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CHANGES IN THE PERIPHERAL DIVISION OF THE AUDITORY ANALYZER IN ACUTE RADIATION SICKNESS

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ABSTRACT

The function of the peripheral section of the auditory analyzer in guinea pigs was estimated with the aid of leads and recording of bioelectricity of the cochlea. In the first group of experiments (10 animals), quantitative evaluation of hearing was carried out. The second group underwent total X-ray irradiation with the dose of 350 R; subsequently, at the height of radiation sickness hearing was evaluated by the same method as above. The ability to hear decreased, on the average, from 3.9 to 9.1 dB.

In otriatrics the first attempts to apply X-rays to the therapy of /29* malignant formations and various inflammation processes go back to 1908 (Gaulin, 1908; Schwarz, 1910). Subsequently Thost (1914), Whiterbee (1921), Hemach (1922), Kottmayer (1923), Forchner (1923), Heidenhain and Fried (1924), Goldmann (1929), V. P. Khrakovaskaya-Chernyak and Ye. B. Germayze (1930), M. A. Odsskaya (1939), Z. I. Rabinovich (1939), V. A. Pyatak and N. S. Khayfets (1939), B. I. Gol'berg and Sh. Kh. Kheynshteyn (1938), Ya. S. Zobin and A. A. Tseytlin (1946), N. S. Sokolov (1952), N. V. Zavadskiy (1959), and others obtained encouraging results when treating moderate otitis (in adults and in children), tubercular otitis, eustachitis, perichondritis of choncha auriculae, etc.

However, from the very beginning of X-ray application to the therapy of otolaryngological diseases and of regions close to the auditory organ, reports began to appear concerning cases when the auditory organ was damaged and its functions were disrupted (Marx, 1909; Meyer, 1925; Moller, 1927; L. Khans, 1933; Ye. D. Dubovyy, 1934; Szmurlo, 1936; Block, 1952, et al.).

*Numbers given in margin indicate pagination in original foreign text.

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These danger signals on disruptions in the auditory organ during the action of radiation energy naturally accentuated the interest of clinicians and experimenters to the study of the biological properties of penetrating radiation. Works of an experimental nature appeared (Marx, 1909; Muta, 1926; K. L. Khilov, 1927; Thieleman, 1929; Girden and Culler, 1933; Kasabach, 1938; T. N. Mil'shteyn, 1939, and others).

The most extensive work in the available Soviet and foreign literature in the field of experimental radiology on the investigation of the state of the auditory organ is the dissertation of Professor I. A. Lopotko. However, this work does not contain data on the functional state of the auditory organ in animals subjected to radiation.

In recent years two works by Novotny (1951) appeared which elaborate on the problem concerning the functional and morphological state of the auditory organ during the local irradiation of the ear region. However, the conclusions of this work are based on only a few facts.

In recent years the Soviet literature also contains individual reports on the variations in the auditory organ during the action of penetrating radiation, but the factual data of the investigations has not been published in the generally available literature (N. A. Pigalev, 1954). At the same time the interest in the study of the state of various organs, and particularly of the functional state of the sensory organs, during general irradiation of the organism with radiant energy is increasing.

For these reasons the otorhinolaryngology department of the Leningrad Institute for the Advancement of Physicians, in collaboration with the Department of Medical Radiology, has formulated problems for the clarification of morphological and functional changes which occur in the auditory organ during radiation sickness. Experiments were performed on guinea pigs.

Hearing was measured by the method of taking and recording the cochlear biocurrents (the Weaver-Brey phenomenon, or the so-called "microphonic effect of the cochlea"), which makes it possible to investigate the functions of the peripheral and auditory analyzer independently of its other sections. At the present time most of the physiologists and otolaryngologists acknowledge /30 the objectivity of the data obtained by this method (Davis, Derbyshire, Lurie and Saul, 1934; Hollpike, 1934; Howe, 1935; G. V. Gershuni, 1937; V. F. Undrits, 1937; L. A. Andeyev, G. V. Gershuni and A. A. Arapova, 1939; N. P. Belkina, 1940; N. V. Timofeyev, 1940).

Simultaneously with the investigation of the function, the morphological studies of the auditory organ in irradiated animals were carried out. This part of the work was carried out in collaboration with the Leningrad Scientific Research Insitute for the Ear, Throat, Nose and Speech Disease.

