XIII. GUINEA PIGS*

A. INTRODUCTION

1. Origin and History

a. **Hystricomorph Rodents**: Guinea pigs are the only members of the rodent suborder Hystricomorpha that are widely used as laboratory animals. The only other member of this suborder which would be familiar to most Canadians is the chinchilla which, although rarely encountered in the laboratory, has been widely bred as a fur animal from time to time over the past 50 years.

Several other hystricomorph species have been raised in captivity, both for their fur and, to a lesser extent, for use as experimental animals. Species that have been used in the latter capacity include the coypu or nutria, the agouti, the acouchi and the wild guinea pig (Weir, 1976). All the Hystricomorpha are indigenous to South America, Central America, or the Caribbean Islands.

b. **Guinea Pigs**: The ancestors of today's laboratory guinea pigs (*Cavia porcellus*) were probably first introduced into Europe from South America some 400 years ago. Several species of wild guinea pigs are distributed through the Andean highlands and the plains of South America and have for centuries been more or less domesticated by the Indians of those regions as a food animal (Wagner, 1976).

A brief but informative review of the history and etymology of the present-day guinea pig or cavy may be found in the Introduction to "The Biology of the Guinea Pig" (Wagner and Manning, 1976) which is a comprehensive general reference work that should be available and familiar to all persons intending to maintain and use the guinea pig for research or test purposes.

During the several centuries that guinea pigs have been raised in Europe and North America as pets, three major varieties have been developed. By far the commonest of these, particularly for laboratory work, is the English or short-haired variety. The Peruvian or long-haired variety and the Abyssinian, with relatively short-hair formed into whorls, are more often encountered as pets.

The Dunkin-Hartley strain of short-haired guinea pig, developed in Great Britain in the late 1920's, and a number of its substrains, are the most widely used in research and testing laboratories today. Several of these substrains, and a few inbred strains with special characteristics, are available commercially (NRC U.S., 1979).

2. Characteristics

a. **General and Behavioral**: Guinea pigs, in common with most rodents of the suborder Hystricomorpha, differ from those of suborder Myomorpha (gerbils, hamsters, mice, and rats) in having a cellular membrane that

closes over their vaginal orifice, excepting at estrus and parturition (the coypu is an exception to this).

Hystricomorphs are also characterized by their relatively long gestation periods, which in most exceed 100 days, and by the precocious state of development of their young at birth (Rowland and Weir, 1974).

In addition to the general group features mentioned above, the guinea pig also exhibits several characteristic behavioral traits, including being nervous but tame and easily handled, a tendency to "freeze" at an unfamiliar sound, and to "stampede" as a group at a sudden, unexpected movement. While male guinea pigs may occasionally fight, there is no fighting between the sexes or amongst females. As the guinea pig has a poorly developed capability for either jumping or climbing, it may be held in a low walled, open topped pen.

b. **Biological Features**: The guinea pig is tailless, has constantly erupting hypsodont teeth and a cervically located thymus that is relatively easy to remove surgically.

The female has only two nipples and mammary glands, located in the inguinal region. Despite this, litters of four or more are commonly raised without difficulty.

The mature male develops extremely large seminal vesicles (vesicular glands) that pass forward as twin horns in the ventral abdominal cavity. These striking accessory male sex glands have, on occasion, been confused with uterine horns and incorrectly linked to pseudohermaphrodism (Russell, 1980).

Physiologically and immunologically the guinea pig may often respond unfavourably to antibiotic therapy and to stress. Smooth muscle contractions of the bronchial tree, in response to the release of histamine, may be extremely severe and even prove lethal in this species (Harkness and Wagner, 1983).

3. **Research Uses**

The preeminent position held by the guinea pig as a research animal during the 19th and early 20th centuries has become enshrined in our vocabulary the use of the term "guinea pig" to describe of us who, willingly or otherwise, are subjected to a test situation.

A number of factors have contributed to the popularity and widespread use of guinea pigs in animal-based research. One of these undoubtedly is the ease with which it may be handled and maintained within the laboratory. Its sensitivity to a variety of infectious diseases that affect man and other animals is a further factor enhancing its usefulness, particularly as a diagnostic test animal in microbiology, its most constant and extensive use having been in that discipline. In recent years, the numbers of guinea pigs used, particularly in tuberculosis testing, have declined greatly with the

development of acceptable in vitro procedures. Despite this, very considerable numbers are still needed in microbiology laboratories and, if anything, increasing numbers are being used as bioassay tools and research animal models in nutrition and other areas of study.

B. HOUSING

1. Environment

The guinea pig can tolerate a wide range of environmental temperatures, particularly if housed in pens on solid floors. Optimal temperatures for breeding and raising guinea pigs range from 16-24°C (61-75°F), with a temperature of 20°C (68°F) being generally quite satisfactory. High temperatures of 32°C (90°F) or above should be avoided, as this species has difficulty in dissipating heat from its body and therefore is subject to heat prostration. A 50-60% relative humidity will be found to be satisfactory.

High relative humidities, low ambient temperatures, undue fluctuations in temperature, inadequate ventilation, and drafts should all be avoided in the guinea pig holding area, as these animals are susceptible to respiratory diseases. Adequate ventilation is of particular importance as ammonia in concentrations as little as 20 ppm can be harmful to guinea pigs (Seltzer, Moum and Goldhaft, 1969).

Sudden noises and unexpected movement may cause these high strung animals to panic and, where housed in large pens, to stampede, with the possibility of injury. Pens with open sides of perforated metal or wire will reduce the likelihood of stampeding and have the added advantages of ease of observation and better ventilation.

