger data sample (30-year monitoring) of individually labeled bank voles from the Il'men' Nature Reserve (a reference biocenosis, Chelyabinsk oblast, Russia). It is important to keep in mind that the ratio of cohorts formed by the fall is retained in an overwintering population and no selective elimination of animals is observed during the fall–winter–spring period [2]. Note that all the information acquired by a population by the fall is transferred through the winter. The presence of animals belonging to different generations born during the previous year in an overwintering group makes it possible to transmit genetic information not only via successive generations, but also directly from the first generation of one year to the first generation of the next year, representing the so-called transgenerational transmission pathway.

It is known [8] that a change in the age structure of a population entails a change in its genetic composition. The knowledge of these aspects is of practical importance in ecological genetic studies with rodents, since, despite a morphophysiological and other similarities, the overwintering individuals have different origins and can qualitatively differ in individual years in the ratio of allelic frequencies. However, it has been shown [9] that allozyme heterogeneity determines a high intensity of metabolic processes, the rate of sexual maturation, age of the first reproduction, and other vitally important characteristics of animals.

The heterogeneity of the overwintering group is a sort of a buffer the presence of which is fundamentally important under extreme conditions, slowing down or preventing the reproduction of underyearlings because of the impacts of various adverse factors (for example, during droughts), including anthropogenic factors [1, 2]. Our previous work [3] has demonstrated that the frac-

tion of overwintering mice in the zone of Eastern Ural radioactive trace amounted to 60–80% in different years. It is reasonable to assume that the higher this fraction, the higher the potential for transgenerational transmission of genetic information.

Indeed, our combined study of genome instability and the specific activity of strontium-90 (the major radionuclide in the zone of Eastern Ural radioactive trace) in the bone tissue of wood and field mice suggests an intensive mutation process [10]. We have found an increase in chromosomal instability, expressed as an increase in the rate of cells carrying chromosome aberrations in the bone marrow, as well as its statistically significant positive correlation with the  $^{90}\text{Sr}$  specific activity in the rodent bone tissue. Note that this cytogenetic study involved the underyearlings that did not reach maturity in the year they were born (the second type of ontogenesis), which in the next year will enter the overwintering group and form the basis for restoration of population, contributing to it with the mutation load they carry as a wide range of genetic and epigenetic abnormalities. According to the current concept, the responses to low-dose irradiation can operate at a distance not exceeding the cell size and are controlled by signaling systems of the cell; in addition, a direct hit is not necessary for a cell to be damaged [11]. This leads to radiation-induced genome instability in unirradiated cells, as well as to changes in gene expression, DNA repair, mutations, and cell death. Several non-target effects have been also described, such as adaptive response, abscopal effect, hormesis, and genome instability, as well as a clastogenic effect at the level of organism. An increase in the rate of minisatellite mutations in mammalian somatic and generative cells has been found [12]. Since the group of overwintering individuals despite their morphophysiological and functional similarities is heterogeneous in its origin (figure), the accumulated genetic and epigenetic load will be transmitted in a transgenerational manner. This route of inheritance of the radiation-induced chromosome aberrations has been observed in experiments with bank voles trapped in the zone of

the Chernobyl nuclear accident [13, 14]. Pregnant females removed from the zone of radiation impact and fed on clean products, as well as their offspring born in a vivarium, do not display any statistically significant decrease in the chromosome aberrations in somatic cells. A long-term retention of the chromosomal instability (for over 24 months) induced by high- and low-intensity doses has been observed in several generations of repopulating hematopoietic stem cells of mice [15].

Thus, the fundamentally new result of the analysis of the fine age structure of mouse-like rodents from the zone of radiation pollution is the possibility of trans-generational transmission of radiation-induced genetic consequences directly from the first generation of one year to the first generation of the next year rather than via succession of generations, shown for the first time. The basis for transgenerational transmission of genetic and epigenetic effects is heterogeneity of the group of overwintering individuals. In turn, the basis for establishment of functional heterogeneity of a population is a dualism of the ontogenetic development of small mammals, representing a powerful mechanism (reserve) for maintenance of population diversity, especially on the anthropogenically damaged territories, including radiation polluted areas.

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