XVIII. MINIATURE SWINE*

A. INTRODUCTION

1. General Characteristics

The general biological characteristics of miniature swine are essentially the same as those of conventional domestic pigs. The one major exception to this is in mature adult weight which in miniature swine will usually level off at from 70 to 90 kg, approximately that of man.

In anatomy and physiology the pig is remarkably like man. Its heart and circulatory system, its diet, its alimentary tract and even its teeth are very similar to those of a human being. Researchers have long been aware of the potential value of these similarities for the development of swine models in specific studies. However, in practice, the use of the standard farm pig has had to be pretty much limited to relatively short-term studies on post weanling piglets, due to its rapid growth (100 kg by five to six months) and ultimate size (250-300 kg or more).

It should be pointed out that the decision to undertake research with either conventional or miniature swine requires both physical resources and people who have, or are willing to develop, new expertise. Work with pigs also places some physical demands on individuals who may not be used to working with strong, heavy animals.

Miniature pigs have become recognized as a useful research animal over the past 20 years, during which period several different strains have been developed and their characteristics described (Weaver and McKean, 1965; Bustad and McClellan, 1966; Bustad and McClellan, 1968; McIntosh and Pointon, 1981; Dettmers and Rempel, 1968; Mount and Ingram, 1971; Pond and Houpt, 1978).

2. Strains and Behavior

The initial two strains to become established were:

a. The Hormel, developed at the Hormel Institute of the University of Minnesota (Dettmers and Rempel, 1968).

b. The Pitman-Moore strain, developed by the pharmaceutical company of that name from a wild variety originally found in a Florida swamp (Bustad and McClellan, 1968).

More recently, several other strains of miniature swine have been developed throughout the United States, Europe, and most recently, Australia (McIntosh and Pointon, 1981). Active breeding programs for the development of further strains continues. Selection in miniature swine is directed towards behavior and reproductive characteristics, as well as size.

Pigs including miniature swine, are usually curious, occasionally aggressive, and inclined to object to being disturbed and handled (Fraser, 1980). Sows with litters are generally protective of their offspring, with the occasional exception of their first litters (Signoret, Baldwin, Fraser *et al.* 1975).

Colorado State University has developed a colony of Yucatan miniature pigs (Mexican Hairless) (Panepinto, 1979; Panepinto, Phillips, Wheeler *et al.* 1978). This strain is reported to be very amenable to handling, as opposed to most others which object to restraint and consequently very often require sedation or anesthesia. A further advantage of the Yucatan strain is the absence of hair, which reduces the need for shaving and results in less odour within the laboratory (Panepinto, 1979). A disadvantage is that colder environmental temperatures must be avoided (Panepinto, Phillips, Wheeler *et al.* 1978).

3. **Research Uses**

The pig offers a closer analogy to man in almost every way than do the commonly used laboratory species such as the rat and the dog. The skin of the pig is similar to that of man, excepting in its sweat glands, while the similarities between the newborn pig and human infant are remarkable, particularly in such areas as carbohydrate and temperature regulation. Young pigs will learn readily and, at least for a few weeks, can be maintained under gnotobiotic conditions.

Miniature swine develop stomach ulcers and cardiovascular diseases resembling those in man. Both standard and miniature pigs have proven particularly useful in the study of heart and vascular disease problems, from coronary circulation through atherosclerosis, with particular regard to the nutritional aspects of the latter condition (Sandes, White, Peterson *et al.* 1978; Weaver, 1968; Rowsell, Mustard, Packman *et al.* 1966; Reitman, Mahley and Fry, 1982). Miniature pigs have also provided many other useful models for the study of a wide range of biomedical problems in such diverse areas as diabetes, dental research, nutrition, oncology and renal physiology (Phillips, Panepinto, Spangler *et al.* 1982; Jump and Weaver, 1966; Strafuss, Dommert, Tumbleson *et al.* 1968; Suarez, 1968).

B. **HUSBANDRY**

1. **Housing**

Miniature swine may be raised in ways comparable to those used for standard domesticated swine herds. However, in the laboratory situation, these animals are usually housed in rooms with metal pens on concrete floors. Each mature animal should be provided with 1.5 to 3.0 square metres of open space per animal. The partitions should be at least 0.6 metres high.

Animals raised on concrete should always be provided with ample bedding, either of sawdust, wood shavings or chips. The behavioral and physical effects of flooring on piglets and sows have recently been explored by Gravas (1979). A suitable dry area where each animal can lie out to its full extent must be available in each pen.

Elaborate and special facilities are not necessary for holding miniature swine and, as a general rule, a facility equipped to handle large dogs may be easily modified to handle them (Panepinto, Phillips and Norden [in press]).

2. Maintenance

The rooting instinct and considerable strength of swine make it essential to firmly secure the feed and water sources in each pen. Sows tend to be clumsy and will often lie on and squash piglets against a solid pen wall. Provision of guard rails in farrowing pens is therefore necessary for the protection of the piglets unless a farrowing crate is available.