2. Caging

a. **Mesh Floors**: Guinea pigs may be successfully raised on wire mesh floors. However, when using this type of flooring, it is important that the wire should be smooth and of a mesh small enough to preclude injuries to the feet and legs of animals of various ages and sizes. Guinea pigs under 350 g require a mesh of approximately 10 mm (3/8 in) made of 10-12 gauge wire; larger animals need a 16 mm (5/8 in) mesh of 9-10 gauge.

   Wire floor cages are frequently used for ease of maintenance in short-term holding and rearing, but are not well suited to either long-term holding or breeding (Ediger, 1976).

b. **Solid Floors**: Cages with solid floors and bedding have decided advantages for holding guinea pigs over extended periods and in breeding colonies. Shavings, woodchips, and similar synthetic materials are satisfactory for bedding. The use of sawdust alone or any other fine material is not recommended because of the tendency of the small particles to adhere to the vulva, scrotum, and prepuce, causing irritation and occlusions, with a resultant reduction in fecundity.

Various types of plastic or metal shoe-box type cages are available commercially. It is preferable that metal cages be of stainless steel, as galvanized surfaces will quickly become damaged from scraping to remove urine scale.

Breeding facility cages will vary with the breeding system in use. Bin type or floor pens are used for harem breeding. Bins are usually 75 x 75 x 25 cm (30 x 30 x 10 in) but may be of any desired dimension that will fit onto the racks available. Bins with low sides should be provided with an inward overlapping guard or be tiered in such away as to prevent escape. A 40 cm (15.7 in) wall is of more than sufficient height to hold adult guinea pigs in their enclosure. Floor pens, though favoured by some on the basis of size and flexibility, have the disadvantage of being wasteful of space and difficult to thoroughly clean; they are, however, both inexpensive and easy to construct.

Based on convenience, economy and ease of sanitization, plastic shoe box experimental cages and plastic drawer-type holding bins constitute the caging of choice for the laboratory guinea pig colony.

C. NUTRITION

1. Nutrient Requirements

a. **General**: The total dietary requirements of the guinea pig are not clearly understood. The National Research Council (USA) has published nutrient requirements for the guinea pig that are generally accepted for use in formulating their rations (NRC U.S., 1978).

There is evidence to suggest that, in stressful situations, the guinea pig may have a requirement for fibre (cellulose) higher than that provided by commercial diets. Such fibre can be provided by feeding hay, greens or carrots. The value of such supplementation has not been clearly defined; however, observations have persisted that the condition and performance of animals so supplemented will be superior to those fed solely on commercial pellets (Ash, 1975).

If supplements of hay or greens are to be fed, care must be taken to assure that their source, selection and storage is such that they will not constitute a means of introducing infection to the animals. It has been recommended that hay be sterilized (Laboratory Animals Centre Diets Advisory Committee, 1977). In this regard, it is inadvisable to make use of superfluous or discarded greens from supermarkets or institutional kitchens. An acceptable criterion for quality of fresh fruits and vegetables for feeding to laboratory animals is that they be fit for human consumption; anything less may jeopardize the health of the colony.

b. **Vitamin C**: Guinea pigs, like primates, are unable to synthesize Vitamin C (ascorbic acid) in sufficient quantity to meet their daily requirements. It is therefore essential that their diet be supplemented with this vitamin.

Insufficient amounts of Vitamin C in the diet will lead to general debilitation, increased susceptibility to disease and, eventually, to scurvy. The immune response may also be altered if Vitamin C levels are less than optimal. Adult guinea pigs require approximately 10 mg/kg of this vitamin daily for growth and maintenance, whilst up to 30 mg/kg will be required during pregnancy (Harkness and Wagner, 1983). Normal daily uptake from a diet containing 200 mg/kg should provide adequate amounts of ascorbic acid, and most commercial guinea pig diets are fortified with Vitamin C to provide this level. However, as this vitamin tends to be unstable, levels may fall below minimal requirements in diets stored improperly or for long periods. Most manufacturers stamp the date of manufacture on the feed bag and recommend that the diets be fed within 30 to 60 days.

Storing the diet in a well ventilated area, in a refrigerated storeroom, will prolong the stability of the vitamin and general quality of the diet.

In order to assure adequate levels of Vitamin C, guinea pig diets are very often supplemented either by:

i. feeding greens, such as kale, cabbage and spinach (see above for precautions), or

ii. adding ascorbic acid to the drinking water. Where the latter practice is followed, it is necessary that a fresh supply of the vitamin be provided daily, in water bottles at a rate of at least 200 mg/L. The reason for this is that ascorbic acid undergoes rapid oxidation, which will be enhanced by heat and catalyzed by copper. If Vitamin C is to be provided at effective levels in the water, a non-copper water delivery system and frequent preparation of the drinking solution are therefore essential.

2. **Feeding**

Food consumption will vary widely with the age, environment and physiological state of the animal. Under normal laboratory conditions, the average adult will eat in the neighbourhood of 60 g/kg in a series of small meals throughout the day.

Commercial pelleted guinea pig feeds will generally prove to be satisfactory provided the precautions referred to above are taken. Most such feeds will contain approximately 20% protein, which will usually prove to be adequate to meet the specific amino acid demands for growth and reproduction in this species (Navia and Hunt, 1976).

Feeds should probably contain about 16% fibre, and those with levels below this should be supplemented with hay or fibrous vegetables such as carrots. The feeding of hay as well as of vegetables has been persistently linked with improved productivity (Ediger, 1976; Ash, 1975; Laboratory Animals Centre Diets Advisory Committee, 1977), although still a subject of controversy (Harkness and Wagner, 1983).

