

CARE OF ANIMALS FOR BIOLOGIC ASSAYS.*

BY PAUL S. PITTENGER.

The accuracy of the biologic test to a marked degree depends upon maintaining the health and vigor of the test animal.

In most laboratories all of the test animals are of necessity kept indoors. If animals are to be kept in a healthy condition indoors for a prolonged period, special care must be exercised in the construction of cages, feeding and the elimination of vermin.

If cages are improperly constructed they cannot be readily cleaned and become offensive and vermin laden. All cages should, therefore, be so constructed that they may be readily cleaned, disinfected and sterilized. Animal rooms containing properly constructed cages can be easily cleaned and kept free from vermin.

When kept indoors some animals require special additions to their food.

White Leghorn Roosters for testing ergot, for example, are normally outdoor animals. When placed in indoor laboratory cages for a period of one year they require more than a mixed grain scratch feed. To be kept in a healthy condition, in addition to mixed scratch feed, they require growing mash, grit and charcoal.

Owing to the fact that they do not have the hard ground and gravel in which to scratch and pick for food, the nails and beak if not properly cared for will become abnormally long. The nails become so long and curved that it is difficult for the cockerel to walk or hold fast to the roost. The beak will grow until it is impossible for the cockerel to close its mouth or to eat. It is, therefore, necessary at regular intervals to clip the beak and nails with bone clippers.

Animals which are allowed but little exercise require less and oftentimes different food than those that receive abundant exercise. The dog, for example, is a carnivorous animal, and meat is his natural diet. When kept indoors, however, and allowed but little exercise, the cooling effect of vegetables is necessary to offset the over-stimulating effect of excessive meat eating.

It is not the object of this paper to treat in detail the methods of housing, breeding, raising and care of each individual laboratory animal, as books upon these subjects are available. Practically all of these books, however, consider the animal only in its natural environment. The author on the other hand has had considerable experience with the housing and care of laboratory animals. The object of this paper, therefore, is to describe simply and briefly the cages and methods which we employ at the present time for housing laboratory animals and keeping them in a healthy condition.

GENERAL PRINCIPLES.

The animal house or room should be so arranged that it will possess maximum comforts for the animals and conveniences for the attendant. It should be dry, cheerful, well ventilated, warm in winter, cool in summer and easy to clean and keep in a sanitary condition. The house or room should have plenty of ventilation

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but *care should be exercised to avoid drafts*. If possible arrange room so it will admit plenty of sunshine.

All cages should be made of metal in order that they may be easily washed, disinfected and sterilized. Cages for all kinds of laboratory animals should be equipped with removable metal trays. Sawdust should be placed in the trays to absorb all drippings. The trays should be emptied, washed and disinfected daily and sterilized at least monthly.

The sawdust removed from trays should be emptied into large galvanized iron ash cans *with lids*. Cans should be emptied and disinfected at regular intervals.

The room should be provided with a large metal sink in which the trays may be washed and scalded. Sinks should be equipped with hot water and if possible live steam. After washing and scalding the trays a small quantity of a non-poisonous disinfectant should be spread over the bottom and clean sawdust placed on top. The trays are then replaced in the cages. In the case of trays for guinea-pig or rabbit cages a bedding of hay should be placed on top of the sawdust.

If this procedure is followed a large number of animals may be kept in the laboratory without objectional odors or danger of vermin.

The cages should be "washed down" occasionally with an antiseptic solution and if live steam is available they should be sprayed with it at regular intervals in order to kill vermin which may be in the crevices, etc.

The animal room can be kept free from roaches, etc., by dusting a mixture of Sodium Fluoride 50% and Sodium Borate 50% into all cracks along the bottom of all partitions, under cages, etc.

All food outside of the cages should be kept in closed metal containers in order that it will not attract rats, mice and other pests.

If the animal house is on the first floor without a basement underneath, the floor should, if possible, be made of asphalt or cement. If a board floor is used it should be built far enough above the ground and with openings large enough to permit small dogs and cats to go under after rats.

CAGES.

Practically all cages should be of all-metal construction. It is more economical, however, in the case of extra large cages to build the framework of wood and make the trays, partitions, doors, etc., of metal. Several coats of aluminum paint should be applied to the wooden parts of such cages to prevent the absorption of moisture. All cages may be more or less of the same general design. Four different size cages usually suffice for the animals required for biologic assays. These may be divided roughly into small, medium large and extra large.

