ZOONOSES OF LABORATORY ANIMALS AND THEIR DANGER TO MAN

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Modern conditions of working in vivaria and during the laboratory use of experimental animals are diverging all the more from the long ago established methods of dealing with such classic experimental animals as dogs, rabbits, guinea pigs, white mice, rats, etc.

In the course of the last ten years the new requirements of experimental science, especially microbiology, virology and oncology, have caused drastic changes in all phases of laboratory animal husbandry. It is enough to point out the following facts: 1) the overall number of animals used has grown immensely, primarily mice (70% of all the species); 2) new species of experimental animals have been brought into use -- the hamster, polecat, cotton rat, vole, gerbil, rainbow trout, bat, hedgehog, toad, etc.; 3) extensive use is being made of monkeys, including anthropoid apes; 4) particular importance has been acquired by pure-strain (inbred) animals with a great diversity of genetic lines; 5) animals grown under sterile conditions (microbe free) are starting to be introduced into laboratory practice, as well as animals free from specific pathogenic microbes (SPF -- Specific Pathogen Free); 6) it has been established that the pathology of spontaneous diseases in laboratory animals is much more diverse than it has been admitted to consider, especially during infections taking place latently, due to "orphan viruses."

These facts and the new problems connected with them in the organization of the entire laboratory animal husbandry, based on the tendency of modern science for the highest degree of standardization of results obtained from the use of experimental animals, stimulated the creation of the ICLA -- The International Committee on Laboratory Animals in London during December 1956. World literature is rapidly becoming enriched with new facts in the stated area, international symposiums are periodically organized, and in many countries special courses are conducted for training zootechnicians, veterinary pathologists and laboratory workers (Metelkin, 1961; Metelkin and Zasukhin, 1960).

Along with this it is necessary to acknowledge that one aspect in this broad activity has still attracted insufficient attention to itself, in spite of its doubtlessly great theoretical as well as practical significance. This is the working conditions of those workers who have a direct relationship to the laboratory animals during their breeding, maintenance and experimental utilization. In world literature there is a complete absence of materials on this problem.

A specific peculiarity of such work is the constant and intimate bond of the workers with many infections and parasitic invasions following their spontaneous spreading among laboratory animals. If their etiological agents are capable of infecting man also following transmission from animals, then their danger for workers in vivaria and laboratories is obvious. Great caution is also required when working with experimentally produced zoonotic diseases. However, it is still necessary to devote main attention to the group of spontaneous infections and invasions, because they, following a spontaneous onset and course and being present in only some of the animals, do not induce a timely sense of caution.

First of all, it is necessary to keep in mind that already the constant residence in premises, usually overcrowded with a great number of animals and moreover small ones, that is, with increased metabolism, reflects unfavorably on the condition of health of the attending personnel. Thus, the high humidity with insufficient ventilation of the accommodations, considerably exceeding the normal (60% relative humidity), disturbs the thermo regulation and promotes catarrhal diseases. The considerable content of ammonia gas in the air of the accommodations from the decomposition of urine and feces from the animals can cause inflammation of the mucous membrane, or be the cause of toxic changes in the blood. The danger of dust-infections is connected with the dust condition of the accommodations as a result of a great amount of hay and litter. Traumatism of the skin of the hands during the cleaning of cages and the bites of animals are a partial reason for inflammatory effects. Even the prolonged semi-bent standing position of the workers when handling a great number of cages causes a rapid tiring of the organism and vacular disorders in the lower extremeties.

Because of constant contact with the urine and feces of the animals it is possible for the service personnel to become infected with such infections as brucellosis, listeriosis, leptospirosis, toxoplasmosis, lymphocytic choriomeningitis, etc., and even invasion by helminths. The possibility is not excluded of infection even through such arthropods as cockroaches, bugs, ants, without mentioning fleas, true-lice, ticks, flies and mosquitoes as biological or mechanical vectors of infections and invasions.

It must be kept in mind that the intensive study of the infectious

pathology of laboratory animals began only a quarter of a century ago and many aspects of it are little known to us yet. In particular, we are insufficiently informed relative to the possibilities of affection of humans by zoonotic infections and invasions. Some of these may proceed in the human organism just as in animals, in a latent state, in the form of "dozing infections" (for example, lymphocytic choriomeningitis, salmonellosis, and others); others may develop immediately and proceed with a sharp syndrome (tularemia, anthrax, necrobacillosis, streptococcal infections, scabies, etc.).

With the discovery of a new series of diseases of laboratory animals, particularly diseases of a viral etiology, the circle of zoonotic infections has expanded by a considerable degree. It is also important to note that not all the diseases of animals are distributed throughout continents and countries to a similar degree (for example, such viral infections affecting only the organism of rabbits, as myxomatosis, papillomatosis of the mouth, Shope papilloma, are completely unknown in vivaria of the USSR). However, under conditions of a rapidly expanding exchange of laboratory animals between countries, the danger is growing of the accidental transporting (particularly by air communication) of infections that are fatal for livestock. The following historical fact serves as an extremely instructive example: A single rabbit, shipped from France to England in 1953, caused the 100% destruction not only of wild rabbits but also laboratory rabbits (in several regions). It is also known that the viral zoonotic infection, lymphocytic choriomeningitis, is distributed among mice in the USA and England but is considerably less known in France.