A supply of fresh drinking water should be available at all times. Adults may drink up to 40 ml or more daily and will often use much more water than that through wastage, as guinea pigs are notorious for playing with emitters. This vice may cause excessive wetting of bedding, or even a severe flood in a shoe box type of cage. Automatic watering systems should not be used with guinea pigs because of this habit. Other bad feeding habits that are common amongst guinea pigs in captivity are those of excessive wastage of feed and of defecating in their food; the latter vice can be controlled by use of a J-type feed hopper.

D. REPRODUCTION

1. Breeding Stock

a. **Sexing**: The guinea pig sow has a vaginal closure membrane: a cellular structure closing off the vaginal orifice except at the times of estrus and parturition. This membrane can be exposed if the area over the genital ridge is gently stretched by thumb and forefinger pressure to each side of it. The membrane, when relaxed, forms a shallow, U-shaped crease between the anal and urethral openings. There is no crevice between the anal and urethral openings of the male. Digital pressure, as described above, will extend the penis. The testes may also be palpable in the male.

b. **Maturation**: Newborn guinea pigs are in a relatively advanced state of development and mature very rapidly. They will usually commence to eat solid foods of their own volition by the fifth day and may be weaned at 14 days if necessary, although 21 days is a preferable age.

Young sows may attain sexual maturity as early as four to five weeks of age, depending on genotype and environment. Early sexual maturation presents a problem in harem mating systems, as the boar may breed his early maturing daughters before they have been separated out. Early maturation notwithstanding, the young sow is best mated at between two and a half to three months of age or at 450 to 600 g. First mating should be undertaken well before six months of age, at which time the pubic symphysis becomes more rigid. Male guinea pigs are slower maturing than their female sibs and, although they may show some sexual activity by about six weeks, they will not produce sperm for fertile matings before about nine weeks of age.

c. **Estrous Cycle**: Duration of estrous cycle will range from 13 to 20 days, averaging 16 days, and is divisible into the standard stages of proestrus, estrus, metestrus and diestrus. Coitus will usually occur at night, during a six to 15 hour period of heat, at which time the vaginal closure membrane may be perforated.

Ovulation is spontaneous, occurring towards the end of the period of estrus. There is also a spontaneous ovulation that regularly occurs a few hours post partum. About 80% conceptions will accrue from post partum matings (Ediger, 1976; Festing, 1976).

Matings can be confirmed by observing the presence of a vaginal plug or by detection of sperm in a vaginal smear.

d. **Gestation**: Normal gestation averages 63 days with a range of from 59 to a maximum of 72 days. Gestations of more than 72 days invariably result in stillborn litters. Stillbirths and neonatal deaths contribute about equally to an approximate total incidence of 18% in this species (Festing, 1976).

   Average litter size at birth should number a little more than four in outbred stock, but usually considerably less in inbred strains.

   The newborn guinea pig, as is typical of hystricomorphic rodents in general, will be relatively mature, with hair, erupted teeth and open eyes.

   The sow becomes extremely heavy during late pregnancy, may double her weight and must be supported when being picked up. Easy access to feed and water should be facilitated for her during this time.

   The useful breeding life of a sow lasts approximately 28 months, after which litters will decrease to one or two young and pregnancies will tend to become intermittent.

e. **Selection**: The requirements of the research program for which breeding is to be undertaken will, of course, largely dictate whether inbreeding or outbreeding, pair or harem type matings, and conventional or gnotobiotic procedures are practised. Regardless of what combination of these procedures may be utilized, the animals selected as breeders should generally be the healthiest and most vigorous available.

   Selection for productivity should be based on numbers of young weaned per sow, rather than on litter size at birth. Selection for breeding performance in both sexes should be routinely practised in inbred strains in order to minimize the decline that will otherwise tend to occur.

   The physical, reproductive, and behavioral characteristics exhibited by outbred stocks can be markedly influenced either through family or mass selection, depending on the heritability of the trait (Festing, 1976; Wright, 1960).

2. **Breeding Systems**

a. **Conventional Colony**: The vast majority of institutional and laboratory requirements for guinea pigs can be satisfied through a conventional system of breeding and raising, as opposed to caesarian derivation and the raising of offspring under germ free or specific pathogen free conditions.

   A wide choice of conventionally raised inbred strains and outbred stocks of guinea pigs is available commercially (NRC U.S., 1979). Whether or not to raise one's own or to purchase should be based on program needs, suitability of facilities, and cost accounting; these points should always be

carefully reviewed before embarking on a breeding program. When an in-house breeding program is in place, it is essential that high standards of hygiene, disease control and record keeping be practised. The fact that a colony is an outbred conventional one in no way justifies carelessness in these matters, particularly if the animals from such colonies are to be relied upon as bioassays or as research models.

b. **Germ Free and Specific Pathogen Free (SPF)**: It is well beyond the scope of this chapter to deal in any detail with the methodology, special requirements, or specific uses for germ free or SPF guinea pigs. Information on this subject has been concisely dealt with in a chapter of "The Biology of the Guinea Pig", which also provides a comprehensive bibliography (Wagner and Foster, 1976). Points that should be kept in mind in reaching a decision in regard to the acquisition of germ free or SPF guinea pigs are that: a) the expense and difficulties in setting up a gnotobiotic guinea pig breeding colony can only rarely be justified when these animals can be acquired commercially (NRC U.S., 1979); and b) the option of obtaining the required germ free animals by hysterotomy from healthy dams from the conventional colony should be seriously considered. Isolator raising of caesarian derived, germ free guinea pigs is made relatively easy by their precocity (NRC U.S., 1970).

