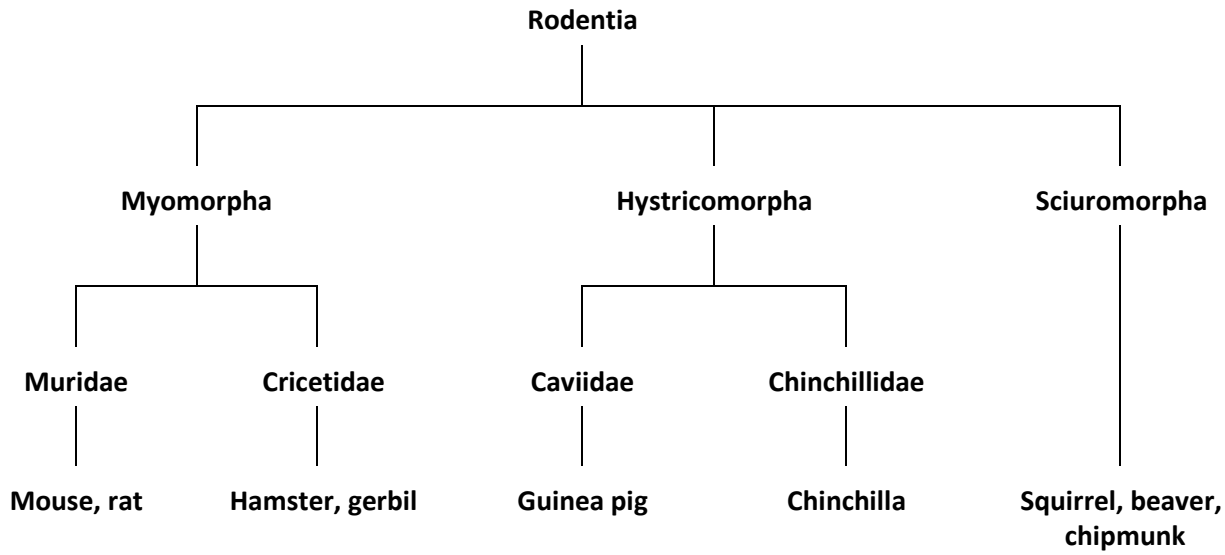
The Mouse, Rat and Guinea-Pig

Rodents are a very successful order of placental mammals which colonise almost all habitats. All members of the order are small, the largest member, the Capybara, being about the size of a small pig. Rodents have a number of distinguishing features: they have open rooted sharp teeth, hindgut microbial fermentation chambers, and are coprophagic.

Rodents can be divided into three suborders, the Myomorpha, Hystricomorpha and Sciuromorpha. Most laboratory rodents are Myomorphs or Hystricomorphs.

Simplified Classification of Rodents



THE MOUSE

The mouse, *Mus musculus*, is the most commonly used laboratory animal. Many well-defined inbred and outbred strains are available, for which the karyotypes are known. In fact, more is known about the genome of the mouse than any other species, which is one reason for its popularity as a research animal. There are many types of genetically modified mice available which are useful models for specific disease entities.

Behaviour

Mice are essentially crepuscular – they are active at dawn and dusk and much of their normal activity takes place during the dark period. They are social animals which can live in harmony once their hierarchy is established. Pheromones act as mediators in communication between mice, and the influence of pheromones must be taken into account when managing a mouse colony. For example, exposure to male pheromones causes synchronisation of oestrus in females (Whitten effect), pheromones from unfamiliar animals can cause stress and aggression, and those from foreign males may cause recently mated females to abort (Bruce effect). Pheromones are used to maintain stability in the colony and if they are removed each time the cage is cleaned, fighting will ensue and subordinate mice will be barbered, or possibly injured. Environmental enrichment, to provide places of refuge, and the technique of leaving a little of the soiled bedding in the new cage to reduce the need to keep re-establishing the dominance hierarchy and territory marking will help to reduce this. There are also strain differences in behaviour. For example, male BALB/c mice are particularly aggressive, and fight wounds are common.

Mice are thigmotactic – they dislike open spaces and prefer to be surrounded on all sides.

Housing

Cages are usually of the shoebox type. Bedding should be provided, such as wood chips or commercially prepared paper-based bedding. Adult males may fight, and are sometimes housed alone. Female mice are less aggressive, and can be kept in groups of familiar females. Females with litters will defend their young and are best separated while nursing.

Mice should be kept in compatible groups, with tubes and objects to climb on in the cage to enrich the environment and reduce stereotypic behaviour such as barbering.

