

## THE HOUSING OF LABORATORY ANIMALS

BY J. I. M. JONES (*Crookes Laboratories*) AND E. C. WOOD (*Virol Ltd.*)

(With Plates 7 and 8 and 1 Figure in the Text)

Two of the most striking features in the application of biochemical studies during the last ten years are the increased use of small animals as laboratory reagents, and the wider application of statistical techniques in the design and interpretation of experiments. The first has made itself particularly noticeable in the industrial field; it is safe to say that the small-animal population attached to industrial firms exceeds in size that of academic laboratories. The second has been brought about by an increasing realization of the variability in behaviour of laboratory animals. This realization has also led to efforts to minimize this variability by attention to methods of breeding and selection, and probably the most obvious and most readily controlled factor is that of environment. This is the subject of the present paper, which was presented as part of a symposium on the care of laboratory animals, organized by the Biological Methods Group of the Society of Public Analysts and Other Analytical Chemists, and held in the spring of 1947.

The experience of any single individual in the matter of housing of laboratory animals is necessarily limited, and it was therefore sought to make a synthesis from the experience of many. To this end a questionnaire was circulated to some forty workers in Great Britain, well over half of whom provided information and views on their existing conditions. The authors would here like to express gratitude for their helpful and often detailed responses.

Though the range of living organisms used by chemists extends from microbes, lice and mosquitoes to monkeys and horses, the only species commonly used in large numbers for bio-assays are mice, rats, guinea-pigs, rabbits, pigeons and chicks. Except for chicks, these are usually bred on the premises. Consideration will therefore in the main be confined to these animals, and in particular to the rat, which is the most widely used.

Out of the twenty-five users of animals who made returns, all but one used rats, as Table 1 shows.

The two points which vitally concern the user of laboratory animals are a regular and sufficient supply, and constancy of quality—in fact, the same requirements as with other laboratory reagents. The quantity and quality of the supply will be closely bound up with the satisfactory housing of the

animals, and this in its turn may be summed up in two words—cleanliness and comfort. The fundamental factors in the comfort of the animals are temperature and ventilation; their cleanliness is the key to prevention of disease. A clean colony, happy and well cared for, will mate better, produce hardier animals and show more uniform experimental behaviour than will a dirty, overcrowded and casually treated one. The provision of hygienic and comfortable quarters is thus not only aesthetically satisfying but economically sound. Every aspect of the design and construction of accommodation needs careful consideration, particularly under present conditions when permits and products, licences and labour are equally hard to come by. Wherever possible, it is better to build a separate specially designed building than to adapt an existing one. Any higher capital outlay will be offset by reduced running costs in the number of attendants needed, the cost of heating and the maintenance of an homogeneously reacting output.

Table 1

Species	Users	Stock per user
Rats	24	100–4000
Mice	15	25–15000
Guinea-pigs	14	10–500
Rabbits	14	10–450
Chicks	9	50–1000
Cats	5	2–13
Hamsters	2	2–40
Monkeys	2	5–8
Dogs	1	2
Ducks	1	500
Pigeons	1	48
Sheep	1	100

### MATERIALS OF CONSTRUCTION

Brick or stone is without doubt the best material of construction, both for permanency and for the minimizing of changes due to weather. Other materials are used only as unavoidable substitutes, though under present conditions (1947) they cannot be ignored. The preference is for a specially designed isolated building, though this is not often realizable in urban areas. Where the accommodation is part of a larger building, some isolation can be effected by

segregating a floor—preferably a basement or top floor so that there is as little traffic and disturbance as possible, since much coming and going not only tends to upset the animals but also adds to the possibility of infection creeping in; even invasion by the atmosphere from other rooms, especially if chemical or dust-producing operations are being carried on, may lead to endless trouble. The problem of isolation in one instance has been solved by erecting the animal house on the roof. Of animal houses described in the twenty-five returns received, ten were isolated buildings, fifteen were specially designed for housing animals, twenty were of brick and one each of stone, concrete, and hollow breeze blocks, while two were of wood.

An important consideration in the choice of constructional materials is the prevention of heat loss. Table 2 gives some data for heat losses through walls.