The following equipment was used in the experiments: (1) shielded cell for the operated animal: (2) amplifier mounted on the Dnepr-5 tape recorder;

(3) type EO-7 cathode-ray oscilloscope and type MPO-2 loop oscillograph; (5) AN-5-48 audio generator; (6) photographic camera for photographing curves from the screen of the cathode-ray oscilloscope.

The animals were selected taking into account their general state, and particularly the state of their auditory organ (the auricular reflex was checked and otoscopy was performed). If there was the slightest doubt concerning the pathology of the auditory organ, the guinea pigs were rejected. Before the experiment the blood of all the animals was tested for the number of leukocytes and the animals were weighed.

Six guinea pigs for each series were subjected to X-ray radiation in a specially designed box without metallic reinforcements. Radiation was carried out by using the RUM equipment with a voltage of 180 kV and a current of 20 mA; the skin-focus distance was 60 cm; the filter consisted of 0.5 mm of copper and 1 mm of aluminum. The dose power was 20.6 R/min, the radiation time was 70 min and the total dose was 350 R.

For several days following the radiation the general state of the animals, changes in the reflexes, the number of leukocytes in the peripheral blood and the weight were carefully checked. The details associated with the development of radiation sickness were noted and during its peak the functions of the auditory organ were investigated.

Biocurrents of the cochlea were always taken in the same manner and under identical conditions. Urethane narcosis was used during the operation (10 percent solution administered subcutaneously in the amount of 2.5 g per kg of animal weight). The bone vesicle was approached using the method developed by V. F. Undritsev and L. N. Yampol'skiy. After the niche of the round fenestra was approached, the active electrode was moved to the niche and fixed in position; the passive electrode was introduced into the surrounding soft tissue. The background signals were measured under constant conditions without generating the acoustic signals. Subsequently, acoustic signals in the range 500-8000 Hz were fed from an audiogenerator through a dynamic speaker connected by a thin tube with the operated ear. As the signals were supplied, they were recorded on the loop oscillograph while the electrical response of the cochlea was photographed from the screen of the cathode ray oscilloscope. In addition to this magnitude of the signal was computed from the screen of the cathode-ray oscilloscope, which was graduated in mV. Subsequently the readings taken in mV were converted into decibels by means of special tables.

After the completion of the experiments the animals were sacrificed for the histological control of variations in the auditory organ. They were either decapitated or underwent intravital fixation by having their circulation system flushed with the Vitmaack fluid.

A total of 154 animals was used in the experiments, of which thirteen perished during the period when the method of narcosis and the recording of cochlear biocurrents was developed. Fifteen were used to obtain hearing norms

for this type of animal; 126 were subjected to X-rays with a dose of 350 R. Of these, 64 animals perished due to radiation sickness while 50 were used to investigate the auditory function during the peak of the /31 radiation sickness. Pyramids for histological control were taken from 24 guinea pigs.

It was established that after irradiation with X-rays of 350 R dose all of the animals developed an acute form of radiation sickness of average degree which, under normal conditions, gives a lethality of 50 percent.

Immediately after irradiation almost all of the animals became passive and sluggish. The olfactory, food and auricular reflexes became retarded. The animals frequently rejected food and water. A reddening of the skin was noted in the region of the neck, chest and ear cavities. In some cases during otoscopy it was possible to note the hyperemia of tympanic membranes. All these phenomena disappeared at the end of the first or second day and by this time the guinea pigs gave the appearance of healthy animals. This state lasted for two to three days. During this period the changes developing in the organism could be detected only by measuring the number of leukocytes in the peripheral blood where on the second day there was already a 40-55 percent decrease in the number of leukocytes; beyond this period the drop increased progressively. By the end of the week the behavior of the animals usually changed: the guinea pigs became sluggish, their appetite dropped and the reflexes were again retarded. The external appearance of the animals also changed, their fur lost its sheen and gathered in lumps in some places, the guinea pigs lost weight, and small hemorrhages could be observed on the skin and on the visible mucous membranes. Subsequently some of the animals exhibited a disruption in the gastrointestinal track and also developed pulmonary rale. All of these phenomena reached their peak by the nine-twelfth day. It was also at this time that the animals perished. One or two days before the animals perished, the number of leukocytes in the peripheral blood dropped to 1200-1000 cells and in some animals to 700-500 cells. The weight loss was 15 percent of the initial weight. During the peak of such manifestations of the radiation sickness we carried out our experiments on the investigation of the functional state of the peripheral end of the auditory analyzer with subsequent histological control of changes in the auditory organ.