Feeding

Mice are herbivores, and have a large caecum which acts as a microbial fermentation chamber. As with all hindgut fermenters, mice are coprophagic: during the dark period pellets of soft faeces are expelled from the caecum and are ingested directly from the anus. This allows the animals to digest the nutrients released by the microbial fermentation. After a second passage through the digestive system, pellets of hard faeces are produced, and these are the ones seen on the floor of the cage. Mice are usually fed ad lib with a complete pelleted mouse diet, from hoppers suspended above the floor to prevent faecal contamination. These should be cleaned twice weekly. Generally **mice will consume 3-5 g of pelleted diet daily,** but there are strain differences, and disease states and pregnancy affect the food requirements.

Water

Water is required for lubrication of the food as well as hydration, so if insufficient fluid is available they have difficulty eating. **The usual requirement is 6-7 ml water daily.** Mice can play with drinking nozzles, so with bottles they may run out and if automated watering systems are used with solid bottomed cages there is a risk of flooding. When ill, mice drink very little and rapidly dehydrate.

Environment

Mice have a large surface area to volume ratio, and therefore lose heat rapidly and are sensitive to changes in ambient temperature. Mice are also susceptible to water loss. They do not sweat or pant to lose heat, as this would cause dehydration. Therefore maintenance of the correct environmental conditions is vital. The Home Office Code of Practice requires temperatures between 19 and 23 ^{o}C, humidity of 40-70 per cent, 12 to 15 air changes per hour, and 12 hours daylight daily. The light intensity should be 350 to 400 lux, except for albino mice. For these it should be less than 60 lux to avoid damage to the retina. Mice are also very sensitive to ultrasound. Normal noise levels may sound quiet to the human ear, but they may be extremely loud for a mouse.

Breeding

Male mice reach puberty at 7 weeks, and females at 6 weeks. Females then cycle every 4-5 days. Oestrus, mating and ovulation tend to occur during the dark phase of the light cycle. Mating results in the formation of a vaginal plug, which can be detected to confirm mating. Gestation lasts 19-21 days, and 1-12 pups may be born, depending on the strain. They are weaned at three weeks by which time they have fur and their eyes and ears are open.

Mice may be bred using a harem system, with one male for 2-6 females, pregnant females being removed from the group to give birth, or may be kept together in a monogamous system. With the latter system, the young are removed before the next litter is born.
Mice will breed until they are 12 to 18 months old.

Handling

When handling small rodents, it may be advisable to remove the lid of the cage, rather than opening the flap in the lid, before catching the animal. Otherwise, they may hide beneath the food hopper which makes them harder to catch and also increases the risk of being bitten._Mice move very fast, so you have to be quick and decisive to catch them.

1. Grasp the base of the tail gently but firmly and lift the mouse. Mice may be carried short distances or transferred between boxes this way.
2. Place the mouse down on a non-slip surface, such as the top of the cage, or your arm, without releasing the tail. You can then lift the tail to sex the animal. The ano-genital distance in the male is approximately twice that seen in the female.
3. Slide the thumb and index finger of the other hand up the animal's body and grasp the scruff of the neck to restrain the head.
4. The animal is then secure and may be examined or injected safely. Extra restraint may be achieved by holding the tail with the 4th and 5th fingers.

When handling newborn mice, transfer the mother to a separate cage first to prevent any aggression. To avoid cannibalism by the mother, rub your hands in soiled bedding material to acquire pheromones before handling the pups. Roll the pups gently into the palm of your hand. Then rub the young with nest material afterwards before replacing the mother. From 10 days of age, they can be handled as adults, but the mother should still be removed first.

Pain and stress recognition

It is important to be familiar with normal appearance and behaviour in order to be able to spot when all is not well. Familiarity with the normal animal is something that can only be acquired with experience and time, Remember that there is a degree of normal variation between healthy animals, which can be due to age, diet or cyclical changes in the female due to oestrus, *etc.* Signs of normal appearance and behaviour include:

- normal behaviour - alert, inquisitive and interacting with others in the group
- well groomed with a glossy coat

- relaxed with a normal gait – no lameness or ataxia, and not hunched or prone
- bright and clear eyes
- normal respiration, not shallow and fast, or deep and laboured
- colour (pink, pale or deep red)
- signs of eating and drinking
- normal faeces and urine
- teeth not overgrown and no malocclusion.
- moderate degree of body fat over the backbone
- normal breeding performance with low neo-natal mortality.

The animal technicians that look after your animals on a day-to-day basis are familiar with normal animals and can advise on cases of abnormality. Different strains of mice may vary in their responses to pain and distress, an increase in sleeping time and weight loss will be seen in animals in pain. Other signs include:

- Piloerection and hunched appearance
- Isolated from the rest of the group.
- Persistent dormouse posture
- Squeals on handling or pressure on affected area
- May become more docile (or sometimes more aggressive)
- May eat bedding or neonates
- Abdominal writhing

Common diseases and health monitoring

Mice which are not kept under barrier conditions are likely to be carrying a number of commensal and potentially pathogenic organisms, and even barrier reared animals can develop infections if there is a breakdown in the barrier. Regular health screens should be performed to ascertain the health status.