Table 2

(Loss in B.T.H.U./hr./sq. ft./° F. temperature difference.)

Brick wall, 4½ in. + plaster	0.55
Brick wall, 9 in. + plaster	0.42
Brick wall, 11 in. (2 in. air cavity)	0.34
Concrete wall, 4 in.	0.57
Glass windows	1.0

The advantage of cavity walls and the disadvantage of large windows is evident. Wooden buildings always have double walls and it is advantageous to fill the cavity with insulating material such as slag wool or glass wool, which helps also to reduce air movement. Dividing the space into cells with cross battens also does this and still further improvement can be made by lining the cavity with aluminium foil. These refinements only apply to buildings of lighter wooden construction and are not necessary for brick; though buildings of 4½ in. brick can be improved by fitting an inner lining of wood or asbestos sheet or one of the proprietary insulating materials, with an air space between it and the brick. Ten buildings in our returns had cavity walls. Heat loss through windows is serious; it could be reduced by having double windows but this is costly, and no return showed this feature. The common-sense solution is to keep the window space as small as possible.

Inside walls should have a hard impervious smooth finish for ease of cleaning and avoidance of lodgement for parasites. For the same reason such details as skirting boards and moulded doors and door frames should be avoided. Doors should be flush and plain and fitted with automatic closers, to avoid heat loss. White glazed tiles are probably the ideal for walls, next to which comes plaster with a coating of washable oil paint. Ceilings should be of plaster with

oil paint. Three buildings had tiled walls, nine oil-painted plaster, and the remainder mostly distempered brick. Floors, too, should be smooth finished so as to retain no foreign matter and be easily washed down. Asphalte is perhaps the best material and our returns showed an equal division between asphalte and concrete. A coloured asphalte floor might have an advantage over the black variety. Quarry tiles for floors have the disadvantage of being noisy to the tread and the joints are frequently a source of trouble. Granolithic paving (a mixture of marble chippings and cement) is sometimes used but it also has the defect of noisiness and is liable to crack and to wear so smooth as to become slippery. The tendency to crack may be overcome by laying it in slabs separated by ebonite or brass strips.

All angles and corners should be rounded and coved, and floors should have a slight slope to a drain to carry off wash water. A single iron gulley trap let in flush with the asphalte in the centre of the room is better than a channel running the length of the room as is usual in laboratories. All except three of the returns showed floors directly connected to drains.

## DESIGN

The most important features of design are avoidance of overcrowding, and provision for separate rooms for different purposes and operational needs. These may be classified as breeding, testing or experimental, cleaning, cooking and storage. The size of the colony and the number of species are the controlling factors, as is shown by the returns to the questionnaire in which the number of rooms ranges from two to eighteen. In the simplest case a minimum of four rooms is required—one to house the breeding colony; an experimental room for housing any animals under observation, such as rats in a vitamin assay or mice in toxicity tests; a kitchen; and a food store. Desirable additions are a laboratory for operations, dissections or pharmacological work, and, if X-ray techniques are to be used, a room for the X-ray apparatus. These rooms are best part of the same building. Cleaning and sterilizing of cages can, in a small colony, be done in the same room as that used for cooking, but a separate store for bulk food is necessary.

The arrangement of rooms is a matter for consideration. It should not be necessary to pass through any animal room to get to another. The rooms should thus open out from a corridor or central hall. Connecting doors should be avoided and in our opinion so should direct communication with the outside.

In deciding the size of the rooms, overcrowding both of the animals and attendants is to be avoided. Width of gangways between cage racks is important. These should not be less than 3 ft. and preferably

wider. It is a mistake also to have the rooms too big; instead of trying to house a big colony in one extra large room, it is better to use two moderately sized rooms. A useful guide is 450–500 sq.ft. of floor area per 1000 rats, the cages being housed in four tiers. This means a room 35 × 14 ft. or 26 × 19 ft.; the first gives two rows of cage racks with 3 ft. gangways, and the second, three rows. As for height, 10 ft. is quite sufficient. This gives five tiers—four for animals and the top one for spare cages.