The author usually designs and builds special cages to suit the particular room in which they are to be used. The stock cages, however, shown in Figs. 1, 2, 3, 4, 5 and 6, built by Geo. H. Wahmann Manufacturing Co., 520 W. Baltimore St., Baltimore, Md., are very satisfactory for practically all purposes.

Small Size Cages.—The small cages shown in Figs. 1 and 2 are of suitable size for housing four or five guinea-pigs or rats. This size cage is also suitable for holding one rabbit or one small cat while under test.

Medium Size Cages.—The cages shown in Figs. 3 and 4 are of a very serviceable size. Each unit is large enough to house 25 guinea-pigs or rats, one small dog,

five small or three large rabbits, three small or two large cats. This size cage is also very satisfactory for holding one or two roosters during the test period.

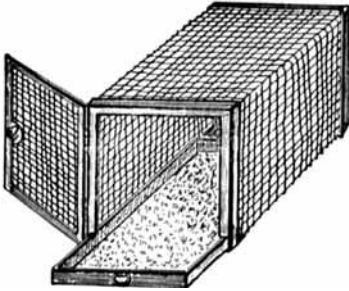


Fig. 1.—*Small Size Cage*.—Dimensions 9" x 15" x 9" high. Made of heavy wire mesh 3 holes to an inch. No. 18 wire. The pan inside is heavy galvanized iron. The cage may also be equipped with a holder for water bottle the same as shown in Fig. 2.

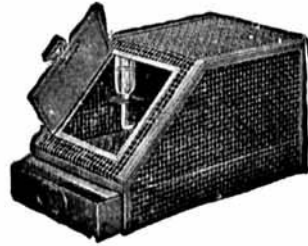


Fig. 2.—*Small Size Cage*.—Dimensions 9" x 9" x 15" deep. Made of galvanized American ingot iron, and galvanized wire cloth. Galvanized iron drawer is removable for cleaning. Provided with water-drinking fountain and holder.

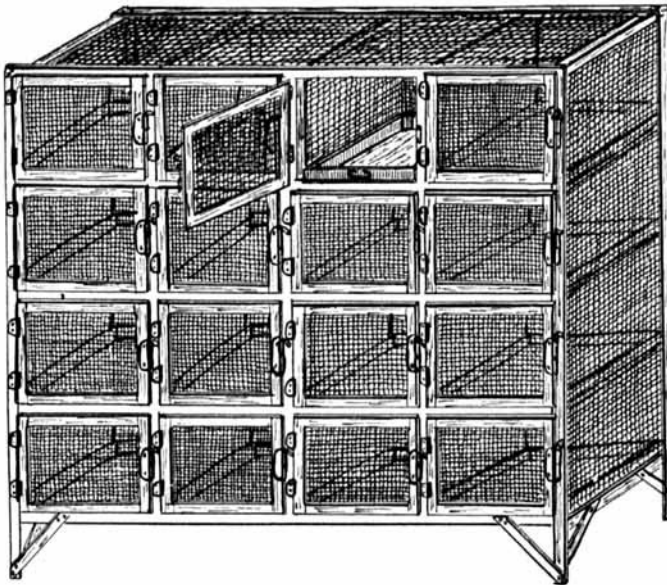


Fig. 3.—*Medium Size Cages*.—Each unit of this cage measures 22" x 20" x 14" high. Made of heavy galvanized iron and stout wire mesh on a frame of angle steel. A cage of this type may be built so that it consists of 4, 8, 12 or 16 units. The galvanized iron trays are removable for cleaning.

They are, however, too small for housing roosters or dogs for longer than the test period.

Large Size Cages.

—Cages of the size shown in Figs. 5 and 6 are satisfactory for housing one large or two small dogs, three or four large cats, five or six rabbits or two roosters. The cage shown in Fig. 5 is made with solid sides and back, two stories high. It may be made as many cages to the row as desired.

The cage shown in Fig. 6 is constructed with a removable wire

floor and tapered bottom for collection of urine for metabolism experiments. Solid galvanized iron extends to one half the height of the sides and door inside to insure the collection of all urine voided. This also prevents dirt from the

upper cage from falling into the lower cage. Two hooks are soldered to the bottom, one on either side of the outlet, for attaching the specimen collecting bottle.