Zoonotic diseases

There should be very few zoonoses in laboratory bred mice in Britain. However, hantaan virus and lymphocytic choriomeningitis (LCM) virus can cause potentially fatal infections in man, and leptospirosis can cause undulating fevers and kidney damage.

Subclinical diseases

Many of the infections of rats and mice do not produce clinical signs in adult animals. However, they may cause disease in neonates or immuno-compromised animals. You should be aware of any infections which are likely to affect your research, and ensure that there is an appropriate screening program in place to detect these infections before any problems are caused.

Respiratory diseases: these increase the risks associated with anaesthesia and surgery. Examples include Sendai virus, pneumonia virus of mice (PVM), and *Pasteurella pneumotropica.*

Virus infections: Mouse hepatitis virus (MHV), can cause a range of signs, from diarrhoea to neurological signs. Mouse rotavirus causes epidemic diarrhoea of infant mice (EDIM). Theiler`s murine encephalomyelitis virus (TMEV) Minute virus of mice (MVM) and lactate dehydrogenase elevating virus (LDHV) affect research data.

Bacterial infections: *Helicobacter spp.* may be of significance in models of oncology and immunology. *Staphylococcus aureus*, *Pasteurella pneumotropica*, *Clostridium piliformis* (Tyzzer's disease), *Citrobacter rodentium* and various streptococcal and mycoplasmal species can cause disease.

Parasite infections: internal infections include pinworms (*Syphacia oblevata, Aspicularis tetraptera)* and protozoa (*Histomonas, Tritrichomonas*, coccidia). External infections include mites (*Myobia musculi* and *Mycoptes musculinus*).

Recommendations for health monitoring of mouse colonies may be found in the Report of the FELASA Working Gp on Health Monitoring of Rodent & Rabbit Colonies. Laboratory Animals (2002) 36, 20-42.

THE RAT

Rats used in research are mainly derived from the brown or Norwegian rat, *Rattus norvegicus*. Outbred and inbred strains are available. Commonly used outbred strains include the Wistar and Sprague Dawley varieties. Fewer inbred strains exist than for mice, but a commonly encountered one is the Lewis rat.

Behaviour

Rats are usually friendly and amenable animals if handled gently, although there are some strain differences. They will become friendlier with more frequent handling. They are social animals and will live together in groups with little fighting provided they are not overcrowded

Rats have a tendency to be nocturnal. Feeding, drinking and mating all usually occur at night. Their eyesight is poor, and blind rats will behave as if perfectly normal. See www.ratlife.org for details of the normal behaviour of the laboratory rat.

Housing

Rats may be kept in metal or plastic cages ideally with solid floors, with bedding. Paper based products, wood shavings, or corn cobs may be used as bedding. Rats like to stand erect, and so cages with high lids are required. Rats are very intelligent and inquisitive animals and need an enriched environment to provide variety and prevent boredom.

Feeding

Rats are coprophagic. They can be fed ad lib on a complete pelleted rodent diet, from hoppers suspended above the floor of the cage. The diet should contain 20-27 per cent protein since higher protein levels than this may reduce reproduction efficiency. Rats are cautious eaters and will reject strange food. **Rats will eat 5g feed per 100g bodyweight daily.**

Water

Water may be provided by sipper tubes or by automated watering systems. **Rats will drink 10ml water per 100g bodyweight daily.**

Environment

Rats are less sensitive to temperature changes than mice, but should be kept between 19-23 ^{o}C. Young rats have much brown fat to assist in thermogenesis, the level of which reduces with age. The humidity should be 40-70 per cent. Low humidity results in ring-tail, in which an annular lesion appears around the tail, which may result in sloughing of the tail distal to the lesion. A 12 hour light period is adequate for rats but, being nocturnal, bright light is deleterious particularly for albino rats and results in retinal degeneration. The level should be less than 400 lux, or 100 lux for albinos. Photoperiod affects the oestrus cycle, and 12 to 16 hours light is best for optimal breeding. Ventilation is particularly important for rats, as many of their pathogens are aerosol borne. Twelve to fifteen air changes per hour is sufficient, provided the air is not recycled or an effective filter is present.

Breeding

Puberty occurs at 50-60 days, and breeding begins at 3 months, when females weigh 250g and males 300g. They breed until they are 12-18 months old. Oestrus occurs every 4-5 days. The Whitten effect is less pronounced in rats than mice, (synchronisation of oestrus in females by exposure to male pheromones), but does occur. Mating usually occurs at night, and a copulatory plug of gelatinous material is left in the vagina for 12-24 hours, which then falls out and can be detected to confirm that mating has occured. Gestation lasts 21-23 days. A litter of 6-12 pups is born in a shallow nest made by the female. Paper or cotton based bedding, wood shavings or specialised nesting materials can be supplied to aid in

nest building. Weaning occurs at 21 days. If a female is disturbed in the immediate post-partum period, she may destroy her young, so extreme care must be taken during this time.