c. **Monogamous Pair Matings**: These are not generally used in outbred colonies due to the numerous boars that must be maintained and the great outlay in caging and personnel time involved. However, the system is the most productive in absolute terms and is well suited to the small colony, particularly where inbreeding and careful selection is to be practised.

d. **Polygamous Group Matings**: A single boar may be set up in a harem with from four to 20 sows, although 10 females is generally considered to be optimal. This system probably provides maximum production per unit of space and expense, and is generally used for out-cross, conventional breeding. A thriving, polygamous group will contain young in all stages from birth to weaning, at any given time. As a consequence, it is important to remove weanlings at 21 days to ensure that they do not get bred by their sires. A further problem encountered is one where older offspring in the group nurse the recently freshened sows (sows will usually permit this) and consequently deprive the neonates of adequate milk. This may be partially prevented by prompt removal of all juveniles; alternatively, the sow and her litter may be removed to a separate cage a few hours after birth (subsequent to post partum breeding). Yet another problem may be stampeding, with trampling of the young, amongst guinea pigs in a heavily populated floor pen harem.

E. HANDLING AND MANIPULATIONS

1. Physical Restraint

Guinea pigs almost never bite and, although nervous, are friendly and very easy to handle. They should always be forewarned before being approached, either by being able to see or hear their would-be handler. They should be lifted by grasping them firmly and gently over their shoulders, with two

fingers behind and two in front of the forelimb. The rump should be supported by the other hand when lifting, particularly in the pregnant sow. Essentially the same grip may be used to immobilize the animal, if the hind legs are grasped and extended and the animal is placed on its back on a table top or counter.

2. **Sampling and Injections**

a. **Blood**: Very small samples of blood may be obtained by nicking the marginal ear vein, cutting the nail, or from the orbital sinus (see chapter on Mice for orbital technique). A procedure for repetitive collection of multiple capillary tube samples using a mechanically activated lancet has been described (Bullock, 1983).

Somewhat large samples of up to 2 or 3 ml may be obtained by venipuncture of one of several veins. Numerous procedures have been described; however, as the blood vessels are thin walled and the appendages in which they are located are short, none of the procedures is easy. The saphenous vein is one of the more accessible.

The only consistently satisfactory way of obtaining larger quantities of blood is by cardiac puncture. Ten to 15 ml may be taken from a 300-400 g guinea pig. This procedure, and in many instances saphenous venipuncture, should be undertaken when the animal is heavily tranquillized or under anesthesia.

b. **Fecal and Urine Samples**: Both may best be obtained by placing the animal in a proper metabolism cage. Fecal samples alone may be acquired by placing the animal in a wire floored cage for a brief period.

c. **Injections**: The most frequently used and convenient route is i.p., whilst the animal is held on its back. The needle should be inserted just lateral to the umbilicus in an oblique and cephalad direction, in order to reduce the likelihood of piercing the bulky abdominal viscera. Injections by the i.v. route are fraught with difficulties, for the same reasons as is blood withdrawal, and should, therefore, be avoided whenever possible.

F. **CHEMICAL RESTRAINT AND ANESTHESIA**

1. **General Comments**

Possibly the only constant and reliable facts concerning analgesia and anesthesia in the guinea pig relate to difficulties in safe administration and the unpredictability of effectiveness. The pertinent scientific literature is rife with conflicting reports on this subject. A number of these have been documented in an excellent review on restraint and anesthesia in Animal Anesthesia, a reference work that also provides specific recommendations based largely on findings from the author's own laboratory (Green, 1979). Other, more recent, brief reviews of this topic are also available (Harkness and Wagner, 1983; Peters, 1981). The notoriously unpredictable responses of the guinea pig to narcotic and anesthetic agents may, in a general way, be attributed to the animal's excitable, stress oriented nature, high metabolic

rate, peculiarities of its respiratory system, relatively inaccessible thin walled veins and tendency to prolonged detoxification due to low blood glucose and/or ascorbic acid levels (Green, 1979; Peters, 1981).

2. **Anesthetic Agents**

   a. **Sedation and Preanesthetic Treatment**:

      i. Atropine at up to 0.03-0.05 mg/kg s.c. should be given 30 minutes before ether anesthesia. It is also frequently used, at much lower doses, prior to induction with other agents; however, there is some doubt as to its value (Green, 1979).

      ii. Diazepam at 5 mg/kg i.p. is an effective tranquillizer but does not produce analgesia (Green, 1979).

      Diazepam 0.1 mg/kg with ketamine at 44 mg/kg i.m. is reported to give rapid immobilization and good muscle relaxation; however, the level of analgesia achieved is questionable (Gilroy and Vaga, 1980).

      iii. Ketamine at dosages from 25 to 44 mg/kg is a dissociative anesthetic agent with a wide margin of dose safety that is very useful in producing restraint and tranquillization. There are, however, numerous reports that in the guinea pig this agent is ineffective in producing surgical anesthesia and a proper level of analgesia, even at very high doses. Ketamine may be used alone or in combination with analgesics such as xylazine (Rompun) for manipulative procedures and for the initial induction of surgical anesthesia when an inhalant gas is to be used, but should not be used alone as a general anesthetic (Green, 1979; Gilroy and Vaga, 1980).