Extra Large Cages.—The two-story cage shown in Fig. 7 was designed by the author for housing roosters, dogs, cats, rabbits or guinea-pigs. Each unit of the cage measures 48" long x 30" wide x 30" high. The framework is made of 2" x 3" white pine planed on all four sides. The sides, doors and fronts are made of perforated black iron. The door frames and supports are of 1" angle iron. The trays are made of heavy galvanized iron supported by three pieces of 1" angle iron. The angle irons are the only means of support for the trays. When the trays are removed, therefore, all dirt may be swept through to the floor. The cages may thus be easily and thoroughly cleaned. The twelve units of the cage are separated from each other by means of sliding removable partitions *A* made of perforated black iron in a frame of heavy galvanized iron. All metal parts are painted with aluminum paint to prevent rusting. The removable partitions make it possible to divide the cage into any desired number of units from two to twelve. In other words it may be made into two very large cages, four extra large cages or six, eight or twelve large cages, depending upon the number and kind of animals to be housed. It is better to house six to eight roosters or three or four dogs in two units (without partition between) of a cage of this size than to house one or two animals in smaller cages. By using two units as one cage the animals have plenty of room for exercise and are, therefore, healthier than when each animal is placed in a smaller cage.

The removable partitions are especially convenient for ergot and cannabis assays for isolating animals during the fasting and testing period. At the beginning of the fasting period all of the roosters may be driven into one of the two units and the partition inserted. The other tray is then emptied and supplied with fresh sawdust. The cocks to be

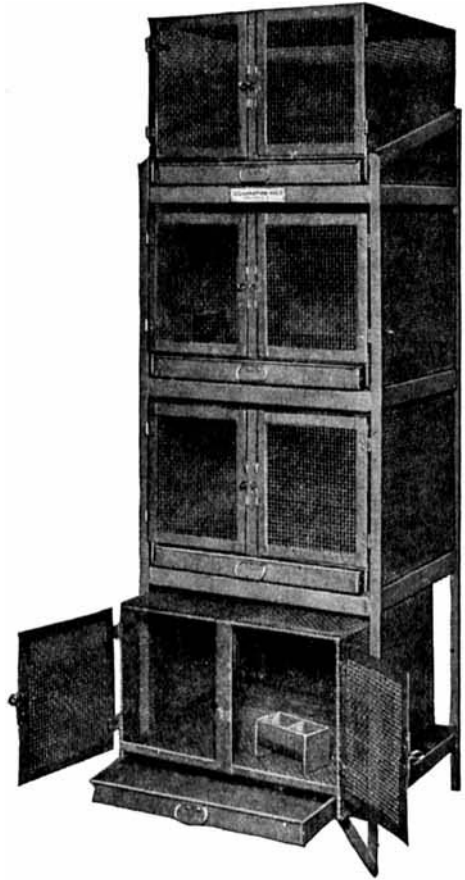


Fig. 4.—*Medium Size Cage.*—This cage is of a slightly different construction than that shown in Fig. 3. This type cage was originally constructed for housing cats, but its peculiar construction makes it satisfactory for all small animals, even small dogs. This cage may be made with as many units as desired. Each unit is 22" wide, 20" deep and 15" high. The four units of the cage shown above are supported by a stand made of heavy angle iron. A solid galvanized iron shelf is placed between each cage to prevent dirt from the cage above dropping into the cage underneath.

fasted are placed in this unit. This procedure precludes the possibility of obtaining scratch feed from previous feedings which may be mixed with the sawdust. All mash hoppers must of course be removed or covered. During cannabis assays the perforated metal partitions are replaced by solid partitions, so the animals cannot see each other.

The galvanized iron forms *B* are used to cover the space between two trays when a partition is removed.

Figure 8 shows a very serviceable three-compartment galvanized iron hopper for holding growing mash, grit and charcoal for cockerels and a hay rack for placing in cage with guinea-pigs, rabbits, etc.