Rats may be bred by monogamous or polygamous mating systems. With a monogamous system, the female will mate at the post partum oestrus, and the young are removed at weaning. This produces the maximum number of litters, but the male may interfere with the young. He can be removed at parturition, and returned to the female after the young are weaned. If the female is lactating during gestation, implantation can be delayed, leading to a 3-7 day increase in the length of gestation. In polygamous systems, one male is housed with 2-6 females. Pregnant females are removed prior to parturition and returned after weaning. Females in this system produce more milk and have larger litters.

Growth

Male rats exhibit prolonged growth, and bones do not become fully ossified until their second year. Inbred and outbred rats differ slightly in their rates of growth.

Handling

There are many ways of handling rats. In general, rats are amenable animals which rarely bite if approached correctly, although there are strain differences.

1. Remove the lid of the cage, and grasp the rat by the base of the tail. Lift the animal from the cage and support it immediately on a non-slip surface such as the arm or cage top. Rats should not be suspended by their tails for any length of time to avoid injury. Once supported on a surface, the animal may be sexed by lifting the tail to expose the perineum, as in mice.
2. To restrain the animal for examination or procedures, once it has been transferred to a non-slip surface as above, slide the free hand up the animal's body to a position behind the shoulders. Position the thumb between the forelimbs so it rests under the chin to restrain the head, with the fingers behind the other forelimb. The animal may then be lifted, and the hindquarters held with the other hand.
3. Alternatively, for added restraint, complete step one then slide the free hand up the animal's body, but press the elbows with the thumb and fingers to cause the forelegs to cross over under the chin. This method may be used if the animal is aggressive/ unfriendly.

Pain and stress recognition

Rats are naturally curious, and will explore in any new situations. Failure to stand erect and take an interest in their surroundings is an indicator of poor health. They are generally docile but become more aggressive, and resist handling during repeated stressful procedures. Acute pain or distress is accompanied by vocalization and struggling. They will lick or guard a painful area and will sit crouched. Sleep patterns will be disturbed and increased if pain and distress are present. The Harderian gland, a modified tear gland situated on the bulbar conjunctiva of the third eyelid, produces a porphyrin-rich secretion which normally lubricates the eye. When the rat is stressed, this secretion tends to overflow onto the face, producing a red ring around the eye, which is characteristic of stress. This is known as chromodacryorrhoea. Red staining may also appear at the nose, as the secretion flows down the nasolacrimal duct. Key signs of pain post laparotomy in the rat are: backarching, twitching and a cat-like stretch, in addition to showing reluctance to move.

Common diseases and health monitoring

Rats are susceptible to a number of diseases. For example, Hantaan virus and Leptospirosis are zoonoses, Sendai virus, pneumonia virus of mice, Rat coronavirus or *Mycoplasma pulmonis* may all have effects on the respiratory system particularly in the stressed animal, and Kilham rat virus may infect transplantable tissues and is teratogenic. Rats are susceptible to pinworms (*Syphacia* spp, *Aspicularis tetraptera*), and the dwarf tapeworm (*Rodentolepis nana*), which has zoonotic potential.

THE GUINEA PIG

The guinea pig, *Cavia porcellus*, is a rodent which originated from South America. There are several different varieties of guinea pig available, including the short-hair (English and American varieties), Abyssinian (which have hair in whorls), and Peruvian (which have long hair). Commonly used laboratory strains are derived from the short-hair variety. The Dunkin-Hartley and Hartley guinea pigs are outbred strains, and strains 2 and 13 are inbred strains.

Behaviour

Guinea pigs are amenable animals which rarely bite. Naturally they are crepuscular, but in the laboratory they will be active for periods throughout the day and night. When startled, guinea pigs have a tendency either to become immobile or to stampede and vocalise, leading to the risk of trampling young and making capture difficult. They should be provided with bolt holes and barriers within the pen, handled frequently to habituate the animals and reduce stress. The approach of a person will cause the animals to scatter: the normal behaviour is for the guinea pig to `resist arrest' and vocalise strongly. If this does not occur it may indicate that there is a problem.

Group housed familiar guinea pigs will soon establish a stable hierarchy, which is male dominated and maintained mainly by olfactory cues, but with some barbering and chewing of subordinate males. If unfamiliar males are placed together fighting will ensue particularly in cramped conditions or if oestrous females are present. Guinea pigs are creatures of habit and become increasingly unable to cope with changes in routine as maturity approaches. If there are any changes in the type of food hopper or water bottle, or in the type of food or water, the guinea pig may be unable to adapt and cease eating and drinking. This is particularly disastrous with pregnant females. Similarly, if there are changes in the type of housing, problems may be encountered.

