HAZARDS OF THE ANIMAL HOUSE

THE Laboratory Animals Centre continued its series of annual symposia with a discussion on "Hazards of the Animal House" at the Royal College of Surgeons of England, London, on May 30. As a first discussion of this problem, the symposium was concerned with the general assessment of the situation, indicating the risks involved in handling animals suffering from natural and experimental infections and outlining the methods by which these risks might be reduced. Attention was also directed to hazards from sources other than pathogenic organisms, including risks involved in experiments with radioactive material, allergic reactions to experimental animals and traumatic risks due to careless handling of animals.

Since, perhaps, the greatest hazard of the animal house is that the worker should be unaware of the risks to which he is exposed, it is natural that many of the papers dealt with various agents which could be transmitted from animals to man. Early in the symposium, Mr. Bywater referred to the fact that, although the first case of infection of man with *B* virus from a monkey took place in the 1930's, it seemed that the risk had not been appreciated until comparatively recently. Rules for the conduct of animal houses, aimed at the protection of not only the scientific worker but also the animal house staffs themselves, have been drawn up in the past few years. Such rules are of obvious value in dealing also with dysentery and other intestinal conditions, which are transmissible from monkey to man. Dr. Sommerville listed the natural infections of laboratory rats and mice which are transmissible to man. Lymphocytic choriomeningitis has not been encountered frequently in man in Great Britain, although it appears to be fairly common in the United States, sometimes producing an influenza-like syndrome, at other times a biphasic illness with an aseptic meningitis. The encephalo-myocarditis virus of mice is also of reasonably frequent occurrence, but other viruses are rare. On the bacterial side, *Pasteurella septica*, although found both in rodents and in man, has not often been clearly demonstrated as having passed from one to the other. However, since it has caused fatal illness in man, it should be taken seriously. Leptospirosis is also of importance.

A second group of infections is caused by viruses and bacteria transmitted from mice or rats inoculated in the laboratory with diagnostic material or with stock viral or bacterial cultures. In this second group, infection is much more frequent than by viruses and bacteria naturally carried by the animals, but the laboratory worker is usually on the lookout for the agent concerned. The worker may not always be ready, however, to realize the ease with which infection may be transmitted by inhalation or ingestion of dust from cages contaminated with excreta or nasopharyngeal material from the rodents.

Mr. McNeil dealt with the more specialized topic of the hazards associated with farm animals. He emphasized the importance of selection of healthy animals for experimental work both by clinical examination and by application of tests such as tuberculin tests and agglutination tests for *Brucellosis*. A quarantine period on arrival is valuable, since it also allows parasitic conditions such as ringworm, lice or mange to be dealt with. Most of the conditions which affect farm animals are likely to be familiar to the staff engaged in handling these species. Careless post-mortem technique, though perhaps not strictly part of the animal house routine, was referred to as a source of infection in such conditions as anthrax and swine erysipelas. Mr. Hodgman dealt with the hazards encountered in dealing with dogs and cats. He considered that the risks from disease are not of great importance in Great Britain, the main hazard being the traumatic one from bites and scratches. Conditions affecting dogs and cats and transmissible to man are more likely to be apparent in owners of pets than in laboratory workers.

Mr. Garratt spoke of the hazards associated with the use of radioactive substances in animal experiments. His main conclusion was that health hazards to personnel from external irradiations are usually negligible and those resulting from internal irradiation after ingestion or inhalation of radioisotopes could be prevented by careful handling. Careful disposal of waste was of great importance. In general, the attitude of the worker with radioactive substances in animal experiments might be summarized by the maxim: "Take care of your experiment and your health will take care of itself". Other specialized problems were dealt with by Dr. Cooper on the handling of large-scale experiments with polio virus, mainly from the laboratory point of view, and by Dr. Rees on precautions against tuberculous infection in the animal house and laboratory. Both these speakers were concerned mainly with the techniques which would reduce risks to the workers with the agents concerned and both referred to the advisability of vaccination of staff. Surgeon Commander Darlow dealt with the general topic of the provision of clean air as a factor in preventing the spread of infection in the animal house. He showed how considerable reduction in the number of airborne organisms could be effected by suitable air filtration. The use of ultra-violet light was recommended as the simplest method for killing airborne organisms. Mr. Porter dealt with the traumatic hazards not only from the animals themselves but also from damaged or incorrectly designed equipment. From the economic point of view, the minor accidents of the animal house (graphically illustrated by Mr. Porter) interfere considerably with efficient working. Cracked water bottles, damaged cages and bins all provide sharp edges on which fingers and hands can readily be cut or scraped, with consequent loss in working time.

Summarizing the discussion, the chairman, Dr. J. B. Brooksby, said that the first point that had been made was the necessity for awareness among research workers of the risks involved in handling any species. A remark had been made from the floor that any worker about to begin experiments with monkeys would do well to consult some of the laboratories concerned in handling the species in large numbers. Similarly, any worker dealing with any new or exotic species should try to obtain all possible information before beginning his experimental work. This symposium might, however, serve as an initial stage in the documentation of the various agents which should be considered as hazardous in the animal house. An important point seemed to be that the various risks were kept in their true perspective. Thus, *B* virus infection from the bite of an apparently healthy monkey was obviously far more serious than the unpleasant, but relatively trivial, infection by ringworm from a domestic animal. Just as the severity of infection varied from agent to agent, so the chances of infection from animal to man would vary, and the proper assessment of the dangers involved in any particular type of work would take into account these factors.