   b. **Injectable Anesthetics**: Guinea pigs' response to injectable agents will vary considerably with age, weight, and physiological state of the subject. Body weight dosages are difficult to estimate accurately unless the animal is fasted for 12 hours, as intestinal content may contribute anywhere from 18 to 40% of the total. Due to the difficulties of venipuncture, injectables are most often administered by other routes, for which dosage can only be approximated and which involve prolonged absorption:

      i. Fentanyl-droperidol (Innovar-Vet) at 22 to 88 ml/kg i.m., produces effects ranging from tranquillization to deep surgical anesthesia. Unfortunately, this combination also sometimes induces a severe inflammatory reaction at the site of injection, with the possibility of necrosis and self-mutilation (Hoar, 1976).

      ii. Ketaset Plus (Bristol), a combination of ketamine HCI (100 mg/ml) promazine HCI (7.5 mg/ml) and aminopentamide sulphate (0.0625 mg/ml) administered i.m., has been reported to give effective anesthesia at 125 mg/kg in guinea pigs (Mulder, Johnson, McKee *et al.* 1979). However, most reports on the use of ketamine, alone or in combination, suggest that its analgesic effects are questionable (Green, 1979; Peters, 1981).

iii. Barbiturates such as sodium pentobarbital 30-40 mg/kg and sodium thiopental at 55 mg/kg administered i.p., produce effective anesthesia, but mortality rates of up to about 15% may occur (Green, 1979). Careful weighing, preanesthesia fasting, and the use of freshly prepared and diluted solutions will help to reduce risk. Ideally, these agents should be administered i.v. to effect, a fact that mitigates against their general use, as this route of administration is technically very difficult in the guinea pig, whilst the commonly used i.p. alternative leads to inconsistent levels of analgesia (Green, 1979).

c. **Inhalant Anesthetics**:

i. Anesthetic gases, particularly methoxyflurane, are the agents of choice for anesthesia maintenance in the guinea pig. However, the use of these agents alone, for both induction and maintenance, is not without its own set of problems in this species. Difficulties arise because the guinea pig is capable of prolonged breath holding, has a rapid respiratory rate (with consequent rapid uptake and high plasma concentration of the gas), has a high respiratory dead space to body weight ratio, and exhibits excessive mucous secretion.

ii. Endotracheal intubation may be used to alleviate several of the problems listed above. Unfortunately, this procedure is itself difficult in the guinea pig due in this instance to a large tongue and narrow, rather inaccessible glottis. However, the techniques that have been described for the intubation of guinea pigs and other small rodents can be successfully performed with practice (Green, 1979; Kujime and Natelson, 1981; Gilroy, 1981). Intubation should be undertaken if prolonged surgical anesthesia is required. Maintenance by drop and nose cone has generally proven satisfactory for shorter procedures.

iii. Methoxyflurane is probably the safest and most useful of the common inhalant anesthetics, particularly if ketamine or a ketamine combination (see above) is used as a preanesthetic or initial inducing agent.

iv. Halothane may be substituted for methoxyflurane but, being rapid acting and somewhat more risky to use than the former, must be administered with extra care, particularly to the frightened animal preferably by an experienced anesthetist.

v. Ether is still a frequently used agent, with induction being undertaken in an improvised chamber followed by mask maintenance. Although this agent gives good muscle relaxation and analgesia, its use in the guinea pig, even following atropine pretreatment to counteract excessive salivation, is risky and should be avoided (Green, 1979; Peters, 1981).

G. HEALTH CARE

1. Drug Therapy

a. **Antibiotic Toxicity**: Many of the antibiotics in common use in animal colonies have proven to be toxic to guinea pigs (Farrar, Kent and Elliot, 1966). This effect may be a direct one as in the case of streptomycin, or indirect as with penicillin (Harkness and Wagner, 1983).

Indirect antibiotic toxicity results from the drug killing off most of the predominantly Gram-positive intestinal flora, permitting overgrowth of Gram-negative organisms. Destruction of intestinal mucosa, bacteremia, enterotoxemia, and death result in from four to nine days after administering the antibiotic. Penicillin does not cause fatalities in germ free guinea pigs. Because of the extreme sensitivity of guinea pigs to these substances, treatment with antibiotics should be undertaken only on expert advice. A discussion on the response of guinea pigs and other rodents to a number of currently available antibiotics is available (Harkness and Wagner, 1983).

b. **Dosage**: A useful table of drug dosages, which should be available to persons responsible for the health care of an animal colony or routinely using guinea pigs in research, has recently been published (Harkness and Wagner, 1983). It is important to realize that guinea pig dosages, particularly of the newer preparations, must largely be based on interspecific extrapolations and often only incidental and limited clinical trials. The therapeutic efficacy of a drug will be influenced not only by species sensitivity and the physiological status of the individual (sex, age, nutrition, etc.), but also by such physical factors as caging, bedding, temperature, and humidity.

c. **Administration**: Drugs frequently are given for both therapeutic and prophylactic purposes, using the drinking water or the feed as vehicles. This is often the only practical way of treating a disease outbreak with agents such as tetracycline and sulfa drugs. However, it must be remembered that bacterial resistance to the agent will inevitably result (Hooper and Hirsh, 1977). This is particularly so following prolonged low dosages (prophylactic regimens), and the use of drugs for this purpose should generally be discouraged. To achieve an effective dose and minimize buildup of resistance, drug concentrations in the vehicle should be at maximal safe levels (based on estimated consumption), freshly prepared and renewed on a daily basis, with all residual water and/or feed being discarded.

Individual animals may also be treated by the above methods under cage isolation conditions, which allows for better control over intake dosage. In either case, drug dosage will have to be calculated on the basis of an estimated average adult guinea pig consumption. These have been estimated for food at 6 g/100 g and water at 10 ml/100 g, with food consumption increasing during pregnancy up to threefold (Harkness and Wagner, 1983). Similarly, consumption may double in the young, active, and growing animals.