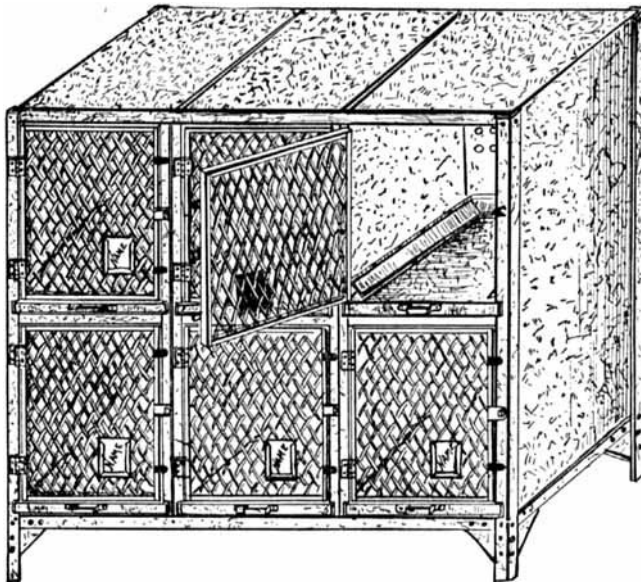


Fig. 5.—*Large Size Cage*.—This cage is specially designed for dogs but is of a very convenient size for cats, rabbits or roosters. Each unit measures 32" x 34" high x 31" deep. Made of heavy galvanized iron throughout. The door is made of galvanized angle iron with very heavy galvanized iron diamond mesh.

They are tropical and heat loving; a few specimens, however, are found in the far North. For example, the tiger in Asia and the Puma in America.

Varieties.—The domestication of the cat occurred at a very early period. The first indication of its connection with man is found in the ancient monuments of Egypt, Babylon and Nineveh.

The *long-haired cats* include the various families known as the Indian, Chinese, Angora and the Persian.

The *short-haired or western cats* include several varieties which are based mostly upon color.

The common varieties include the tortoise shell, tortoise shell and white and the tabbies. The tabbies are divided into four classes: The brown, spotted, blue or silver and the red.

Short-haired cats are preferable for laboratory use.

Housing.—The cat as a rule is a very clean animal and when kept in the laboratory should be provided with means for remaining so. The sawdust in the

CATS.

The cat is a mammal belonging to the order *carnivera* and, therefore, prefer to go in quest of their own prey and kill it.

All cats have the same general type of structure, the variations being only in minor characteristics which are very slightly related to their habits.

Cats are found all over the world except in Australian regions, Madagascar and the West Indies.

trays of the cat cages should be changed daily. Figures 3 and 4 show cages suitable for housing cats.

Exercise.—Animals which are kept for a prolonged period should be provided with some means for exercise. It is good practice to keep several sections of a cage of the type shown in Fig. 7 for use as an exercising cage. Several animals

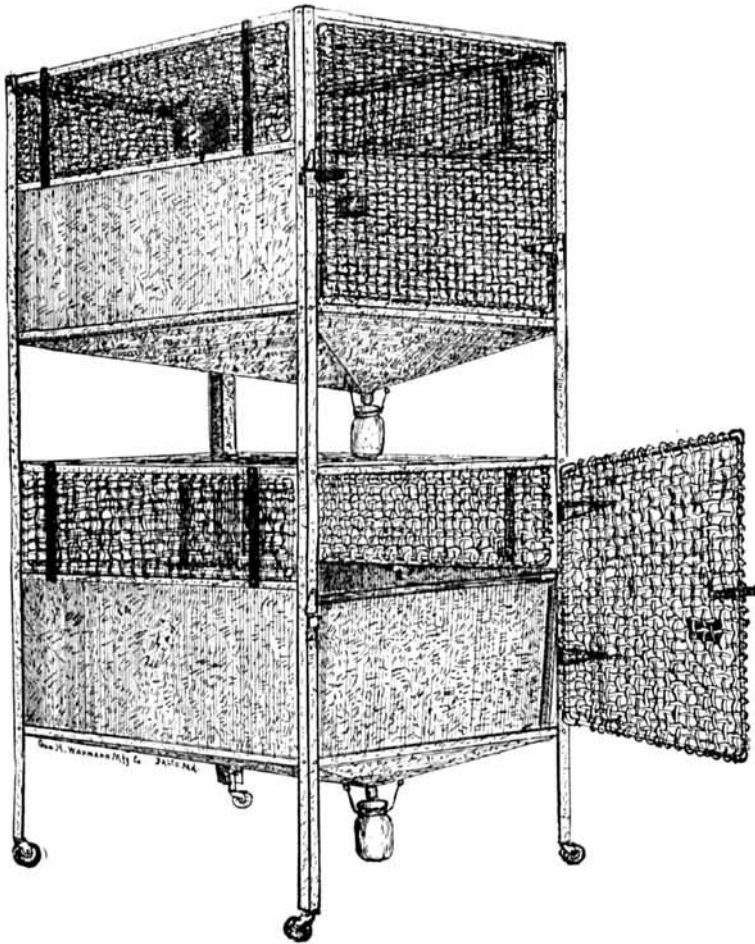


Fig. 6.—*Large Size Cage.*—The inside measurements of each cage are 22" wide, 32" deep, 22" high. The framework is of heavy angle iron. The door and sides are constructed of very heavy special steel wire mesh made over a framework of pipe. The bottom, slanting pans and sides are of heavy galvanized iron. The framework is of one piece from bottom to top to insure rigid construction.

should be removed at a time from the small individual cages and placed in the large cage for twelve to twenty-four hours.