From these positions, particular attention is merited by the recently observed extensive introduction into laboratory practice of monkeys from various parts of the world. They may be carriers, not only of tuberculosis, bacterial and amebic dysentery, or some helminthiases, but also concealed viral infections which are spread to humans. It is sufficient to recall that the recently discovered monkey B virus has already caused the death of laboratory workers (following the symptoms of myelitis). Such a danger may be presented by little known infection in new species of laboratory animals (for example, in susliks and marmots it is possible to encounter known cases of carrying the causative agents not only of tularemia but of plague). Recently a mass contamination was described (more than 100 persons) by viral hemorrhagic fever as a result of the careless handling in the laboratory of spontaneously infected wild rodents -- extremely persuasive proof of the necessity of special care when handling "new species" of experimental animals with still insufficiently studied manifestations of their pathology (Kulagin et al., 1962).

The following circumstance may serve as a convincing example of the great significance of hidden viral infections which are being uncovered with

the development of the virological sciences. A new virus, accidentally discovered (Armstrong and Lilly, 1934) in tests with neuroviruses on monkeys caused characteristic histological changes in the central nervous system following experimental infection of monkeys and mice and was therefore named the virus of lymphocytic choriomeningitis. Soon it turned out that it was widely distributed in mice, and also in rats, guinea pigs, hamsters, pole cats and dogs, and is transferred by mosquitoes, fleas, lice, ticks and cockroaches. Infection also takes place on contact through urine and feces. The same virus has also been detected in humans with aseptic meningitis, and in a number of laboratory workers it has been established by serological investigation of the cerebrospinal fluid during a latent infection. Several cases are known of the death of humans as a result of their infection from laboratory animals; usually the course is latent or similar to flu with meningeal manifestations; recovery begins in 2-3 weeks.

The following list (of anthropozoonoses) gives a representation of the distribution of spontaneous zoonotic diseases among laboratory animals: 1) bacterial infections -- strepto-, diplo- and pneumococcal, streptobacillosis (causative agent - Streptobac. moniliformis[1]), salmonellosis, dysentery (of monkeys), erysipeloid, tuberculosis, listeriosis, brucellosis, tularemia, plague (suslik, marmot), necrobacillosis, tetanus, leptospirosis, spirochetosis of "rat bite" (wild and white rats, mice); 2) rickettsioses -- rat exanthematous fever (wild rats), vesicular, Q fever, etc.; 3) viral infections (primarily neurotropic) -- lymphocytic choriomeningitis, B virus (monkeys), pseudorabies, encephalytis, psittacosis-ornithosis; 4) mycoses -- trichophytosis, favus, actinomycosis, blastomycosis; 5) protozoan invasion -- lambliasis, balantidiasis, amebic dysentery (monkeys), leishmaniasis (gerbils); 6) ectoparasitic invasions -- scabby ticks, mouse ticks (Dermanissus muris), fleas; 7) helminthiasis -- transmitted by means of parasite eggs or intermediate hosts.

Footnote 1. Inhabitant of the nasopharynx in rats. It possesses a strong pathogenicity for mice (infectious arthritis) and is transferred to man following the bite of a rat.

It must be recognized that in zoonoses, the interrelationship between the animal, as the source of infection, and the man who is susceptible to it is more complex than between man, as the source of infection, and a healthy man. This is explained by the species biological differences between animal organisms and the differences in the forms of contact between them. Therefore, the course of the infectious process during zoonoses in the organism of man may often take place in a latent form or with weakened clinical manifestations, and its true nature is cleared up only by the detection of the specific antibodies in the organism. Such a reaction of the human organism is caused apparently both by changes in the virulent properties of the causative agents of the infection during their residence in various organisms and by the effect of constant immunization with small doses of antigen during daily contact with infected animals.

At the same time the possibility cannot be left out of the spreading of zoonotic infections by man among laboratory animals (such facts are known in regards to tuberculosis, salmonellosis, mycoses, etc.). This situation requires a careful attitude towards the selection of personnel who attend the animals (especially monkeys) and the establishing of a laboratory control of them with the aim of exposing carriers of pathogenic microbes and parasites.

The diagnosis of zoonotic infections, especially their latent forms, is carried out by microbiological, parasitological, and allergic (tuberculosis, glanders, brucellosis, toxoplasmosis, etc.) methods. In some cases, medical treatment is practicable only with the use of modern antibiotics, sulfanilamide and other chemotherapeutic preparations.

Preventive treatment is the main method of combatting the spread of zoonotic infections both among animals and among their handlers. In regards to the animals, it is necessary to have a rational organization of work, strict observance of veterinary-sanitary rules, isolation of patients and those suspected of having the disease, observance of the correct quarantine terms, conducting of phasic and strict calendar disinfection and disinfestation, and in rare cases -- the use of prophylactic biopreparations. The entry of stray animals (dogs, cats, rodents) into the vivaria and feed storehouses must be prevented, unauthorized persons must not be permitted in the vivaria, grass from public squares and from lawns must not be used for feed or even for the litter, and when sawdust is used for the litter it must be preliminarily heated.

It is necessary to recommend the following measures in regards to persons constantly coming into contact with zoonoses under conditions of work: Sanitary instruction, control over the execution of official duties and compulsory sanitary-hygienic rules with the aim of protection of labor; in individual cases (for example, when working with experimental zoonoses) the use of vaccines and sera is necessary (anthrax, tetanus, tularemia, poliomyelitis, etc.).

The problem of zoonotic infections in laboratory animals must be given more attention in the experimental science of the present day.

Literature

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