It may also be appropriate to provide diversions within the pen, such as a suspended tire, as a relief from boredom, particularly where pigs are caged singly.

Weaning usually takes place at about six weeks of age and litters of weanlings may be placed together in large holding pens prior to segregation by sex and placement into smaller (experimental) groups. This practice will help to prevent the fighting and the possible injury which can occur when animals are first separated and then placed back together. Segregation according to sex should be undertaken by approximately four months of age.

If tie stalls need to be utilized, the same care in acclimatization and monitoring the pigs' comfort must be practised as is recommended for conventional (farm) pigs in Volume 1 of this Guide.

3. Nutrition

The nutrient requirements of the pig are similar to those of man and are well known, which enhances its value as a model for the study of certain nutritional problems in man (St. Clair, Bullock, Lehner *et al.* 1971; Tumbleson, Tinsley, Corwinn *et al.* 1969; Baker, Anderson and Eash, 1970; Hartsock and Graves, 1976; NRC [U.S.], 1973).

Commercial pelleted hog rations will prove quite satisfactory for growth and maintenance. Information on a specific all purpose diet for these animals is also available (Panepinto, Phillips, Wheeler *et al.* 1978). Water should be provided *ad lib*.

Given the opportunity, miniature swine become markedly obese. It is therefore beneficial to restrict food intake. Their appetites will not usually be affected, even temporarily, by changes to any one of a variety of experimental diets, a characteristic that enhances their usefulness in studies into the effects of various diets on body systems.

4. Breeding

The reproductive physiology of the miniature pig is essentially the same as that of the various breeds of domestic swine. First estrus usually occurs at approximately 200 days (range of 150 to 250). Cycle duration is 21 days with

a range of from 19 to 23 days. Estrus will last from three to five days. During the proestrus stage, which lasts from one to three days, the gilt is alert and conscious of the approach of the boar. She will have a tendency to mount others and permit other diestrus females to mount her; however, she will not allow the boar to mount.

Estrus is recognized in the gilt by swelling and reddening of the vulva, and a vaginal discharge. Other signs include restlessness, mounting other females and frequent urination. The sow will permit coitus over a two, sometimes even a three day period during estrus. Ovulation usually occurs from mid to late estrus. Diestrus follows, during which time the gilt will fiercely reject the boar.

The average gestation period is 114 days.

Spermatogenesis will occur in the boar by six months; however, it is preferable if he is not used for breeding until eight months of age.

C. HANDLING

1. Identification

As with all laboratory animals, proper identification of the individual in a laboratory herd is essential. Temporary marking can be carried out by the use of crayons or metallic or plastic ear tags. More permanent identification will require the use of such techniques as tattooing and freeze branding. These are preferable to the ear notching techniques that are commonly encountered in swine herds.

2. Physical Restraint

Swine, in general, tend to resist most forms of physical handling and although they are rarely vicious many can be quite aggressive; consequently, care must be exercised at all times. Gentle but forceful application of appropriate methods and techniques by experienced individuals will usually effect the necessary restraint required. A popular device readily available is a snare which may be tightened around the upper jaw just caudal to the canine teeth. The snare should be of such material as to minimize the trauma to the gingiva and other soft tissues.

In the laboratory, placing the animal on its back in a "V" shaped trough may sometimes be a satisfactory way of controlling smaller pigs for such procedures as blood collection and injections. This method of restraint will require the participation of two or more individuals, depending on the size of the animal. If manpower is in short supply, the use of chemical restraint may be necessary.

A method of restraining small laboratory swine using a restraining rack and canvas sling has been described (Tumbleson, Dommert and Middleton, 1968). It has been claimed that manipulations such as blood sampling may be

performed on the docile Yucatan miniature pig by one person alone with the sling restraint procedure (Panepinto, Phillips and Norden [in press]).

3. Chemical Restraint

The method of choice in chemical restraint will usually be dictated by the procedure contemplated. The chlorpromazine, acepromazine tranquilizers are generally quite satisfactory when used at dosages ranging from 0.5 to 4.0 mg/kg. Diazepam has also proven a very satisfactory tranquillizing agent in miniature pigs when used at a dosage level of approximately 0.5 mg/kg i.m.

D. ANESTHESIA

Prior to administering general anesthesia to members of this species, one or more of the excellent textbooks available that deal with anesthesia in domestic animals, should be consulted (Soma, 1971; Lumb and Jones, 1973).

1. Sedation Procedures

Minor surgical procedures can be carried out using various neuroleptic agents. A combination of acetylpromazine (10 mg/ml) and etorphine (2.25 mg/ml), at a dosage rate of 0.5 ml/50 kg is rapid acting, producing recumbency in approximately two minutes (Booth, 1977). The etorphine antagonist, diprenorphine, at a dose of 0.5 ml/kg will reverse this effect.

