The Laboratory Rabbit

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ANZCCART Facts Sheet

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Introduction

Rabbits (*Oryctolagus cuniculus*) are classed with hares, pikas, and American cottontail rabbits in the Order Lagomorpha. The domesticated rabbit is derived from the European wild rabbit, apparently native to continental Europe and perhaps North Africa. The species is most common in southern and Mediterranean Europe, particularly Spain, and has been domesticated at least since Roman times.

Wild rabbits have been introduced to many countries, including Britain, since the Middle Ages, and Australia and New Zealand in the 19th century. All significant establishments of introduced rabbits have been the result of deliberate introduction of wild rabbits. Escaped domesticated rabbits have not been involved. The term 'feral' is inappropriate in this sense. Wild rabbits have never become established in North America, probably because of the presence of well established native predators of cottontail rabbits.

Wild rabbits have adapted to a wide variety of conditions from semi-arid to sub-tropical, but do best under temperate pastoral conditions. In Australia they have never established in the tropical north. This adaptability is attributable to their efficient pseudo-ruminant digestive system and high reproductive potential.

Domesticated rabbits are raised for meat, fur and pelts. Rabbit hair is the finest mammalian hair, and Angora fur breeds have been developed. Rabbits are important livestock in some parts of the world, including Europe and China. As meat producers, they are highly efficient converters of low grade plant materials (e.g. hays, forage crops, cereal by-products) to animal protein, with best feed conversion ratios of around 2.5 : 1.

As laboratory animals, rabbits have been particularly used for anti-serum production, pyrogen testing, cardio-vascular studies including atherogenesis, teratology, and ocular studies. Their advantages as laboratory animals include good access to blood vessels, size, reproductive rate, and suitability for cage housing. Laboratory rabbits used in Australia include the following breeds:

- *New Zealand Whites*: these are large-bodied albinos with erect ears, developed as meat rabbits. Mature body size 4-5kg.
- *Lop -eared Rabbits*: these are large coloured rabbits with broad pendulous ears, used originally for ear chamber implantation studies. Mature body size is about 4kg.
- *Dutch Belted and English Multicoloured rabbits*: these are smaller coloured rabbits with erect ears. Mature body size is about 3kg.

Apart from body and ear size, there seems little objective evidence that any strain is preferable for a particular experimental purpose. Inbred strains have been developed but are not in general use. Sources of laboratory rabbits can be found in the publication *Survey of Laboratory Animals and Tumour Cell Lines Maintained in Australia* (7th Edition), ANZCCART 1992.

Husbandry and housing

thermoneutral zone	5°C-30°C
optimal environmental temperature	15°C-20°C
optimal environmental relative humidity	45%-65%
light/dark ratio for reproduction	14hr/10hr

The available evidence indicates the need for space to permit sufficient exercise for normal skeletal structure development, and for direct social contact with other compatible rabbits. Rabbits have a very light bone structure (8% of body weight compared to 13% in cats), which is significant with regard to vertebral fractures (Harkness and Wagner, 1989).

Group pens represent an excellent form of environmental enrichment and should be considered wherever appropriate (BVAAWF *et al.*, 1993; Whary *et al.*,

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1993; Love, 1994). Otherwise, cages large enough to accommodate two or three rabbits and utilizing various forms of environmental enrichment should be used where appropriate. However, in some circumstances, group housing is not possible. For example, groups of mature intact males kept together will always result in trauma to subordinate males. Group breeding of females will increase pre-weaning losses (Harkness and Wagner, 1989; Post-Graduate Committee in Veterinary Science, 1990).

Stock Rabbits

It is recommended that group pen housing of stock rabbits could be considered appropriate in the following circumstances:

- use with compatible adult female rabbits, young rabbits of either sex up to 10 - 12 weeks of age, or castrated adult males;
- use particularly for long term holding purposes (over six weeks);
- place no more than six to eight rabbits in a group;
- preferably form the group from weaning or as soon after as possible;
- use with animals free from infection with *Pasteurella multocida*, ear mites, and coccidiosis;
- provide micro-environments including retreating and hiding places.