Housing

Guinea pigs like to be housed in groups. This may be in floor pens, or large plastic or steel cages. Although guinea pigs rarely jump, cages should have sides at least 23 cm high, and more height is required for open-topped floor pens. Mesh floors may predispose to foot pad ulcers and increased stress levels, and are certainly contraindicated with experiments involving joints and feet.

Bedding materials provide comfort and a substrate for rooting behaviour. Materials such as wood shavings, paper based bedding, ground corn cobs or sawdust may be used, together with hay. Fine shavings and sawdust alone may cling to moist areas such as the perineum and probably are best not given to breeding guinea pigs. Larger shavings are better for these animals. Guinea pigs are messy animals and will disperse opaque, creamy coloured urine and faecal pellets throughout the pen. Removal of urine scale may require the use of acidic cleaning agents.

Feeding and Watering

As guinea pigs are messy, food and water bowls placed on the floor will soon become soiled with bedding, urine and faeces, and should be suspended above the floor or cleaned frequently. There is a tendency to play with drinkers, which leads to messy floors, and bottles quickly become empty. Automated watering systems ensure a constant water supply, but in solid floored systems, care must be taken to prevent flooding. All watering systems need to be checked and cleaned frequently. Any changes in watering system will upset the routine, and the guinea pig will need help to adapt. **The water requirement of a guinea pig is 10-40 ml per 100g bodyweight daily.**

Guinea pigs need vitamin C in their diet, and need 5mg/kg daily, or up to 30mg/kg if pregnant. This can be supplied in the food or water, or by giving cabbage, kale or oranges. Food with added vitamin C must be used within 90 days of manufacture, or the vitamin C will degrade. Guinea pigs are fastidious eaters and

will reject unfamiliar food. They require a pelleted, freshly milled complete guinea pig diet, not one designed for any other species. Supplements of hay or greens may be given, but with care as digestive disturbances may result from an excessive amount. **The food requirement is 6g per 100g bodyweight daily.** However because much of the food is wasted more should be supplied. The food should contain 18-20 per cent crude protein, and 10-16 per cent fibre. Coprophagy does occur in the guinea pig, but may not be essential.

Breeding

Female guinea pigs reach puberty from 5-6 weeks, and males from 8 weeks. The average is 9-10 weeks. Pairing should be done when the female is 400g (at 2-3 months), and the male 650g (3-4 months). One boar can be housed with one to ten females. The oestrous cycle of the female lasts 15-17 days, and she is receptive for 6-11 hours. The vagina is covered by an epithelial membrane which is intact except during oestrus and parturition, both of which are signalled by perforation of the membrane. Gestation lasts 59-72 days, depending on litter size. In the last week of gestation, the pubic symphysis separates under the influence of the hormone relaxin, and once the gap reaches 15mm parturition will take place within 48 hours. Females should have their first litter before reaching 7-8 months of age, or the symphysis will be unable to separate sufficiently and will have difficulty giving birth (dystocia). In any case, there is often a high incidence of dystocia and fetal death. Abortions and stillbirths are common.

Female guinea pigs can breed until they are 20 months old. Thereafter, the litter size tends to drop and dystocia is more common. Neonatal guinea pigs are precocious, weighing 60-100g, and they begin to eat solid food within a few days. The young are not hungry until 12-24 hours after birth, and can then be fed cows' milk or soaked guinea pig pellets. If the females are not kept in harem groups, the young may be removed at birth and hand reared, to allow the sow to be mated at the post-partum oestrus. Otherwise, weaning takes place at 180g (15-28 days), or 21 days (165-240g). Weaned males intended for breeding need to be weaned late or group housed to allow development of normal adult reproductive behaviour.

Handling

Guinea pigs are easily startled, and they will vocalise and try to avoid capture when approached. They should be grasped quickly and smoothly, placing the thumb and fingers of one hand on either side of the shoulders, then lifted and the free hand placed beneath the hindquarters to support the weight. The guinea pig can then be turned over for i.p. injections or sexing. Positioning the thumb under the foreleg and beneath the chin as in the rat will provide additional restraint. Alternatively, one hand may be placed under the thorax and the other under the rear feet. It is particularly important to support pregnant females with two hands.

Recognition of pain and stress

Guinea pigs are alert, apprehensive animals who will try to avoid capture and restraint. Any unusual sign of acceptance indicates the animal is unwell. Loud vocalization accompanies even minor and transient pain. They often appear sleepy when in pain and rarely show aggression. They are stoical animals and it can be difficult to assess whether they are in pain from a single glance. A carefully used pain scoring assessment method should be employed.

Common diseases and health monitoring

Relatively few infectious diseases are seen in guinea pigs. Guinea pigs are unique among non-primates in having a dietary need for vitamin C however, and will develop signs of deficiency if fed diets which are not designed for guinea pigs, which have been stored incorrectly, or fed after the use by date, since vitamin C is labile and will degrade over a period of time. Most infectious diseases seen in guinea pigs are bacterial, with abscesses and non-specific infections most commonly encountered. However, guinea pigs can carry lymphocytic choriomeningitis virus (a zoonosis) and Sendai virus.