A ketamine dosage rate of 20 mg/kg is useful as a sedative for minor surgical procedures and also can be used as a preanesthetic agent. Diazepam (10 mg/kg) is an effective sedative, which maintains its effect for up to six hours.

2. Intravenous Anesthesia

The intravenous administration of sodium pentobarbitol at the usual anesthetic dose of 20-30 mg/kg, usually via an ear vein, provides satisfactory anesthesia, especially when prolonged sedation is desirable. Sodium pentothal, 10-15 mg/kg intravenously, will produce general anesthesia of approximately 15 minutes duration.

A useful anesthetic combination in miniature swine is to pretreat with atropine sulfate (0.04 mg/kg) 10 to 20 minutes before giving a combination of ketamine hydrochloride (25 mg/kg) and acepromazine (0.5 mg/kg). This immobilizes the pig and is eminently suitable for manipulations, such as blood sampling, that require less than 20 minutes. There is a wide margin of safety with this combination and higher dosages have not caused problems. Prolonged anesthesia following ketamine/acepromazine pre-treatment can be maintained with thiopental sodium to effect (6-10 mg/kg).

3. Inhalation Anesthesia

Inhalation anesthesia in the pig should be preceded, approximately 15-20 minutes, by premedication with atropine, at a dosage level of 0.04 mg/kg. If reflex bradycardia occurs during surgery, up to 0.05 mg/kg in addition may be required to return to normal sinus rhythm.

As with other species, initial anesthesia is usually induced with intravenous barbiturates, with surgical anesthesia being maintained with halothane. Halothane is delivered through a vaporizer by means of oxygen. Nitrous oxide may also be used in combination with the oxygen at a ratio of about 1:2, thus reducing the amount of halothane required. With oxygen alone, 4% halothane is usually necessary during the induction period and approximately 2% is necessary to maintain surgical anesthesia.

4. Special Precautions

Because endotracheal intubation is somewhat difficult for anatomical reasons, specially constructed laryngoscopes with long blades should be considered. In the pig, endotracheal tubes should be used to assure ropery delivery of the anesthetic gases, and thus a safer anesthesia. A properly fitted endotracheal tube also overcomes the risk of aspiration of vomitus. Anesthesia for both standard and miniature swine has been the subject of several specific publications (Roberts, 1971; Piermattel and Swan, 1970).

A potentially lethal hyperthermia occurs with some frequency, in certain breeds of swine, particularly when exposed to halothane (Nelson, Jones, Venable *et al.* 1972). Succinylcholine appears to act as a potent activator to the malignant hyperthermia (MH) syndrome in both swine and humans (Harrison, 1979). MH is closely linked to porcine stress syndrome, a condition responsible for significant economic losses to the pork producing industry. The prevalence of these conditions in swine in Ontario, and the greater sensitivity of the halothane/succinylcholine screening test over halothane alone has recently been reported (Seeler, McDonell and Basrur, 1983). An investigation on MH induction by comparison of five inhalant anesthetics in MH sensitive swine has shown nitrous oxide and methoxyflurane to give a significant reduction in MH reactions (McGrath, Rempel, Jessen *et al.* 1981).

E. SPECIAL CONSIDERATIONS

1. Blood Sampling

The miniature swine as a laboratory animal poses some problems with respect to accessibility of blood vessels for vein puncture and blood sampling. The external jugular is not superficial and presents some difficulty in achieving a good venipuncture. The ear veins can be used for injections or blood withdrawal; however, repeated venipuncture is not well tolerated.

Ragan and Gillis (1975) reported on a technique for the venipuncture of the anterior vena cava, in either standing or dorsally recumbent pigs, which involves a "blind procedure" that apparently, with practice, is easily mastered.

In smaller sized miniature pigs, venipuncture may be reliably carried out using the saphenous vein, employing essentially the same technique as that used in the dog. However, because the skin of pigs is much thicker than that of the dog, venous distention must be palpated rather than visualized. Small blood samples may also be obtained from the orbital sinus of swine (Tumbleson, Dommert and Middleton, 1968; Huhn, Osweiler and Switzer, 1969).

2. **Catheterization**

Chronic catheterization is frequently employed in research on miniature swine. Chronic indwelling catheters must always be well protected and close confinement, often with sedation, is usually considered necessary when conducting these sorts of chronic experiments. However, a small, sturdy metal box device has been described for this purpose which reportedly allows for relative freedom of movement, and does not dictate use of a specially prepared or individual pen, as the animals were unrestrained for 14 days in the study reported (Wachtel, McCahan and Alford, 1976).

3. **Devocalization**

One objection to working with pigs has been their squeal, which may prove particularly unacceptable in certain research laboratory settings (such as those associated with hospitals). Pigs may be surgically devocalized as a means of overcoming this problem (Mackey, Anderson and Kubicek, 1970).

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