Where rabbits are held in cages, it is recommended that:

- to provide sufficient space for adequate exercise, cages should provide room for hopping or jumping (a horizontal dimension of at least 0.8-1m) and vertical space for stretching upright (45-50cm) (Lehmann 1987);
- rabbits should be caged in compatible groups of two or three animals where possible in sufficiently large cages (BVAAWF, 1993; Whary *et al.,* 1993);
- where rabbits are held in smaller cages which do not provide room for adequate exercise, access to exercise pens for several hours should be provided at least several times weekly. Such access can also be used for singly caged rabbits for opportunities for social interaction with other compatible rabbits;
- environmental enrichment such as toys, sticks, climbing surfaces, and retreating and hiding places within the cage should be provided (Stauffacher, 1992);
- cage floors of stamped out sheet metal or plastic are preferable to wire floors. However more frequent cleaning of cage floors may be required;
- after weaning, young stock rabbits should be held in sufficiently large cages in litter mate groupings for as long as practicable and while the animals are compatible. Intact males must be separated by 12 weeks of age;
- singly caged rabbits must always be able to see other rabbits in adjacent or facing cages;
- wherever possible, experimental rabbits should be held in single cages for short term purposes only (6 weeks or less).

Breeding Rabbits

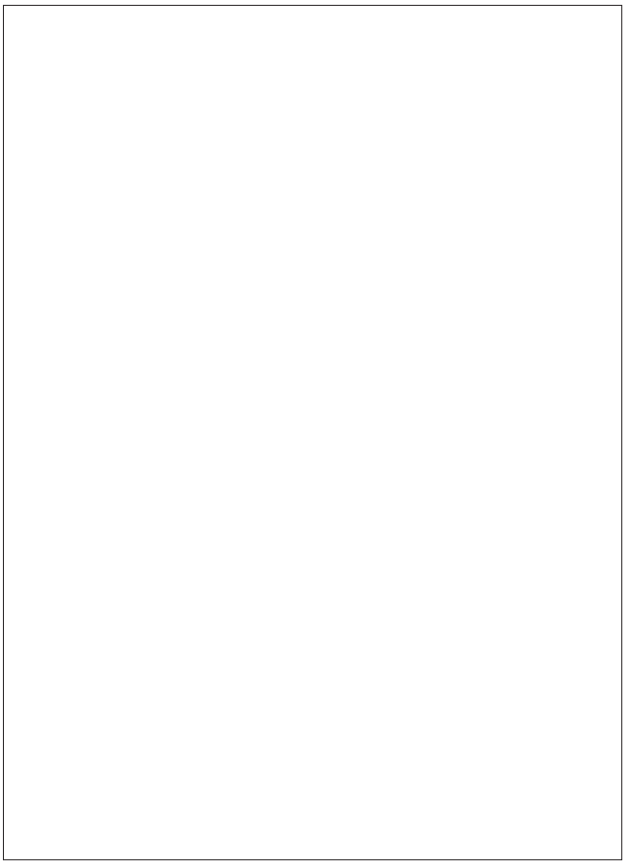
More work needs to be done to assess the usefulness of a large enriched group breeding cage holding two or three female rabbits with or without the permanent presence of a male rabbit, as suggested by Stauffacher (1992). The concept of an enriched group mating pen as described by Stauffacher containing one male and five or six females also has much merit but will not hold many rabbits per unit of room floor area, rendering it impractical for most situations, and it may cause higher pre-weaning mortality rates.