Anaesthesia in the Small Laboratory Animals

Anaesthesia in small laboratory animals is potentially difficult and presents a significant risk. Their small size makes access to blood vessels difficult and increases heat loss during anaesthesia, resulting in hypothermia. Also, fasting before or after anaesthesia may result in the development of hypoglycemia. Pre-anaesthetic fasting is unnecessary since these animals cannot vomit. It may be required if surgery on the upper GI tract is to be undertaken but even then, since coprophagy is not prevented, removing the animal's food may not result in an empty stomach.

Anaesthesia should only be induced in healthy, stress free animals. Small animals need to be kept warm during and after anaesthesia, to prevent hypothermia, and may need supplementary fluids to prevent dehydration and encourage return to normal physiology in the post anaesthetic period.

Inhalation anasthesia

Isoflurane is the inhalation agent of choice for small animal anaesthesia. It has a very high safety margin for all species and is rapidly excreted from the tissues via the lungs, which results in rapid recovery. There is virtually no biotransformation, making it the most suitable agent for studies that require maintenance of normal drug metabolising ability.

Isoflurane may be used to induce anaesthesia in rodents by exposing them to a high concentration of the agent. This may be administered via a facemask, or more usually via an anaesthetic chamber. These methods are suitable for mice, rats and guinea pigs, but not for rabbits, which breath-hold for a long period and become anoxic.

Alternatively a short-acting injectable agent may be given to produce initial unconsciousness, with anaesthesia then being maintained with a volatile inhalation agent. Once an animal is unconscious, anaesthesia can be maintained by passing an endotracheal tube and administering a low concentration of volatile agent in oxygen. This is safe for both the animal and the operator. However, passing an endotracheal tube in the small laboratory species can be difficult, and it may be necessary to use a facemask.

Injectable anaesthesia

Injectable agents can be given by a number of routes. In all cases, the intra-venous route is to be preferred, as the effect is immediate and the dose can therefore be titrated against the effect, making it much safer. However, difficulty accessing veins in some of the smaller animals, especially guinea pigs and mice, makes intra-peritoneal route more common in these species. With this route, the dose has to be pre-determined against body weight and then administered in one injection. There are several disadvantages to the i/p route: the total dose is always larger than if given i/v, absorption is slower, and therefore induction is slower. Any residual drug effects will persist for longer and so recovery is usually also prolonged. It is also never possible to be absolutely certain that you have administered the injection into the peritoneal space, and occasional mis-injection into other tissues, such as fat, may account for the variable results that may sometimes be seen following injection.

Many injectable agents are available. Some of these are listed in the tables.

Drug dose rates for anaesthesia in rodents and rabbits, all i/p administration unless otherwise stated

Drug	Type of small animal										Comments	Duration of anaesthesia	Sleep time
	Guinea-pig		Mouse		Rabbit		Rat		Hamster				
	mg/kg	Route	mg/kg	Route	mg/kg	Route	mg/kg	Route	mg/kg	Route			
Medetomidine (ug/kg)	-	-	30-100	s.c			30-100	s.c	100	s.c	Sedation only. Reverse with atipamezole 1mg/kg s.c	-	-
Hynorm (ml/kg) (fentanyl/fluanisone)	0.65 20 min	i/m	0.5 60 min +		0.22	i/m	0.4	i/m	0.5	i.m	Sedation only. Good analgesia Poor relaxation	-	-
Alphaxalone (mg/kg)	40	i/v	10-15	i/v	6-9	i/v	10-15	i/v	150	i.p.	Surgical anaesthesia only if i/v	5 mins	10 min
Hypnorm (ml/kg) + diazepam (mg/kg)	1 2.5	i/m	0.4 5		0.3 2.5	i/m i/p or i/v	0.3 2.5	i/m	1 +5	i.m or i.p	Good surgical anaesthesia	45-60 mins	3-4 hours +
Hypnorm (ml/kg) + midazolam (mg/kg)	8*		10*		0.3 2	i/m i/p or i/v	2.7*		4*	i.p	Good surgical anaesthesia	45-60 mins	3-4 hours +
Ketamine (mg/kg_ Diazepam(mg/kg)	100 5		100 5		25 5	i/m i/m	75 5				Light anaesthesia	20 mins	2 hrs
Ketamine (mg/kg) + Medetomidine (mg/kg)	40 1		75 0.5		35 0.5	i/m	75 0.5		100 +0.25		Surgical anaesthesia	20-30 mins	2-4 hrs +
Ketamine (mg/kg) + Xylazine (mg/kg)	40 5	i/m	80-100 10		35 5	i/m	90 +10		50-200 +5-10		Surgical anaesthesia	20-30 mins	2-4 hrs +
Propofol (mg/kg)	10	i.v	26	i/v	10	i/v	10	i/v	10	i.v	Surgical anaesthesia only if i/v	5 mins	10 mins

i/m intramuscular i/p intraperitoneal i/v intravenous

* Mixture of 1 part Hypnorm, 2 parts water for injection and 1 part midazolam.
+ Recovery time reduced if specific antagonists are administered