Feeding.—The cat thrives best on a mixed diet of milk, meat, fish and vegetables. If fed too much meat or fish it will refuse vegetables. It is best, therefore, to finely grind the meat or fish and vegetables and thoroughly mix so it will be impossible for the animal to separate the meat or fish from the vegetables. The

meat may be either raw or cooked. Animals with a limited amount of exercise, however, should not be given an abundance of raw meat. When fresh fish is not available, canned salmon may be used to advantage. Oatmeal porridge serves as a variation which is acceptable to most cats.

Water.—Water should be supplied in vessels that may be quickly and thoroughly cleansed. Do not allow drinking water to remain day after day without change. Frequent change of water should be provided and placed where the sun will not shine upon it.

Fleas.—As a precaution against fleas the cages should occasionally be washed down with a solution of Sanax and steam sterilized. The tray supports should be dusted with a mixture of Sodium Borate and Sodium Fluoride. If the animals became infected with fleas, spray the cages and room with kerosene and wash the animals in a weak solution of Sanax. Care should be taken

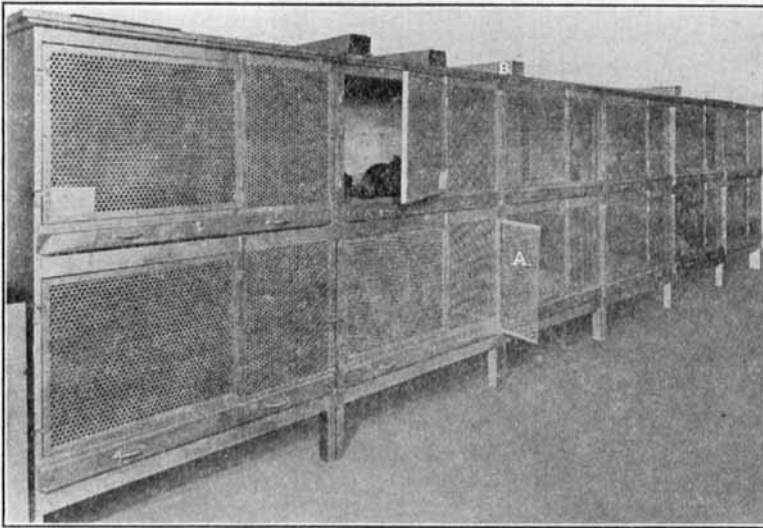


Fig. 7.—*Extra Large Cages.*—Designed by the author for housing roosters, dogs, cats, rabbits or guinea-pigs. The removable partitions make it possible to divide cage into any desired number of units from two to twelve. Each unit of the cage measures 48" long x 30" deep x 30" high.

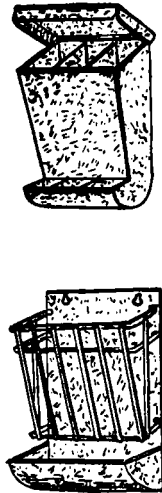


Fig. 8.—Three-compartment mash, grit and charcoal hopper and hay rack.

to thoroughly wash out the antiseptic solution with fresh water to prevent possible irritation of the skin.

Worms.—Are very often found in both the stomach and intestines of laboratory cats. The usual symptoms are those of intestinal irritation and the unthrifty appearance of the animal. The fur becomes harsh and dry and the abdomen distended.

The animal should be fasted for 12 hours and then given by mouth from $\frac{1}{10}$ to $\frac{1}{4}$ grain of Santonin with $\frac{1}{4}$ to 1 grain of Calomel depending upon the size and age of the animal. This should be followed after four to five hours with a dose of $\frac{1}{2}$ to 1 ounce of mineral oil administered by stomach tube.

Mange.—Two forms of this disease attack the cat, sarcoptic and follicular. Both are produced by a parasite which multiplies rapidly.