For breeding rabbits held singly in cages, it is recommended that:-

- cages should provide room for hopping or jumping (a horizontal dimension of at least 0.8- 1m) and vertical space for stretching upright (45-50cms) (Lehmann 1987);
- breeder rabbits held in smaller cages should be given access to exercise pens for several hours at least several times weekly;
- cages should provide some secluded area for nesting purposes for does with young litters;
- Litters should be weaned by four to five weeks, or does should have retreating areas where they can escape attention from their offspring;
- does should be kept breeding (i.e. remated by the time of weaning the previous litter) or else housed with one or two other compatible females in sufficiently large cages in between litters. Aggression between breeding does is quite likely. Some large facilities in Australia use a single doe floor-penned breeding system successfully. Such systems ensure that the does have full environmental and behavioural enrichment without the unattractive aesthetics of caging and without the problems of group floor pens.

Grasping and lifting a rabbit

Grasp by the scruff of the neck and support the body with the other hand



General*

Scientific classification: Species Oryctolagus cuniculus, Order Lagomorpha, Class Mammalia

diploid chromosome number (2n)	44
general activity	crepuscular (dawn + dusk twilight) but adaptable to environmental influences
life span	5-10 years
productive life span for domestic production	2-3 years or 10 litters
birth weight	30-100gm (average 50-70gm)
adult weight	2.5-5kg
growth rate	15-20gm/day to 8 weeks
	100-150gm/week to 26 weeks
body temperature	38-40°C
body surface area	9.5 x (wt in grams) $^{2}/_{3}$
energy requirement for growth	180-280 kcal D.E./day
skeletal weight	7-8% of total body weight

*See Harkness and Wagner; (1989); Williams, (1976); Weisbroth et al., (1974).

Reproduction**

sexual maturity	18-22 weeks
oestrous cycle	prolonged pro-oestrus
ovulation	induced
post-partum mating	yes (if permitted), usually fertile
gestation period	31-32 days
average litter size	4-10
weaning age	30-35 days
placenta	discoidal, classified variously as haemochorial or haemoendothelial
transfer of passive immunity	mainly or entirely via yolk sac
uterus	2 horns, 2 cervixes (duplex)
egg diameter	160 μm
time to early blastocyst	72-80 hr post-conception
time to implantation	160-170 hr post-conception
mammary glands	4 pairs (1 thoracic, 2 abdominal, 1 inguinal)
milk composition***	water 73-74%
	protein 10-15% (av. 10.4-12.5%)
	fat 10-16% (av. 12-13%)
	carbohydrate 2%
	ash 2-3%
age testicles descend	10-12 weeks
maximum female reproductive output	1 offspring weaned/female/week
	(most colonies average 0.5-0.8)
young - eyes open	7 days
young - start eating solid food	3 weeks
volume of ejaculate	0.5-0.8 ml
sperm density	200-500 x 10^{6}/ml
daily sperm output	170 x 10^{6}/day
success of natural matings	75-80% mate successfully of which 90% conceive
expected perinatal and weaning mortality	20%
hormonal induction of ovulation (dose)	20-40i.u. of human chorionic gonadotrophin or 2.25ml luteinising hormone releasing hormone ('Receptal', Hoechst, Bomac)

**See Adams, (1972); Hafez, (1970); Harkness and Wagner, (1989); Poole, (1987); Weisbroth et al., (1974); Williams (1976).
***Does only feed their young once or twice a day. This can often be mistaken for mismothering.

Circulation and Haematology

heart rate	150-300 per minute (average 200-240)
arterial blood pressure - systolic	90-130mmHg (average 110)
diastolic	60-90mmHg (average 80)
blood volume	45-75 ml/Kg B.wt (average 60)
haematocrit (packed cell volume)	30-50% (average 36-44%)
red cell count	3.9-7.0 x 10^6/mm^3 (average 4.8-6.3)
haemoglobin	8-17gm/100ml (average 10-14)
white cell count	2.5-12.5 x 10^3/mm^3(average 5-11)
differential count	neutrophils - 20-75% (as heterophils)
	lymphocytes - 20-90%
	monocytes 2-16%
	basophils 2-10%
anaphylactic shock target organs	pulmonary artery constriction, right heart dilation, Ag/Ab complexes precipitate in pulmonary capillaries
aural circulation	central artery, anterior and posterior marginal veins