Results of Auditory Investigations in Guinea Pigs (in the norm).

This series of experiments includes the investigation of hearing in 15 intact guinea pigs. The conditions of investigating the hearing were the same in all experiments. After the background was checked and recorded, biocurrents were taken from the cochlea during the action of various-frequency sounds (from 500 to 800 Hz inclusive) with a loudness of 120 dB and a voltage of 4 V.

As a result of the experiments, it was established that in all of the 15 test guinea pigs the electrical response of the cochlea recorded in millivolts

is approximately the same for corresponding frequencies. The small difference in the threshold response which was detected did not exceed 3 mV in all of the recordings.

Proceeding from these data we established the values of normal hearing for guinea pigs in millivolts for various frequencies (table 1).

In determining the threshold of hearing in decibels we obtain data /32 which are close to the results of other investigators who determined the threshold of hearing in guinea pigs using the same method (Davis, Derbyshire, Kemp, Lurie, Upton, 1935; Cowell and Black, 1936).

Results of Auditory Investigations in Irradiated Animals.

After the hearing norm was determined for this type of animal we proceeded with the second series of experiments determining the cochlear function of the inner ear of guinea pigs during the peak of radiation sickness produced by the action of a sublethal dose of X-rays (350 R). Since 64 of the 126 animals perished, the auditory investigations were conducted on 62 animals of which 8 perished during the experiment.

Observing the development of radiation sickness we noted interesting changes in the auricular reflex. In the first hours after irradiation the auricular reflex in most of the animals (85 percent) was sharply retarded, but we did encounter animals with inadequately pronounced reaction (15 percent). During the latent period in the sickness, the reflex was normal and then fell off in the subsequent days but remained discernible at all times. From these coarse investigations we could judge that the acuteness of hearing in the test animals gradually decreased as the sickness developed but the hearing didn't disappear completely. The biocurrents of the cochlea were taken on the 7-14th day after irradiation. The data obtained were recorded in the form of curves on the loop oscillograph and photographed on the screen of the cathode ray oscilloscope. The screen of the cathode ray oscilloscope was graduated in mV; therefore, by comparing data obtained for irradiated guinea pigs with the average hearing norm we obtained the hearing loss in mV. Later by means of special tables the millivolts were converted into decibels. From the comparison of hearing norms with these data we established a certain loss in the hearing of guinea pigs during the peak of radiation sickness (table 2).

TABLE 1. HEARING NORMS FOR GUINEA PIGS IN MILLIVOLTS

Frequency (Hz)	500	1 000	2 000	3 000	4 000	5 000	6 000	7 000	8 000
Hearing Norms (mV)	9,47	17,5	15,75	15,75	13,3	10,5	8,3	5,25	3,08

TABLE 2. GENERAL DATA ON HEARING LOSS IN DECIBELS

Frequency (Hz)	500	1 000	2 000	3 000	4 000	5 000	6 000	7 000	8 000
Hearing loss (dB):									
Minimum	5.0	2.0	3,0	2.0	3,0	3,5	3,5	2.0	2.5
Maximum	25	24	19,5	19,2	22	20	18	12,5	9,2

We can see from table 2 that hearing in different animals varies for each of the frequencies. We may assume that this is due to the individual peculiarities in the course of the radiation sickness.

All the irradiated guinea pigs can be divided into three groups according to the degree of cochlea biocurrent decrease: the first group has pronounced hearing loss (31 percent of the animals), the second group has moderate hearing loss (41 percent of the animals) and the third group has an insignificant hearing loss (28 percent of the animals).

From these results we may assume that during the peak of radiation sickness produced by general X-ray irradiation in the dose of 350 R there is a reduction in the bioelectrical potential of the cochlea in guinea pigs at all of the test frequencies.

Histological Investigations of the Auditory Organ /33

Twenty-seven pairs of pyramids were used for the histological control of changes in the auditory organ during the peak of the radiation sickness. Of these, 16 were obtained by decapitating the guinea pigs, while 11 were obtained by intravital fixation of the animals. Both ears were subjected to investigations. One investigation was carried out after investigating the cochlear biocurrents. In addition, the pyramids from three guinea pigs not subjected to radiation were investigated only after the biocurrents of the cochlea were taken.