The biggest single room in the returns was 32 × 23 ft.—nearly 750 sq.ft., but the general run was from 15 to 25 ft. long and 10 to 15 ft. wide. Experimental rooms are smaller, and a room 15 ft. square will accommodate comfortably 160 cages in four tiers. This gives sufficient rats for about thirty 5-point assays for vitamin D, using 70 rats per pair of assays, with 7–10 rats per cage, and gives a theoretical output of 250 assays per annum. This figure presupposes an even flow of assays, a constantly available supply of animals, and a highly organized routine. It is probably safer to assume a figure of 150–200.

Food storage requires considerable space—practically as much as the breeding colony. There is a tendency to put sacks of food in any old corner, but this is a mistake. If not carefully stored they become pest ridden and there may be large losses.

### LIGHTING

The kind of lighting in animal rooms does not seem to be important as long as there is enough light to see what one is doing. The practice of providing large window spaces which characterizes modern industrial architecture is to be condemned for animal houses. Large windows increase heat loss and add to the difficulty of temperature control both in winter wind and summer sun. Fig. 1 shows a temperature record chart which illustrates how summer sun affects the temperature when windows are large. The sun did not shine directly on the recorder and though the thermostatic control was set to 70° F., temperatures rose daily to 80° as the sun moved round to the windows. Window joints are also a source of draughts. Metal window frames are to be preferred; wooden ones may harbour vermin. Double windows to avoid heat loss have already been mentioned. A point about windows which has troubled some workers is that they form a source of ingress for sparrows, who constitute a major nuisance, and also flies. Screening the windows prevents this. If only rats and mice are kept, comparatively narrow windows running horizontally near the ceiling are sufficient. Where Vitamin D assays are being done, direct sunlight should not be allowed to fall on the stock rats and daylight should be excluded from the test room. Windows or glass panels in the roof are possible in

single-story buildings and on top floors, and these are used, along with wall windows, in several laboratories. Chicks require good lighting, otherwise they do not feed.

Some form of artificial lighting is also required and nowadays the fluorescent type is favoured. A very satisfactory light is obtained by indirect lighting—the light being reflected from the ceiling.

### HEATING AND VENTILATION

By far the most important factor in housing is heating, and since in practice ventilation systems are often combined with heating systems, both may be considered together. Moreover, the removal of heat generated in metabolic processes is of considerable importance and this is primarily a matter of ventilation.

Many investigations on the effect of environmental temperature on growth and health of animals have been made; the ground has been well covered by Mills (1945). Only a brief recapitulation is given here.

It has been well established, for both mice and men, that the basal metabolic rate varies with the external temperature, increasing when the temperature falls and vice versa. Growth is retarded in animals kept in hot rooms and is accompanied by adaptation in heat loss organs as, for example, larger tails in rats and mice and larger ears in rabbits. Food consumption is much reduced; the onset of sexual functions is delayed and there is loss of fertility. Restoration of all these functions occurs on transferring the animals to a colder environment. The retardation of growth and development in hot surroundings can be overcome by increasing the dietary protein, choline or vitamin B<sub>1</sub>. Resistance to infection is diminished and the animals become hypersensitive to the action of drugs if kept in a hot environment. Changes of temperature, particularly in hot environments, result in a considerable incidence of colds and pneumonia.

These experimental facts emphasize the need for uniformity in environmental conditions if uniformity in behaviour is to be attained, and there is no doubt also that this constancy of temperature within a relatively narrow range is essential for the successful maintenance of animal colonies.

The general consensus of opinion is that 70–75° F. is the optimum temperature for the smaller laboratory animals. Some workers prefer 65° F. for breeding rooms and 70° for experimental rooms. Mills (1945) prefers 76–78° F. for suckling young and 68–72° F. for the animals before delivery because this results in higher vitality in the young after weaning. The Wistar Institute aims at 72° F., but the tolerated range is 65–75°. Temperature tends to rise in summer, but is controlled by increased ventilation.

Chicks when received at 1-day-old require a higher temperature, at about 85° F., but this is achieved in the brooders themselves. The important thing in all cases is to prevent wide or sudden fluctuations. A temperature of 70–75° F. enables one to dispense with bedding except for newborn litters.