Respiration

respiratory rate (adult)	32-65/minute (average 35-56)
tidal volume (at rest)	20ml (4-6ml/kg)
0_2 consumption (at rest)	0.42-0.48ml/gm/hr
breathing type	obligate nose breathers
lung structure	2 left lobes, 4 right lobes

Excretion

urine	thick, turbid, crystalline, creamy yellow or occasionally orange red, moderate proteinuria
urine pH	8.2
urine excretion rate	50-130ml/kg/day (average 50-90)

Plasma Clinical Chemistry***

total protein	4.0-8.5gm/100ml (average 5.4-7.4)
albumin	55%
α globulin	15%
β globulin	15%
γ globulin	15%
glucose	3-8mmol/l
cholesterol	10-80mg/100ml (average 35-55)
urea	7-13mmol/l
bilirubin	3-7mmol/l
calcium	2.4-3.4mmol/l
magnesium	0.5-0.8mmol/l
sodium	125-148mmol/l
potassium	3.3-4.1mmol/l
alkaline phosphate	10-50i.u./l
AST (SGOT)	10-98i.u./l
ALT (SGPT)	10-80i.u./l

***See Harkness and Wagner, (1989); Poole, (1987); Post Graduate Committee in Veterinary Science (1990); Weisbroth, et al., (1974); Williams, (1976).

Digestion

digestive mode	herbivorous, monogastric, enlarged caecum and colon with hind gut fermentation, coprophagic, nocturnal passage of caecotrophs
food consumption (dry pellets)	5% body weight/day
water consumption	8-10% body weight/day
dentition	no deciduous teeth, open rooted, continuous growth
dental formula	incisor $^2/_1$, canine $^0/_0$, premolar $^3/_2$, molar $^3/_3$
gastric pH	1-2 (adult), 5-6 (pre-weaning)
gastro-intestinal transit time	4-5 hr
fasting time to empty tract	9 days
gastro-intestinal antibiotic tolerance	penicillin and all penicillin derived antibiotics are likely to be toxic
gall bladder	present, separate bile and pancreatic ducts, bile pigment mostly biliverdin

Dietary Recommendations

crude protein levels		growth - 15-19% pregnancy and lactation - 16-20% maintenance - 12-15%
energy content of food		2200-3200 kcal D.E./kg
optimum energy/protein ratio		23.5 kcal D.E. per gm D.C.P.
fibre		14-22%
fats		3-5% (up to 15% satisfactory)
vitamins	A	10,000i.u./kg (carotene will replace)
	D	1,000i.u./kg (over 3,000 is toxic; rabbits do not seem to have any essential requirement)
	E	100mg/kg
	K	2mg/kg (caecal synthesis)
	B_1	19mg/kg (caecal synthesis)
	B_2	6mg/kg
	B_3	40mg/kg
	B_{12}	0.1mg/kg (caecal synthesis)
	biotin	0.2mg/kg
	folic acid	1mg/kg
	pantothenic acid	20mg/kg
	ascorbic acid	not required
	salt	0.25-0.5%
	calcium	0.6-1.0%
	phosphorus	0.4-0.7% (Ca:P-1:1 to 1.5:1)
	potassium	0.6-0.9%
	magnesium	400mg/kg
	iron	100mg/kg
	copper	6mg/kg
	zinc	40mg/kg
	manganese	40mg/kg
	iodine	0.3mg/kg
	fluorine	less than 20mg/kg

Antibiotics

Penicillin*	40mg/kg i/m
Chloramphenicol	15mg/kg i/m
Oxytetracycline	15mg/kg s/c
Trimethoprim 40mg/ml and Sulphadiazine 200mg/ml (as a solution)	0.2ml/kg s/c

*Penicillin and related antibiotics may cause digestive upsets due to interference with gut flora.