The method of the histological processing of pyramids is conventional with fixing in the Vitmaak fluid, decalcification in nitric acid, alcohol series and a subsequent pouring into celloidin. The cuts were dyed in hematoxylin-eosin.

Every three to four cuts were examined while in the cochlear region every second cut was examined. All specimens were checked by the staff member L. N. Yampol'skiy of the Leningrad Institute of Otorhinolaryngology. As a result of the histological investigation of the auditory organ it was possible to note, in most of the specimens, a small quantity of homogeneous exudation in the

middle and, to some extent, in the inner ear. The vessels of the middle ear mucous membrane were englarged and the mucous membrane itself had peeled off from the osseous bulb. Small hemorrhages in the various sections of the middle and inner ear were the basic signs of damage to the auditory organ (figs. 1 and 2).

Hemorrhage can be observed on specimens obtained after the decapitation of guinea pigs as well as on specimens from the intravitally fixed animals. Some of the cuts showed changes in the membrane of the round fenestra in the form of

Figure 1. Microphotogram. Hemorrhage near the wall in the internal auditory passage. Magnified 10 X 8.

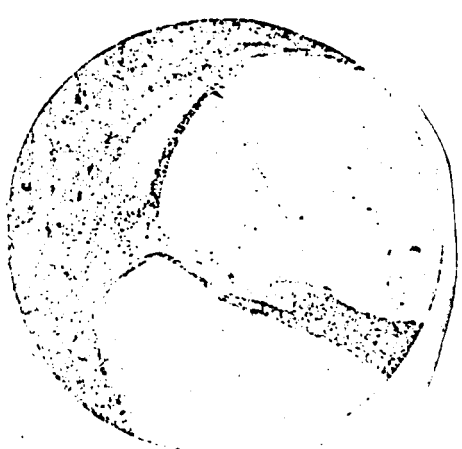

Figure 2. Microphotogram. Hemorrhage in the basic helix of the cochlea during the normal structure of the cormear organ magnified 10 X 8.

its infiltration, thickening and separation into fibers frequently correlated with the exudate or hemorrhage in the basic helix of the cochlea (fig. 3). It was not possible to detect any changes in the sensitive and nervous apparatus of the inner ear during this investigation. Apparently the morphological changes in the auditory organ during the peak of radiation sickness are /34 associated with the systematic disruption of blood supply to all the organs, with variation in the permeability of vessels and in the biochemical composition of the cellular fluids.

The morphological and functional data which have been obtained correspond to a certain degree to changes described by investigators who use the same methods (Novotny et al.).

Conclusions

1. The method of recording cochlear biocurrents is the most objective and convenient one for investigating the function of the peripheral end of the auditory analyzer in animals.

2. A dose of 350 R is the one which produces the acute form of radiation sickness of average degree in guinea pigs.

3. During the peak of the radiation sickness there is a drop in hearing of animals which is indicated by the drop in the auricular reflex and the drop in the bioelectric potential of the cochlea.

4. The decrease in hearing has been recorded for all frequencies from 500 to 8000 Hz inclusive.

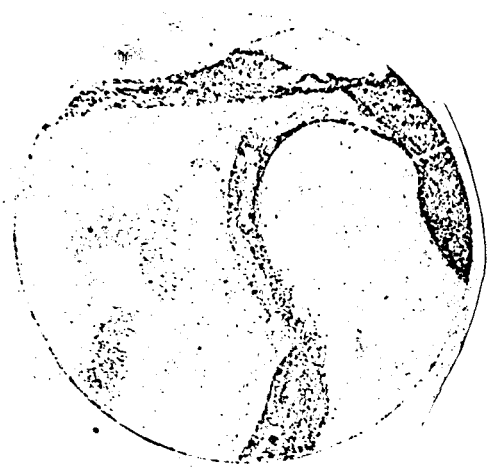

Figure 3. Microphotogram. Infiltration and flaking of the round fenestra membrane and hemorrhage in the basic helix of the cochlea. Magnified 10 × 8.

5. Morphological changes in the auditory organ indicate that it has undergone injury associated with the general disruption of the blood supply system to organs during radiation sickness and the disruption of vessel permeability.

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