2. **Caesarian Derivation**

In the guinea pig this is a relatively easy procedure, as noted earlier under Breeding. Thus, by obtaining animals aseptically and rearing them in a more or less isolated environment known to be completely free of the specific pathogenic contamination affecting their parents, a specific infectious disease cycle can be broken and a desired genotype (strain) maintained.

H. INFECTIOUS DISEASES

1. Bacterial Diseases

a. **Enzootic Cervical Lymphadenitis**: This is a suppurative disease seen with some frequency in guinea pig colonies. The causative organism is the Lancefield Type C, *Beta hemolytic streptococcus* (Fraunfelter, Schmidt, Beattie *et al.* 1971).

The disease is manifested clinically as bilateral swellings or discharging lesions, either under the jaw or in the neck region. There is abscessation of the affected lymph nodes and usually, but not always, a severe debilitation of the affected animals. Cervical lymphadenitis frequently runs an acute course with fatal termination, particularly in young animals. Peritonitis, focal hepatic necrosis, purulent otitis media, fibrinous pericarditis and pleuropneumonia may occur as sequelae to the acute disease. The organism gains entrance to the body through breaks in the oral mucosa and some enzootics have been attributed to oral injuries during the ingestion of hay. Animals exhibiting the disease should be removed and either destroyed or treated separately. Both the affected animals and their penmates may be treated with an appropriate antibiotic.

b. **Bacterial Pneumonias**: Those that commonly occur in the guinea pig are caused by either *Bordetella bronchiseptica* (Ganaway, Allen and McPherson, 1965), *Diplococcus pneumoniae* (*Syn. Streptococcus pneumoniae* or *Pneumococcus*) or group *C hemolytic streptococci* (Harkness and Wagner, 1983). Streptococcal pneumonia due to *D. pneumoniae* is often seen as a chronic condition accompanied by such signs as pleuritis, pericarditis, peritonitis, otitis media, and meningitis (Peters, 1981). This type of pneumonia can reach epizootic proportions amongst guinea pigs. The detection of hematuria is helpful in differentiating this disease from acute salmonellosis (Harkness and Wagner, 1983).

c. **Salmonellosis**: This zoonotic disease, although not commonly encountered in guinea pig colonies in Canada, has frequently been diagnosed in colonies elsewhere (Habermann and Williams, 1958). Because of its lethality and the dangers of transmission to man and other animals, salmonellosis remains a disease of considerable importance. Acute diarrhea and sudden death may occur, as may extensive lymph node enlargement, within 48 hours of infection (Peters, 1981). Several species, including *S. typhimurium* and *S. enteritidis*, have been isolated from guinea pigs. These organisms may be latent in animals in the colony or may be introduced on feedstuffs and bedding contaminated with wild

rodent excreta (Peters, 1981). Treatment should not be attempted. Suspected outbreaks should be immediately and strictly isolated and infected animals destroyed once a positive diagnosis has been made. Strict hygienic methods should be implemented and a quarantine maintained until the outbreak is completely over.

d. **Pseudotuberculosis**: This condition in the guinea pig rather resembles salmonellosis and is characterized by areas of caseation necrosis in tissues such as the mesenteric lymph nodes, liver, and spleen. The causal organism is *Yersinia pseudotuberculosis*, and the disease is of some significance in this species. It is usually manifest as a chronic, emaciating disease, with diarrhea and enlargement of the lymph nodes. Death often occurs in three to four weeks. Treatment is impractical and affected animals should be destroyed. Spread is through ingestion and may be controlled by strict sanitation. It has been suggested that the organism may be introduced on contaminated greens (Townsend, 1975).

2. **Viral Diseases**

a. **Naturally Occurring Virus Infections**: At least 16 naturally occurring virus infections have been identified in the guinea pig (Van Hoosier and Robinette, 1976). The significance of some of these viruses to the guinea pig itself is as yet undetermined other than perhaps as a difficult to access, potential nuisance in other types of experiments.

b. **Herpes and Herpes-like Viruses**:

i. Cytomegalovirus (CMV) and "salivary gland virus" is due to a herpes virus organism which normally exists in salivary gland tissue as an inapparent or "latent" infection (Smith, 1979). CMV infection rarely occurs as a generalized disease.

ii. Herpes-like virus infection is relatively widespread in certain strains of guinea pigs and apparently is present as a latent infection in these animals (Bhatt, Percy, Craft *et al.* 1971). This virus has been isolated from kidneys with segmental nephrosclerosis. It has been suggested by some investigators that such kidney lesions in the guinea pig may be vascular in origin (Takeda and Grollman, 1970). Although initially correlated with cases of leukemia in the guinea pig, a specific role for the virus in any disease entity in this species has yet to be determined.

iii. Lymphocytic choriomeningitis, although not of common occurrence in guinea pigs, is of particular significance, as other species, including man, are susceptible. Wild mice are considered a natural reservoir of the virus and consequently control is achieved by isolating laboratory animals from contact with wild rodents (Takeda and Grollman, 1970). The disease in guinea pigs is manifest by neurological signs of meningitis and hind limb paralysis. Suspected outbreaks should be handled with the same precautions and methods as outlined for salmonellosis.