The ordinary or sarcoptic mange is due to a small parasite which burrows under the skin, where it deposits its eggs, which upon hatching become very irritating to the skin, as the young insects grow and tunnel out to the surface, where they breed for the next generation to burrow and deposit its eggs.

The sarcoptic mange may appear first on the face and cheek, or upon the insides of thighs and armpits, and may extend over the whole body. On account of the intense itching the animal will scratch itself, which produces abrasion, which scabs over and when scratched off becomes sores.

In follicular mange the parasite affects the nose around the muzzle, the skin of the chin and the skin of the paws, surrounding the claws, where it burrows in beside the roots of the whiskers and larger and grosser hairs, and into the sebaceous glands. On examination around the roots of the whiskers and on the skin of the paws, we find dark red pimples or pustules about the size of a pin head.

A cat with mange should be separated from the other animals, washed with antiseptic soap or a weak solution of Sanax or other antiseptic solution and one of the standard mange remedies applied.

Other Common Diseases of the Cat include catarrh, distemper, pleurisy, pneumonia, bronchitis, constipation and diarrhoea.

Constant attention should be devoted to the prevention rather than the cure of these diseases.

DOGS.

In the case of dogs for laboratory use, attention should be paid primarily to cleanliness, feeding, exercise and affection.

Kindness runs strong in a dog's nature. All domestic animals are sensitive to the kindness of their owners and attendants, but no animal is so dependent upon human sympathy as the dog. Laboratory dogs may, therefore, be handled more easily by an attendant who is fond of and kind to the animals than by one who simply cares for them as part of his necessary daily tasks.

Varieties.—For *blood pressure work* any type or breed of dog may be satisfactorily employed. Usually, however, a common mongrel, short-haired, medium-sized dog is to be preferred.

For *testing Cannabis* medium-sized fox terriers are the best. If there are not any available, medium-sized, short-haired, long-legged dogs are preferable to long-haired, short-legged dogs.

Housing.—Dogs which are kept indoors should be placed in cages of the design shown in Figs. 5 and 7. Trays should be filled with sawdust and changed daily. If the animals are kept outdoors they should be provided with kennels. The kennels should be protected from rain and cold and should be ventilated from the top in order to prevent drafts. The animals should not be allowed to sleep on cement floors as cement is often cold and damp and will cause rheumatism and lameness. If the floor is made of cement a bed of straw should be provided and frequently changed. The kennel entrance should be from the side rather than from the front to safeguard against rain and wind. If possible shade should be provided in summer.

Exercise.—Small and medium-sized dogs such as used for laboratory purposes require plenty of exercise. If the dogs are not given sufficient exercise they overeat, become sluggish and oftentimes sickly.

If the size of the animal house permits, three or four dogs should be housed together in two or more units of a cage of the type shown in Fig. 7 rather than kept in individual cages of the type shown in Fig. 5.

In the large cage the dogs play and run and romp together thus getting plenty of exercise. If lack of space makes it necessary to house each dog separately,

one large exercising cage should be provided in order that the animals may be exercised in groups.

Feeding.—Dogs especially when kept indoors are better off a little hungry rather than overfed.

Feeding but once a day is the custom at most large kennels, but I consider twice a day much preferable. Twenty-four hours is too long a period for the stomach to go without food, and the animal so fed will usually bolt the food without proper mastication. This is one of the chief causes of indigestion.

Dogs should not be fed continually upon the same diet of cooked or raw meat, starchy food or corn bread. Dogs thus fed suffer from fermentative indigestion. No one food contains the necessary protein, fats and carbohydrates. A single meat diet creates a distaste for other and more varied foods. Do not feed such meats as pork, veal, etc. Feed beef, mutton and, occasionally, liver. Do not feed lights or offal from slaughtering.

If the dogs are fed twice a day dog biscuits are an ideal food for *the morning meal*. They should be fed dry. For small dogs the biscuits should be broken into small pieces. Dog biscuits contain beef, cereals, ground bone and flour and, therefore, furnish a well-balanced diet. The hard biscuits provide exercise for the teeth and prevent bolting.

The evening meal should vary—otherwise it will become distasteful. Boiled vegetables, with meat should be fed during the summer months. Vegetables of all kinds except potatoes and corn (which are too difficult for a dog to digest) should be mixed with the boiled meat.