The action to be taken to avoid the hazards of the animal house would obviously relate to the degree of risk. Commander Darlow's paper indicated the way to the ultimate degree of protection possible, by designing a special building with air-filtration and all other apparatus necessary for restriction of airborne micro-organisms. Various practical steps could, however, be taken to reduce risks in accommodation already available. Several speakers emphasized the need for taking only healthy animals into the animal house. The value of tuberculin testing in monkeys was discussed, and there was some divergence of opinion as to its value. Restriction of risk in operative procedures could often be achieved by the use of hoods, anti-splash guards and other equipment of this sort. The point had also been made that spread from an animal often occurred after the object of the experiment had been achieved and there was no case, for example, for keeping tuberculous guinea pigs after the primary lesion had developed; they could be destroyed before caseation supervened. Another problem which was of great importance was staff discipline, particularly where large numbers of animals were being handled and much of the work was necessarily undertaken by staff recruited untrained. Training took place after appointment, when new staff members were undertaking potentially dangerous work. Attention to proper sterilization techniques and to the disposal of bedding and dirty equipment was most important. The use of proper equipment in a good state of repair was also a prime necessity for the avoidance of undue risks.

It will be realized that many of the steps that must be taken to control hazards are also those which would be taken in any animal house dealing with infective agents, in order to prevent cross-infection among the animals themselves, and the instruction of workers in the health hazard may help to achieve the discipline which will, in turn, prevent both the health hazard and the hazard to the experiment itself.

USE OF ANIMAL CELL, TISSUE AND ORGAN CULTURES IN RADIOBIOLOGY

FOR nearly fifty years the tissue culture method has proved a valuable experimental tool for radiation studies. By isolating a group of cells outside the body the effect on blood- and nerve-supply and the reaction of the organism as a whole are eliminated and the direct effects of radiation can be accurately assessed. The establishment of clone cultures and the introduction of chemically defined media in the past decade have brought a further simplification and standardization of experimental conditions which make it possible to obtain precise quantitative data. At a symposium convened by the New York Academy of Sciences in February 1961, the effects of ionizing radiations on cell structure and differentiation, on mitosis and growth of cells in tissues grown *in vitro* were reported and correlated with changes in synthesis of deoxyribonucleic acid (DNA); the influence of oxygen tension, sensitizing and protective agents on radiation action was outlined, and variations in radiosensitivity discussed.

L. J. Tolmach (St. Louis) and J. E. Fogh (New York), using HeLa *S*3 and *FL* amnion cells, reconfirmed the well-known fact that radiation affects cell division much more than cell growth. Cells unable to divide continue to increase in size, reaching a maximum 2–4 days following exposure.

Y. Onuki, A. Awa and C. M. Pomerat (Pasadena) investigated the effect of radiation on the chromosomes of leucocytes cultured from the human buffy coat. A dose of 400 r. increased the number of tetraploids by 7 per cent and the number of cells showing chromosomal damage by 50 per cent. F. E. Osgood (Portland) interpreted the effect of radiation on normal and malignant human hæmic cells *in vivo* and *in vitro* in terms of his α-cell–*n*-cell concept. The potentially dividing α-cells give rise, as a rule, to another α-cell and a differentiating *n*-cell. Doses of 10–400 r. immediately inhibit the division of α-cells while the number of fully differentiated and longer-lived *n*-cells remains, at first, unchanged. Their number begins to drop when the reduced α-cells fail to replace *n*-cells which have reached the end of their natural life-span. In this range of dosages, radiation did not seem to inhibit synthesis of DNA of α-cells as they continue to incorporate tritiated thymidine after their increase in number is stopped. Comparisons of hæmic cells as regards their radiosensitivity show that normal and malignant lymphocytes are the most sensitive cells though even in these cells there is a marked individual variation in sensitivity.

The great sensitivity of lymphocytes was also emphasized by Schrek and Trowell. R. Schrek (Hines, Ill.) examined the immediate and delayed effects of radiation on human and animal lymphocytes. A dose of 1,000 r. produced severe intranuclear vacuolization and death within 24 hr. following exposure, while 10 r. reduced the 10 per cent survival-time from 9·7 to 6·1 days. There was no difference in radiosensitivity of human lymphocytes from blood or lymph nodes, but lymphocytes from rats, guinea pigs and rabbits were slightly less sensitive than human lymphocytes. O. A. Trowell (Harwell) described the influence of various gas mixtures on the action of radiation on lymphocytes from rat mesenteric lymph nodes and stressed the importance of choosing the right effect and end-point for measurements. For example, by counting dead nuclei 5 hr. after exposure an oxygen sensitivity factor of 12 was found, while counts of surviving nuclei 24 hr. after irradiation gave a sensitivity factor of 2·7—a value which agrees well with most other biological materials. Trowell attributes his original result to a slowing down of pycnosis by oxygen.