Suggested dose rates of analgesia in small animals

Analgesic	Type of small animal														
	Mouse			Rat			Guinea-pig			Hamster			Rabbit		
	Dose (mg/kg)	Route	Interval (hourly)	Dose (mg/kg)	Route	Interval (hourly)	Dose (mg/kg)	Route	Interval (hourly)	Dose (mg/kg)	Route	Interval (hourly)	Dose (mg/kg)	Route	Interval (hourly)
Buprenorphine	0.05-0.1	s/c	8-12	0.01-0.05	s/c	8-12	0.05	s/c	8-12	0.5	s/c	8-12	0.01-0.05	s/c, i/v	8-12
Butorphanol	1-5	s/c	4	2	s/c	4	1	s/c	24	0.4	s/c	8-12	0.1-0.5	i/v	4
Flunixin	2.5	s/c, i/m	12	2.5	s/c, i/m	12	-	-	-	2.5	s/c	12	1.1	s/c, i/m	12
Ibuprofen	30	per os	4	15	per os	4	10	i/m	4	-	-	-	10	i/v	4
Meloxicam	5	s/c	24	1.0	s/c, per os	12-24	0.1-0.3	s/c, per os	24						
Morphine	2-5	s/c	2-4	2-5	s/c	2-4	2-5	s/c, i/m	4	-	-	-	2-5	s/c, i/m	2-4
Pethidine	10-20	s/c, i/m	2-3	10-20	s/c, i/m	2-3	10-20	s/c, i/m	2-3	20	s/c	2-3	10	s/c, i/m	2-3

i/m intramuscular i/v intravenous s/c subcutaneous

See Flecknell and Waterman-Pearson (2000) Pain management in animals. WB Saunders.

Biological data, mouse

(NB: There are strain variations especially in genetically modified mice)

Biological Data		**Breeding Data**	
Adult weight (grams)	Male 20-40 Female 18-40	Puberty (days)	28-49 (Average 42)
Diploid number	40	Age to breed male (days)	70
Food intake	15g/100g bodyweight	Age to breed female	60-84
Water intake	15ml/100g bodyweight	Gestation (days)	19-21
		Litter size	4-12
Rectal temperature (^{o}C)	38-39	Birth weight (grams)	1-1.5
Heart rate/min.	310-840	Weaning age (days)	18-21
Blood volume (ml/kg)	60-75	Oestrous cycle (days)	4-5
Tidal volume	0.18	Post partum oestrus	Fertile

Haematological Data		**Biochemical Data**	
RBC (x10^{6}/mm^{3})	7-12.5	Serum protein (g/dl)	3.5-7.2
PCV (%)	39-49	Albumin (g/dl)	2.5-4.8
Hb (g/dl)	10.2-16.6	Globulin (g/dl)	0.6
WBC (x10^{3}/mm^{3})	6-15	Glucose (mg/dl)	62-175
Neutrophils (%)	10-40	Blood urea nitrogen (mg/dl)	12-28
Lymphocytes (%)	55-95	Creatinine (mg/dl)	0.3-1
Eosinophils (%)	0-4	Total bilirubin (mg/dl)	0.1-0.9
Monocytes (%)	0.1-3.5	Cholesterol (mg/dl)	26-82
Basophils (%)	0-0.3		
Platelets (x10^{3}/mm^{3})	160-410		

From Wolfensohn and Lloyd (2003).

Biological data, rat

Biological Data		**Breeding Data**	
Adult weight (grams)	Male 450-520 Female 250-300	Puberty (days)	60-63
Diploid number	42	Age to breed (days)	65-110
Food intake	10g/100g bodyweight	Gestation (days)	20-23
Water intake	10ml/100g bodyweight	Litter size	6-12
Rectal temperature (^{o}C)	36-40	Birth weight (grams)	5-6
Heart rate/min.	250-450	Weaning age (days)	21
Blood volume (ml/kg)	54-70	Oestrous cycle (days)	4-5
Respiratory rate/min.	70-115	Post partum oestrus	Fertile
Tidal volume (ml)	0.6-2		

Haematological Data		**Biochemical Data**	
RBC (x10^{6}/mm^{3})	7-10	Serum protein (g/dl)	5.6-7.6
PCV (%)	36-48	Albumin (g/dl)	3.8-4.8
Hb (g/dl)	11-18	Globulin (g/dl)	1.8-3
WBC (x10^{3}/mm^{3})	6-17	Glucose (mg/dl)	50-135
Neutrophils (%)	9-34	Blood urea nitrogen (mg/dl)	15-21
Lymphocytes (%)	65-85	Creatinine (mg/dl)	0.2-0.8
Eosinophils (%)	0-6	Total bilirubin (mg/dl)	0.2-0.55
Monocytes (%)	0-5	Cholesterol (mg/dl)	40-130
Basophils (%)	0-1.5		
Platelets (x10^{3}/mm^{3})	500-1300		

From Wolfensohn and Lloyd (2003).

