

# Animal Health Research and Laboratory Animals

By TAKAYOSHI INO

Chief, Laboratory of Animal Research Section, 1st Division,  
National Institute of Animal Health

## Circumstances with great importance put on laboratory animals

Since 1950, as a distinctive feature of the scientific research trend at home and abroad, the investigating researches, examinations on the qualities, and expansion and completion of experimental equipment for laboratory animals have become remarkable as a matter of great concern in various branches of science—medicine, veterinary medicine, pharmacology, experimental psychology and biology.

As for the circumstances that have aroused such trend, it could be considered as follows:

1) Generally, researchers increasingly focused their attention to the quality of laboratory animals.

2) It is indispensable to use animals of good quality to perform research on the important subjects that still remain unsolved in the fields of medicine, veterinary medicine and pharmacology (tumor, high blood pressure, heart disease, diabetes, diseases of the aged, span of life, hereditary physical constitution and chronic infectious diseases).

3) The need to procure laboratory animals of good quality has been increased to testify the effect and safety of drugs produced by the pharmaceutical industry, and to examine the toxicity and safety of the food and its additional substances produced by the food industry.

Laboratory animals of good quality could be

specified as follows:

Their breeds and strains must be clearly classified, they must have adequate susceptibilities and resistivities to meet the demands of certain experiments, and they must be free from all pathogenic microbes and parasites as specific pathogen free animals.

Since 1950 in Japan, laboratory animal centers have been established at universities, national or private institutes in the fields of medicine, veterinary medicine and pharmacy, and then the system of production and supply of animals of good quality was developed progressively. And commercial animal breeders have also successively joined this project.

In Japan, research, production and supply of laboratory animals have been carried out by the investigators who graduated from the faculty of veterinary medicine or of zootechnical science. Recently, the schooling on laboratory animals has been promoted in the course of veterinary medicine at universities.

## Correspondence between animal health research and laboratory animals

Generally speaking, the kind of animals in our laboratory could be specified as follows: mouse, rat, hamster, guinea pig, rabbit, ferret, dog, cat, domestic animals (cattle, horse, sheep, goat, pig), poultry (chicken and quail) and furthermore the primates, reptiles, amphibia and the fishes.

The specification of the laboratory animals

for the researches on animal health in our institute is as follows: cattle, poultry, horse, sheep, goat, pig, chicken and honeybee, and as small laboratory animals, mouse, rat, hamster, guinea pig and rabbit.

The usage of these animals and poultry is as follows: cattle, horse, pig, chicken and honeybee are used for researches on their bacterial, virus, parasitic and metabolic diseases, and they are also used for the exploitation and examination of biological products, as vaccine. Sheep and goat have been used as the substitutions of cattle rather than for researches of their own diseases.

The small animals (mouse, rat, hamster, guinea pig and rabbit) have been used for the following purposes: (1) infection test, immunity test and evaluation test of bacteria and viruses. (2) Efficacy test, safety test and toxicity test of biological products. (3) Stock culture and serial passage of bacteria, viruses and parasites. (4) Preparations of tissue culture cells, immune serum and complement<sup>2)</sup>.

Until 1960, these laboratory animals had been supplied by dealers. Consequently, their strains and ages were obscure. Sometimes they were ill-fed and infected with parasites or pathogenic microbes; therefore, many obstacles arose in the performance of experiments and bioassay.

During 1961-1962, the laboratory animal center was established in the National Institute of Animal Health to produce and supply the inbred strains of small animals (mouse, rat). During 1965-1966 facilities for SPF pig production and a laboratory for infection experiments on SPF pig were set up. As for the chicken, an avian leukosis virus free flock and a flock susceptible to leukosis virus were produced.

These home-production systems of laboratory animals have been established in our and other institutes with the intention of producing and supplying healthy animals, instead of inadequate animals supplied by dealers.

These animals should be genetically con-

trolled as inbred strain, mutant strain and closed colony, and also they must be free from all pathogenic parasites and microbes.

The laboratory animals that were supplied by dealers up to this time were not so good. Occasionally, they were obscure with their strains and ages, and they were often ill-fed, and the parasites or microbes were kept in them.

Thus since 1961, the system for production and supply of laboratory animals of good quality has been promoted progressively in our institute.

In 1971, a laboratory was newly established for laboratory animal research. Research on genetic and disease control of animals, and their heredity and production will be carried out in this new laboratory.

## Summary of experimental results

The researches on the laboratory animals conducted at the National Institute of Animal Health could be classified as follows.

1) Researches on small animals (mouse, rat, etc.).

2) Researches on the production and infection experiments of SPF pigs.

3) Researches on the production of chicken flock free of avian leukosis virus and the production of chicken strains susceptible to avian leukosis virus.

### 1) Results of experiments on small laboratory animals

In 1961, 13 inbred strains of mice (C3H/He, C57BL/6, CFW, CF<sub>1</sub>, AA, DDD, DDK, DSD, DDY, KK, NC, RR, SS) and one strain of rats (Wistar-Imamichi) were introduced to our laboratory, and their productive qualities (growth, reproduction, milk production), their sensitivity and resistibility against bacteria and viruses, and their reactions to hormones and medical drugs were examined<sup>1),2)</sup>.