The best method of maintaining satisfactory temperature conditions is by the forced circulation of

heating and ventilation requires regular attention, but the only point that needs mention is the cleaning of the air filters. If they are situated in a fan house, they may easily be forgotten and become blocked, so that the fans continue to revolve without ventilating. A periodical test of air flow is useful.

The size of fan and heater depends on the volume of air to be handled. The temperature should be

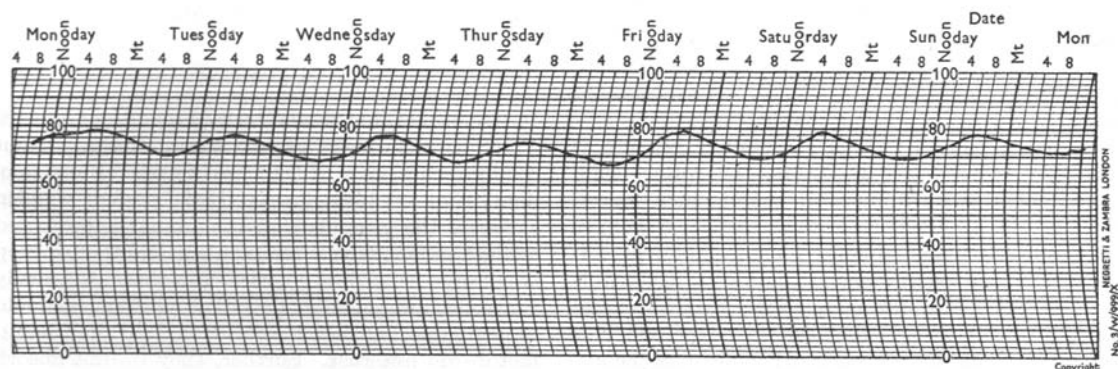


Fig. 1. Effect of summer sun on the temperature of an animal room.

heated air. This, of course, effects ventilation at the same time and both temperature and humidity can then be automatically controlled. Fresh air taken into the system is driven by fans over heat exchangers and passes into the rooms by suitably arranged ducts and grilles near floor level, being taken out again through grilles in the ceiling. Care must be taken in the placing of these grilles to give even distribution, having due regard to the heat loss through windows. Baffling may be necessary to avoid direct draughts on the animals. The amount of air admitted at any one of the grilles can be controlled by shutters placed in the duct.

The air taken in should be filtered and preferably humidified to about 50% R.H. Air which is too dry is considered by some to foster respiratory infections. The weather can be relied on in this country to provide plenty of humidity, which is probably why no case of humidity measurement or control has been reported to us, though in one instance the circulating air is washed. The rate of ventilation should be such as to give at least six changes per hour. For heat economy some of the air may be recirculated, about 20% fresh air being taken in with each circulation. Some economy may also be effected by taking in the air from some other warmed building, but one must then guard against pollution. This circulation rate keeps the animal rooms fresh and without any offensive smell, except possibly for chicks, which seem to produce more excreta per kg. of body weight than any other test organism.

As with anything mechanical, such a system of

thermostatically controlled, and if in summer it rises even when the heat is cut off, the fans can be speeded up. The fan intake should not be placed where flue gases or other obnoxious vapours can be drawn into the system. The position of the thermostatic element also requires consideration. It should be near the centre of the room at about 5–6 ft. from the floor.

Steam is the usual and most economical means for heating the air to be circulated, and is generally available in industrial laboratories. There are, however, no annual or statutory holidays for animal houses and it may be uneconomical to keep steam up even for week-ends, so that some supplementary form of heating will be required. Electric heating of the circulated air gets over this difficulty, except when there is 'shedding of the load', but is more expensive. Some standby for emergencies is always advisable, but gas should be avoided—leaks may be dangerous. Good oil stoves are satisfactory.

Some details of two heating systems may be of interest. That in laboratory A comprises a forced circulation of heated air as explained above. The building is flat roofed and the circulating fans and main heaters are housed on the roof, the warm air being led into and out of the animal rooms by insulated ducts. The heaters are electric and are made in sections which may be switched on or off independently and automatically by thermostatic controls in the rooms. The fan and heaters are designed to give six air changes per hour in the building and to maintain a temperature of 70° F. against an external air temperature of 30° F.