Biological data, guinea pig

Biological Data		**Breeding Data**	
Adult weight (grams)	Male 850-1200 Female 700-900	Puberty	Male 60 days Female 30 days
Diploid number	64	Age to breed male	3-4 months,
Food intake	6g/100g bodyweight		600-700g
Water intake	10ml/100g bodyweight	Age to breed female	2-3 months,
Lifespan (years)	4-8		300-450g
Rectal temperature (^{o}C)	37.2-40	Gestation (days)	59-72
Heart rate/min.	230-380	Litter size	2-5
Blood pressure systole (mmHg)	80-94	Birth weight (grams)	70-100
Blood pressure diastole (mmHg)	55-58	Weaning age	3-4 weeks
Blood volume (ml/kg)	69-75	Oestrous cycle 15-17 days	
Respiratory rate/min.	42-104	Post partum oestrus	Fertile
Tidal volume (ml)	2.3-5.3		

Haematological Data		**Biochemical Data**	
RBC (x10^6/mm^3)	4.5-7	Serum protein (g/dl)	4.6-6.2
PCV (%)	37-48	Albumin (g/dl)	2.1-3.9
Hb (g/dl)	11-15	Globulin (g/dl)	1.7-2.6
WBC (x10^3/mm^3)	7-18	Glucose (mg/dl)	60-125
Neutrophils (%)	28-44	Blood urea nitrogen (mg/dl)	9-31.5
Lymphocytes (%)	39-72	Creatinine (mg/dl)	0.6-2.2
Eosinophils (%)	1-5	Total bilirubin (mg/dl)	0.3-0.9
Monocytes (%)	3-12	Cholesterol (mg/dl)	20-43
Basophils (%)	0-3		
Platelets (x10^3/mm^3)	250-850		

From Wolfensohn and Lloyd (2003).

REFERENCES AND FURTHER READING

BVA Animal Welfare Foundation online tutorials: http://www.bva-awf.org.uk/resources/tutorials/

BVA Animal Welfare Foundation et al. Refinements in rabbit husbandry. Second report of the BVAAWF/FRAME/RSPCA/UFAW Joint Working Group on refinement. **Laboratory Animals**, 27 301-29.

Conlon, K.C., Corbally, M.T., Bading, J.R., and Brennan, M.F. (1990). Atraumatic endotracheal intubation in small rabbits. **Laboratory Animal Science**, 40(2), 221-22.

Davies, A., Dallak, M. and Moores, C. (1996). Oral endotracheal intubation of rabbits (Oryctolagus cuniculus). **Laboratory Animals 30**, 182-183.

FELASA Working Group on Health Monitoring of Rodent and Rabbit Colonies. (2002) Recommendations for the health monitoring of rodent and rabbit colonies in breeding and experimental units. **Laboratory Animals** 36, 20-42

Flecknell and Waterman-Pearson (2000) **Pain management in animals**. WB Saunders

Foster, H.L., Small, J.D., and Fox, J.G. (eds.) (1983). **The mouse in biomedical research** Vol. III. Academic Press, New York.

Harkness J.E. and Wagner J.E. (1989). **The biology and medicine of rabbit and rodents** Lea and Febiger

Hillyer E.V. and Quesenberry K.E. (1997). **Ferrets, Rabbits and Rodents: clinical medicine and surgery** W.B. Saunders

Hubrecht R. and Kirkwood J. (eds) (2010). **The UFAW Handbook on the Care and Management of Laboratory Animals.** Eighth Edition. Wiley, Chichester.

National Research Council (1996). **Laboratory animal management: rodents**. National Academy Press.

Popesko. P., Rajtova, V. and Horak, J. (1992). **A colour atlas of anatomy of small laboratory** animals Volume 1: Rabbit, guinea pig. Volume 2: Rat, mouse, hamster. Wolfe Publishing Ltd.

Rodent Refinement Working Party (1998). Refining rodent husbandry: the mouse. **Laboratory Animals** 32, 233-259

Tuffery AA(ed) (1995). **Laboratory Animals an Introduction for Experimenters** 2nd Edition

Wolfensohn S and Lloyd M (2003). **Handbook of laboratory Animal Management and Welfare** Third edition. Wiley Blackwell.