As for the bacteria, each strain was tested

for the sensitivity to *Bacillus anthracis*, *Microbacterium johnei*, and *Staphylococcus aureus*, and for the sensitivity and immunity against tetanic toxin. And as for viruses, each strain was tested for sensitivity to Japanese encephalitis virus, rinderpest virus, bovine ephemeral fever virus, Ibaraki virus and bluetongue virus. And experiments were carried out in succession on their infections<sup>1),2)</sup>.

With the results of these investigations, it has been shown that there exists a difference in sensitivity to bacteria and viruses among the various strains of mice and that therefore, the strains of laboratory animals used for infection experiments or toxic quantitative analysis of bacteria and viruses must have been carefully selected before the experiments are undertaken.

As for the reactions to hormones and medical drugs, the human chorionic gonadotrophin (HCG), pregnant mare serum gonadotrophin (PMSG), malformation inducing activity of cortisone and diabetes caused by alloxan were examined. It has been recognized that there also exists a difference in reaction among the strains and that this difference is controlled by the law of heredity<sup>2)</sup>.

### 2) *Results of experiments on the production and infection of SPF pigs*

During 1965-1966, facilities for the production and a laboratory for infection of SPF pigs were established in the National Institute of Animal Health. They were the first of their kind in Japan. Young's method has been practically applied to these establishments, but the operating hood, isolator, germ-free diet and artificial milk have been exploited and improved originally<sup>3),4)</sup>.

The SPF pigs that were produced at facilities were free from all known pathogenic bacteria and viruses, and negative for *Lep-tospira*, PPLO (*Mycoplasmatales*) and *Toxoplasma*.

From the results of microbiological examination, it has been certified that the SPF pigs produced in this institute were available widely for the experiment of pig disease<sup>5)</sup>.

Furthermore, in this institute, infection experiments on transmissible gastroenteritis in pigs (TGE), Japanese encephalitis and swine enzootic pneumonia (SEP), research on hog cholera and its live virus vaccine, research on the developmental mechanism of scours in piglets, and immunoglobulin research have been carried out with these SPF pigs, and many important results have been obtained from them.

### 3) *Production of avian leukosis virus free strain of chickens, and production of a strain of chickens susceptible to avian leukosis*

Avian leukosis is a well known disease that causes considerable damage to poultry raising in the world. Therefore, to produce a virus free strain of chickens and a strain of chickens susceptible to this disease is a very important problem for research on this disease and for the exploitation of its vaccine.

Since 1964, Shimizu et al. have succeeded in exploiting a virus free strain of chicken by the resistance inducing test (RIF) with the selecting method for propagation on the White Leghorn which has been contaminated with the viruses of this disease, and also, they have succeeded in selecting out from these flocks the dam and sire which have susceptibility or resistivity to this disease.

And they have examined the genetic factor which rules these susceptibilities or resistivities by the experiment on the hybrid of these dam and sire. Consequently, they have manifested that these susceptibilities and resistivities are controlled by heredity of a single gene, and that the susceptibility gene (SS) dominates over the resistivity gene (ss).

At present, in our institute, researches on avian leukosis are carried out with these virus-free or virus-susceptible strains.

In future, laboratory animals with well defined qualities, genetical factors and disease-controlled will become indispensable to make clear the unsolved important themes of animal health research.

## References

- 1) Imagawa, T.D.: Propagation of rinderpest virus in suckling mice and its comparison to murine adapted strains of measles and distemper. *Arch. Ges. Virusforsch.*, **17**, 203-215 (1965).
- 2) Ino, T.: Laboratory animals: Main problems and results of research. *Bull. Nat. Inst. Anim. Hlth.*, No. 62, 237-251 (1971). [In Japanese.]
- 3) Kashiwazaki, M. et al.: Studies on the rearing of germ-free pigs. 1. A germ-free rearing isolator apparatus and procurement of baby pigs. *Bull. Exp. Anim.*, **16**, 85-92 (1967). [In Japanese with English summary.]
- 4) Kashiwazaki, M. et al.: Studies on the rearing of germ-free pigs. 2. Rearing of germ-free pigs in isolators. *Bull. Exp. Anim.*, **16**, 93-98 (1967). [In Japanese with English summary.]
- 5) Namioka, S. et al.: Microbiological evaluation of an isolation facility for the production of specific pathogen free pigs. *Japan Jour. Vet. Sci.*, **29**, 21-32 (1967). [In Japanese with English summary.]
- 6) Shimizu, T. et al.: Development of a chicken flock free of avian leukosis viruses. *Bull. Nat. Inst. Anim. Hlth.*, No. 57, 9-15 (1968). [In Japanese.]
- 7) Young, G. A.: SPF swine. *Adv. Vet. Sci.*, **9**, 61-112 (1964).