Inside the rooms are auxiliary tubular electric heaters on the walls near floor level. These are also controlled thermostatically, but separately, so that if the fan heaters fail to maintain the temperature for any reason, the tubular heaters are switched on. The maximum electricity consumption in winter, including power for fans as well as heating, is 25 kW./hr. An estimated actual average figure is one-half this, viz. 12.5 kW./hr. The costing of industrial electric power is full of intricacies. Though the nominal charge may be  $\frac{1}{2}d.$  per unit, other charges, which vary with the intensity of the consumption, make the average cost per annum about 1.2*d.* per unit.

In laboratory *B*, which is smaller, heating is effected by hot-water radiators, the water being heated by electric immersion heaters in a lagged storage tank of sufficient thermal capacity to supply the needs of the animal house for some hours even if the electric supply is cut off. Thermostatic controls in the animal house stop or start the flow of water and simultaneously switch the heaters off or on. This system, though not circulating hot air, has the advantage of being able to utilize the specially low tariff that some supply companies will quote for 'off-peak' current, i.e. current which is cut off by a time-clock during periods of maximum demand by other consumers. Supply stoppages occasioned by breakdowns or 'load-shedding' are also without effect unless of unusually long duration. Ventilation in this laboratory is by means of a fan which withdraws air through ducts placed near the ceiling. Table 3 gives some comparative data. Costs will evidently be reduced if there is no forced ventilation, since there is much less loss of heated air from the system.

Table 3

Laboratory	<i>A</i>	<i>B</i>
Volume of rooms (cu. ft.)	18,600	3555
Volume of air circulated (cu.ft./hr.)	111,600	14,220
Electricity consumed (units per week)	2100 (estimated)	500 (metered over 12.5 kW./hr.)
Cost per unit	1.2 <i>d.</i>	0.7 <i>d.</i>
Total weekly cost	£10.5	£1.5

The present-day cost of installation *A*, including motors, fans, ducts, tubular heaters, thermostats and wiring, is about £500.

Of those laboratories making returns, four employ heated-air circulation—two using steam, and two electricity for heating the air. The most popular method of heating is by hot-water pipes and radiators supplemented by electric fires. Steam pipes in three cases, and gas stoves in one, were used as a supplementary supply. Nearly all find auxiliary

heating necessary in winter. Ventilation is effected mostly by opening windows. Most laboratories have thermostatic temperature control and also make regular observations of temperature. This is necessary, for thermostatic devices sometimes fail. About one-third use continuous temperature recorders. These are extremely useful and sometimes enable one to trace abnormalities in the behaviour of animals to temperature fluctuations. Charts showing weekly records are convenient.

### EQUIPMENT

Lastly, something should be said about equipment, which means chiefly cages. Again, the important requirements are comfort, ease of cleaning and freedom from vermin. Farris (1942) prefers wooden cages on the grounds that the animal is protected against sudden falls in temperature and that upkeep is less since wood does not rust. In a thermostatically controlled animal house temperature changes should be negligible, and metal cages galvanized after manufacture do not rust. Further, they do not absorb urine, are less liable to harbour vermin than wooden cages, and are much more quickly cleaned and dried. Only four out of the twenty-five returns used wooden cages, and only one of these used them for rats, while all stated that they would prefer metal.

Most workers have their own ideas of cage design; the main point to be emphasized is that simple arrangements of readily interchangeable parts should be used. Fig. 2*a, b* shows a convenient arrangement in which there are three parts—the cage itself with hinged top, a removable wire base which rests about 1 in. above the bottom, and a galvanized tray in which the cage stands. Fig. 3 shows the complete assembly. Excreta fall into the tray and are removed with little trouble; the raised wire bottom prevents coprophagy. It is an advantage to reinforce the corners of the trays before galvanising since the rats choose the corners in which to urinate and corrosion is apt to occur in the corners of the trays while the rest remains quite sound.