Soups that are not too greasy make excellent food and add variety to the diet. Dry broken bread or broken dog biscuits added to soupy food also adds variety.

In our laboratory we prepare the evening meal fresh daily. Small pieces of beef necks, flanks or butchers' scraps and bones are placed in a large pot and thoroughly boiled with plenty of water and a little salt. The bones are then taken out and a quantity of vegetables added and boiled to shreds. For variety the vegetables are replaced with rice, broken bread or dog biscuits.

Each dog is given some of the thoroughly cooked bone. This induces the dog to exercise his teeth and salivary glands while the small particles of bone gnawed off constitute nutriment to the bony structure.

Care should be exercised in the feeding of bones. Many dogs are injured by careless feeding of bones with sharp points or pieces which break off and are swallowed. Chipped bones are always dangerous. Small bones, such as chicken bones, splinter very easily and should never be fed as they are liable to cause trouble either by lacerating or puncturing the stomach or intestines.

Never let food stand around after meals. After the dog is through with its regular meals, remove all food, otherwise he will eat too often and too much.

Water.—Same as for cats. For dogs housed outdoors a pan placed under a dripping spigot makes an ideal dog fountain.

Fleas.—Same as for cats.

Worms.—If a dog has a ravenous appetite, does not seem to thrive and has a bloated appearance of the abdomen while thin elsewhere treat it for worms in the same manner as described for cats.

Mange.—Same as for cats.

Lice.—Lice cause great irritation which causes the animal to scratch and worry constantly. They live on all or any part of the body, but are usually most abundant about the head and face, the eyes, roots of ears and along the top of the back where it is hard for the dog to get at them. By closely examining the animal's skin, red streaks and spots of blood will be seen where the louse has been feeding.

A mixture of 40% Sodium Fluoride and 60% Talcum dusted upon the skin will kill the lice. Lice may also be killed by washing the animal in a solution of Sanax or some similar anti-septic. Care should be taken to prevent the solution from coming into contact with the animal's eyes.

If the cages and animal quarters are kept clean and are frequently sterilized, the animals will be free from lice unless the lice are brought into the cages by "new animals."

Nails.—The lack of hard ground and gravel in which the animal may scratch results in an abnormal growth of the nails. This makes it difficult for the animal to walk. The nails should, therefore, be clipped occasionally with bone clippers. Care should be taken not to clip the nail too close to the toe as this will cause bleeding. By careful observation the extent to which the blood enters the nail can be seen and by carefully avoiding the cutting of this part, bleeding will not occur.

(To be continued)

REPORT OF CONTACT COMMITTEE ON TABLETS.

The contact committees of the American Drug Manufacturers' Association and the American Pharmaceutical Manufacturers' Association have submitted to the Food, Drug and Insecticide Administration, United States Department of Agriculture, an extensive report in which they have indicated the degree of accuracy within which properly manufactured medicinal tablets can be made under present-day manufacturing methods. The report includes also methods of analysis for the tablets.

This is the third report submitted by the committees to the department. The previous reports related to hypodermic tablets.¹ The present one, in addition to amendments to the previous reports, includes suggested tolerances for ten of the more common compressed tablets.

The Food, Drug and Insecticide Administration, which is charged with the administration of the Federal Food and Drugs Act, has stated that in its activities in connection with the enforcement of the law it will give careful consideration to the recommendations of associations of manufacturers of products subject to the act. In promulgating the report of the contact committees the department invites comment from manufacturers, distributors, prescribers and any others interested in the preparations involved.

The tolerances recommended by the contact committees are as follows:

Hypodermic Tablets.			
Atropine sulphate	7.5 to 12% ²	Morphine sulphate	7.5%
Cocaine hydrochloride	9%	Nitroglycerin	15 %
Hyoscine hydrobromide	7.5 to 12% ²		
Compressed Tablets.			
Acetanilid	7.5%	Codeine sulphate	9 %
Acetphenetidid and salol	10 %	Phenolphthalein	7.5%
Calomel	7.5%	Salol	9 %
Calomel and soda	7.5 to 10% ²	Sodium bromide	7.5%
Cinchophen	7.5%	Strychnine sulphate	7.5 to 12% ¹

Complete copies of the report, including recommended assay processes for the various tablets may be obtained from the Food, Drug and Insecticide Administration, United States Department of Agriculture, Washington, D. C.

¹ See JOURNAL A. PH. A. for 1926, pp. 112 and 302. ² Depending upon the grainage.