3. **Parasitic Diseases**

a. **Ectoparasites**: These are considered generally to be of little significance in the guinea pig. Guinea pig lice (*Gryopus ovalis* and *Gliricola porcelli*) may be fairly common on animals from certain commercial sources, but infestations are rarely severe enough to give clinical signs. In extreme cases, excessive scratching may result in a rough coat or even some alopecia (hair loss). These parasites can be controlled by dusting with a 0.2% pyrethrim powder or by short exposures to dichlorvos vapour (vapona strip), repeated two or three times at two week intervals to destroy successive generations of newly hatched eggs.

The guinea pig fur mite (*Chirodiscoides caviae*) is another fairly common ectoparasite of laboratory guinea pigs. Signs of heavy infestations and treatment are similar to that described for lice (above). Diagnosis may be confirmed by microscopic identification of the parasite or its eggs.

The observation of alopecia in guinea pigs should not automatically lead to the conclusion that ectoparasites are the cause. Their presence should be confirmed visually, as other reasons for this condition are not uncommon in this species (see below).

b. **Endoparasites**: Of the internal parasitic diseases encountered in this species, coccidiosis is the most significant. Although usually not pathogenic, extremely heavy infestation with Eimeria caviae will produce a typhlitis and colitis, which may be manifested clinically by diarrhea, anorexia, lethargy and occasionally death. The disease is diagnosed by finding the characteristic oocysts in the feces. The condition can be controlled by improved sanitary and husbandry practices and the use of coccidiostats.

I. MISCELLANEOUS DISEASES

1. **Reproductive Conditions**

a. **Ketosis (Pregnancy Toxemia)**: This syndrome occurs in guinea pigs in advanced pregnancy with fair frequency. The condition is characterized by acidosis, ketosis and a fatty liver usually leading to a fatal termination. Obese guinea pigs, carrying three or more fetuses, subsequent to the 56th day of pregnancy are especially susceptible to this disease (Ganaway and Allen, 1971). Pregnancy is not, however, an essential prerequisite, as obese, virgin guinea pigs may die in a similar manner under stress. Experimental evidence indicates that obesity and stress, especially from fasting during late pregnancy, may induce the syndrome (Seidel, Hughes, Bertolet *et al.* 1979).

The disorder is considered a metabolic disease; however, it has been suggested that the massive fetal displacement that develops under these conditions may compress the aorta in advanced pregnancy, resulting in on impaired circulation that precipitates the pregnancy toxemia (Festing,

1976). A genetic predisposition to the condition has also been implicated (Peters, 1981).

b. **Alopecia**: Hair loss in the form of a fairly uniform thinning of the hair, is seen predominantly in albino guinea pigs in the latter stages of gestation or immediately post partum. Hair growth will usually begin again immediately after parturition and the hair coat will have returned to normal by three to four weeks. This condition is minimal or not usually encountered in first litter sows; however, the probability of its occurrence increases with each succeeding pregnancy. Severely affected animals may become almost totally bald.

   The occurrence of this type of alopecia is not confined to pregnant sows, but is also seen in mature animals that are subjected to stresses associated with experimentation. Males are rarely affected.

   The cause of this condition is not understood although it is unquestionably stress-related. The fact that some colonies that breed their own animals are much more severely affected than others, suggests that heredity is implicated. However, attempts to eliminate the alopecia by selective breeding have not been successful.

2. **Miscellaneous Disorders**

   a. **Soft Tissue Calcification**: This is most frequently seen in animals over one year of age, occurring in such tissues as liver, heart, lung, and kidneys (Sparschu and Christie, 1968). The disease may be due to an imbalance in dietary calcium, phosphates, magnesium and potassium. Careful control of these elements in the diet is imperative for the proper maintenance of acid-base balance and the prevention of soft tissue calcification.

   b. **"Slobbers"**: Chronic drooling results in the fur under the chin and down the neck being constantly wet and matted. Overgrowth of the continuously erupting rodent incisors may be the cause; however, it is also seen when teeth are normal, and in these cases the cause remains obscure.

REFERENCES

ASH, G.W. When is a husbandry method proven-after 10 years? Guinea Pig News Letter 1975; 9: 27.

BHATT, P.N., PERCY, D.H., CRAFT, J.L. and JONAS, A.M. Isolation and characterization of an herpes like (Hsiung-Kaplow) virus from guinea pigs. J. Inf. Dis. 1971; 123: 178.

BULLOCK, L.P. Repetitive blood sampling from guinea pigs (*Cavia porcellus*). Lab. Anim. Sci. 1983; 33: 70.

EDIGER, R.D. Care and management. In: The Biology of the Guinea Pig (J.E. Wagner, P.J. Manning, eds.). Academic Press, New York NY 1976: 5-12.

FARRAR, W.E., Jr., KENT, T.H. and ELLIOT, V.R. Lethal gram negative bacterial superinfection in guinea pigs given bacteracin. J. Bact. 1966; 92: 496.

FESTING, M.F.W. The guinea pig. In: The UFAW Handbook on the Care and Management of Laboratory Animals. Churchill Livingstone, London UK 1976: 229-247.

FRAUNFELTER, F.C., SCHMIDT, R.E., BEATTIE, R.J. and GARNER, R.M. Lancefield type C streptococcal infections in strain 2 guinea pigs. Lab. Anim. 1971; 5: 1.

GANAWAY, J.R. and ALLEN, A.M. Obesity predisposes to pregnancy toxemia (ketosis) of guinea pigs. Lab. Anim. Sci. 1971; 21: 40.

GANAWAY, J.R., ALLEN, M.A. and McPHERSON, C.W. Prevention of acute *Bordetella bronchiseptica* pneumonia in a guinea pig colony. Lab Anim Care 1965; 15: 156.