As to size, most workers express a preference for standard sizes but in regard to these same standard sizes, it appears that *quot homines, tot sententiae*. One of us uses cages 15 × 12 × 6½ in. for mating and resting does, and 10 × 12 × 5½ in. for litters and test animals; the other uses cages 18 × 12 × 8 in. for litters and groups of animals on the same diet, and 9 × 12 × 8 in. for mated pairs. The present-day cost of an 18 × 12 × 8 in. cage assembly is 32*s. 6d.* of which the cage itself is 14*s.*, false bottom 5*s.* and tray 13*s. 6d.* in galvanized iron (or 18*s.* in aluminium). Aluminium or duralumin trays are lighter and much less corrodable—one of us has used them for nearly a year and they have proved very satisfactory. Guinea-pigs and rabbits can be housed in cages of



Fig. 1. A typical cage and rack assembly.



Fig. 4. Apparatus for radiographing chicks, showing lead protection.

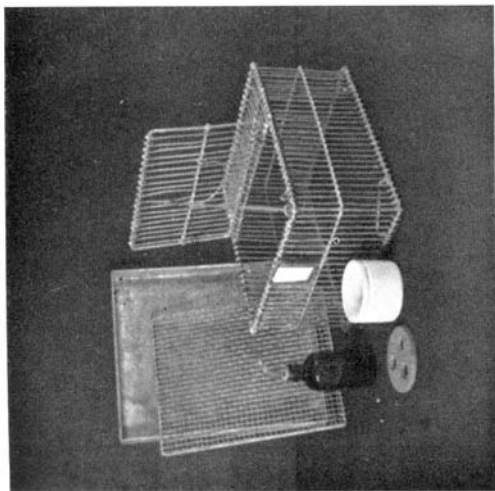


Fig. 2.

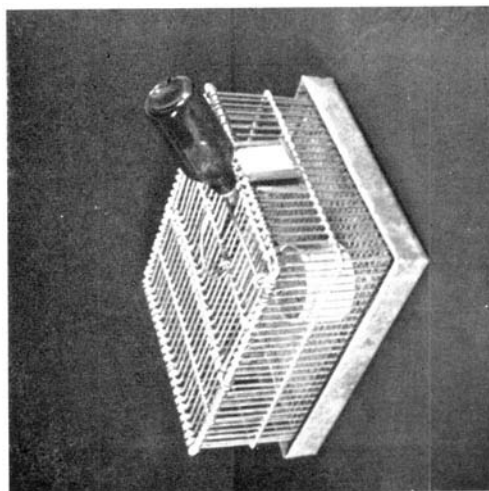


Fig. 3.  
Figs. 2, 3. A cage assembly for rats.

the same type with the front hinged instead of the top.

Before leaving this question of cages, attention may be drawn to a cage designed to prevent coprophagy and described by Gayer, Gayer, Derse, Zinkin, Elvehjem & Hart (1947). The animal is kept in an endless circular runway and is unable to turn round to lick itself. Comparative growth figures for this type of cage compared with the ordinary square type are 106 and 167 g. respectively on a basal diet and 189 and 210 g. respectively when a liver powder supplement was given.

Exercising devices are conspicuous by their total absence in British animal houses, though several papers have been published showing the benefit of exercise on weight, organs, fertility and longevity (cf. Dunn, Murphy & Rockland, 1947).

Cages are kept on racks or shelves. The view of the authors is that these racks are best suspended from the ceiling so as to leave the floor quite clear for cleaning. Pl. 7, fig. 1 shows an arrangement. There are five tiers, but only the lower four are used for cages. The bottom is 20 in. from the floor and there is 15 in. between tiers. The top tier carries fluorescent lighting tubes which throw their light on to the ceiling. These racks are made in units from angle iron. Each unit is 5 ft. 6 in.  $\times$  2 ft. 2 in.  $\times$  5 ft. 2 in. high and weighs about 1½ cwt. They are three large or six small cages long and two wide so that one unit carries 24–48 cages. Only five returns showed hanging cage racks; most laboratories had racks standing on the floor, but in all except five of these, the racks were movable, being equipped with wheels or castors. Shelves on walls are not recommended; one should be able to get all round the rack for cleaning.

In America, the Wistar Institute (Farris, 1942) has used racks equipped with paper rolls to collect the excreta instead of metal trays. These do not appear to have been tried in this country.

The best type of feeding pot for use with powdered or paste diets is the glass or china ointment jar, from 4 to 12 oz. capacity. This is not easily upset and holds a reasonable amount of food. It has the drawback that the rats can sleep in it and that they soil the food with excreta. These drawbacks are avoided to some extent by providing perforated disks which rest on top of the food (see Pl. 8, fig. 2). These also help when it is desired to measure the food consumed. Glass is probably the best material for the disks—metal or plastic is gnawed by the rats—but earthenware has been found to be satisfactory. If food cubes are used, they can be put in a container which hooks on to the cage so that the animals have access to it between the bars.

None of the laboratories making returns had water laid on to the cage racks as used in part at least by the Wistar Institute. This has the advantage of saving

time and breakages in cleaning and filling bottles, but is probably only feasible for fixed cage racks. Most workers use inverted bottles provided with glass licking-tubes. Cleaning is the difficulty with bottles and for this reason tubes of the pattern shown in Pl. 8, fig. 1 are sometimes preferred. Glass is essential in order to see both the amount and the condition of the contents. Water should be laid on to the rooms for filling the drinking bottles, as well as for washing down.

Cleaning facilities are, of course, essential. Cages must be cleaned regularly in a separate room; they are allowed to soak in hot soapy water, then removed and scrubbed. If the cleaning is done at least weekly, not much scrubbing is required. They are rinsed in water containing a disinfectant. Feeding pots should also be cleaned at least weekly. This cleaning, of course, necessitates a stock of spare cages and feeding pots. The cleaning room should not communicate directly with the animal rooms and some provision such as a small fan should be made to remove steam. If cleaning is really thorough, sterilization can be reduced to a minimum or even omitted, unless work involving the use of pathogens is being done. The converse is not true, however; a cage coated with sterile filth is a horrid sight. A really large sink or tank, with scrubbing tables or boards of adequate size at the right height in a well-lit and ventilated room will assist in ensuring that the uninteresting but vital job of cage-cleaning is done cheerfully and well.

For mixing small quantities of special diets a mechanical mixer is useful, having a capacity of 6 or 7 lb. If this is not available, hand mixing on a large enamelled or glazed table, though laborious, can with care be as efficient. For stock diets, if not bought ready mixed, a large 2 cwt. mixer is almost essential. In addition, a grinder may be needed if maize and other grains are bought whole. An ordinary gas stove, or at least a gas ring, is also required for food preparation.

The convenience of an automatic balance should also be mentioned, particularly where animals have to be weighed in large numbers. These are available to weigh up to 500 g. with an accuracy of 1 g.; or to 250 g. with an accuracy of 0.5 g.

Finally, a word may be said about protection in working with X-rays, which enter a great deal into vitamin D assays. Lead-lined gloves should be used and the table on which the animals are placed should be lead covered. A convenient screen for holding chicks when X-raying their legs consists of a lead covered board with a slot through which the leg passes (Pl. 8, fig. 4). Only one glove need then be used, the operator's other hand being protected by the screen.

This communication has been concerned with the



housing and environment of experimental animals, and it must not be forgotten that the human environment of the animals is no less important than their material environment. Efficient and sympathetic attendants are highly necessary; the laboratory animal has a psychological side like his human counterpart and unskilled or unsympathetic handling can have untoward results, as, for instance, in its effect on the temperature changes of rabbits. The experimenter is largely in the hands of his animal attendants, and their selection and training is a matter deserving much care. The holding of periodic conferences of animal attendants, as is being

carried out by the Laboratory Animals Bureau of the Medical Research Council, is a very welcome and useful measure.

#### SUMMARY

A survey of both the prevailing and the desirable conditions for housing small laboratory animals, with particular reference to rats and mice, is described. The data surveyed are confined to laboratories in Great Britain and include requirements of space, heating, ventilation and building construction, with such accessories as cages, feeding devices and other equipment.

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