GILROY, B.A. and VAGA, J.S. Use of ketamine-diazepam and ketamine-xylazine combinations in guinea pigs. VM/SAC 1980; 75: 508.

GILROY, B.A. Endotracheal intubation of rabbits and rodents. J. Am. Vet. Med. Assoc. 1981; 179: 1295.

GREEN, C.J. Orders Lagomorpha, Rodentia, insectivora and Chiroptera. In: Animal Anesthesia. Laboratory Animal Handbooks 8. Laboratory Animals Ltd., London UK 1979: 131-161.

HABERMANN, R.T. and WILLIAMS, F.P. Salmonellosis in laboratory animals. J. Natl. Cancer Inst. 1958; 20: 933.

HARKNESS, J.E. and WAGNER, J.E. The biology and medicine of rabbits and rodents (2nd Ed.). Lea and Febiger, Philadelphia PA 1983: 17-24.

HOAR, R.M. Biomethodology. In: The Biology of the Guinea Pig (J.E. Wagner, P.J. Manning, eds.). Academic Press, New York NY 1976: 13-20.

HOOPER, D.G. and HIRSH, D.C. Changes of resistance of enteric bacteria in mice given tetracycline in drinking water. Am. J. Vet. Res. 1977; 38: 565.

KUJIME, K. and NATELSON, B.H. A method for endotracheal intubation of guinea pigs (*Cavia porcellus*). Lab. Anim. Sci. 1981; 31: 715.

LABORATORY ANIMALS CENTRE DIETS ADVISORY COMMITTEE. Guinea-pigs. In: Dietary Standards for Laboratory Animals. Medical Research Council, Carshalton UK 1977: 16-17.

MULDER, J.B., JOHNSON, H.B., McKEE, G.S. and SELLERS, S.E. Anesthesia with ketaset plus in guinea pigs and hamsters. VM/SAC 1979; 74: 1807.

NATIONAL RESEARCH COUNCIL (U.S.). Gnotobiotes: Standards and guidelines for the breeding, care and management of laboratory animals. National Academy of Sciences, Washington DC 1970.

NATIONAL RESEARCH COUNCIL (U.S.). Nutrient requirements of the guinea pig. In: Nutrient Requirements of Laboratory Animals (3rd Ed.). National Academy of Sciences, Washington DC 1978: 59-69.

NATIONAL RESEARCH COUNCIL (U.S.). Animals for research: A directory of sources (10th Ed.). National Academy of Sciences, Washington DC 1979.

NAVIA, J.M. and HUNT, C.E. Nutrition, nutritional diseases and nutrition research applications. In: The Biology of the Guinea Pig (J.E. Wagner, P.J. Manning, eds.). Academic Press, New York NY 1976: 235-267.

PETERS, L.J. The guinea pig: An overview Part II. Comp. Cont. Educ. Pract. Vet. 1981; 3: 403.

ROWLANDS, I.W. and WEIR, B.J. (eds.). The biology of hystricomorph rodents. Symp. Zool. Soc. London UK 1974: 34.

RUSSELL, R.J. (Letter). Vesicular glands in guinea pig incorrectly identified. VM/SAC 1980; 75: 538.

SEIDEL, D.C., HUGHES, H.C., BERTOLET, R. and LANG, C.M. True pregnancy toxemia (pre eclampsia) in the guinea pig (*Cavia porcellus*). Lab. Anim. Sci. 1979; 29: 472.

SELTZER, W., MOUM, S.G. and GOLDHAFT, T.M. A method for the treatment of animal wastes to control ammonia and other odors. Poult. Sci. 1976; 4B: 1912.

SKINNER, H.H., KNIGHT, E.H. and GROVE, R. Murine lymphocytic choriomeningitis: The history of a natural cross infection from wild to laboratory mice. Lab. Anim. 1977; 11: 219.

SMITH, M.G. The salivary gland viruses of man and animals (*Cytomeaalic* inclusion disease). Prog. Med. Virol. 1959; 2: 171.

SPARSCHU, G.L. and CHRISTIE, R.J. Metastatic calcification in a guinea pig colony: a pathological survey. Lab Anim Care 1968; 18: 520.

TAKEDA, T. and GROLLMAN, A. Spontaneously occurring renal disease in the guinea pig. Am. J. Pathol. 1970; 60: 103.

TOWNSEND, G.H. The guinea pig: General husbandry and nutrition. Vet. Rec. 1975; 96: 451.

VAN HOOSIER, G.L., Jr. and ROBINETTE, L.R. Viral and chlamydial diseases. In: The Biology of the Guinea Pig (J.E. Wagner, P.J. Manning., eds.). Academic Press, New York NY 1976: 137-152.

WAGNER, J.E. Introduction and taxonomy. In: The Biology of the Guinea Pig (J.E. Wagner, P.J. Manning, eds.). Academic Press, New York NY 1976: 1-4.

WAGNER, J.E. and FOSTER, H L. Germfree and Specific Pathogen-Free. In: The Biology of the Guinea Pig (J.E Wagner, P.J. Manning, eds.). Academic Press, New York NY 1976: 21-30.

WAGNER, J.E. and MANNING, P.J. (eds.). The biology of the guinea pig. Academic Press, New York NY 1976.

WEIR, B.J. Laboratory hystricomorph rodents other than the guinea pig and chinchilla. In: The UFAW Handbook on the Care and Management of Laboratory Animals. Churchill Livingstone, London UK 1976: 284-292.

WRIGHT, S. The genetics of vital characteristics of the guinea pig. J. Cell. Comp. Physiol. (Supplement 1; November) 1960; 56: 123.