Injectable anaesthetic dose rates

Barbiturates	contra-indicated
Ketamine/Xylazine	Ketamine 50mg/kg and Xylazine 5mg/kg as combined i/m injection, or Xylazine 5mg/kg i/m and then Ketamine 10mg/kg i/v after 5 minutes
Saffan	7mg/kg i/v (variable effects are reported)
Diazepam and Fentanyl/Droperidol	Diazepam 2mg/kg i/m and Fentanyl/Droperidol 0.3ml/kg i/m
Acepromazine/Propofol	Acepromazine 1mg/kg i/m and Propofol 10mg/kg i/v
Buprenorphine (analgesia)	0.02-0.05mg/kg/8hr i/m

Disease and Aetiology	Clinical and Pathological Signs	Transmission, Control, Treatment
Pasteurella multocida infection 'Snuffles'	Respiratory form - purulent nasal and/or ocular discharge, rhinitis, sinusitis, sub-acute or chronic pneumonia. May be septicaemic spread to metritis, mastitis, orchitis, etc.; in group housed rabbits it is often associated with abscessed or infected bite wounds.	Direct transmission - requires close contact. Aerosol spread seems relatively ineffective. Spreads mother to offspring (may occur at birth) or horizontally particularly amongst group penned weaners. Systemic antibiotics e.g. tetracyclines, chloramphenicol, may alleviate clinical signs but disease will tend to re-occur due to sequestration of organisms in para-nasal sinus cavities. Vaccines may give partial protection. Best control is by identification of carrier does by nasal swab and plating on selective media, to eradicate and produce a clean breeding herd. It may be desirable to cull the entire herd and repopulate with SPF animals.
Myxomatosis - myxoma (pox) virus	Solid neoplastic subcutaneous swellings, particularly around face and ears; swollen eyelids and conjunctivitis with watery eye discharge becoming purulent, leading to blindness; loss of appetite and anorexia; death usually in one-two weeks. May be complicated by P. multocida infection. Domestic rabbits generally highly susceptible.	Spread by direct contact or insects (fleas, mosquitoes). Live vaccine used overseas, not permitted in Australia. Control by quarantine and prevention of insect entry to rabbit housing. Some affected animals may recover with nursing, hand feeding, and antibiotic cover for secondary bacterial infections.
Rabbit haemorrhagic disease. (Calicivirus)	Short incubation (one-two days), fever, lethargy, high mortality (90%) within five days. Rabbits less than two months old recover. At necropsy, good body condition, food in stomach, pale swollen friable liver, enlarged spleen, widespread haemorrhages which may not be observed very close to time of death. Less acute and chronic forms of the disease have also been described.	Planned use as a biological control agent, although the effect of the recovery of young exposed rabbits on the epizootiology of the disease may be contradictory. No control measures at present but it is to be hoped that a killed vaccine will be available to protect domestic rabbits if this disease is introduced into the wild population. The virus is highly infectious, very stable and resists drying. Direct spread or via contaminated feed, bedding, or clothing.
Enterotoxaemia (Clostridium spiroformé toxinogenic strains produce toxins similar to iota toxin of C. perfringens)	Acute enteric disease with passage of dark fluid faeces which may show signs of blood and/or mucus, and usually gas bubbles. At necropsy, large intestines are hyperaemic and distended with foul smelling dark fluid contents and gas. Confirm by mouse toxin test - 0.5ml of filtered supernatant of gut content injected i/p will kill a mouse in less than one hour.	No effective treatment. Emtryl (dimetradazole) in drinking water at 2.5g/l may lessen the severity of outbreaks. Outbreaks are predisposed by stress, particularly transport, dietary change, use of penicillin derived antibiotics, introduction of carrier rabbits, and low crude fibre diets. Changing from a low fibre diet to a diet with at least 14% crude fibre content has been effective in stopping one outbreak.
Mucoid enteropathy - unknown aetiology	Passage of scant quantities of hard dry faecal pellets and large quantities of firm mucus. Thought to be due to secretory hypertrophy of intestinal mucosa due to unknown gut irritants. Possibly a low level chronic form of Clostridium spiroformé infection. Loss of appetite and body condition leading to death after several weeks.	Symptomatic treatment usually ineffective. Transmission and control measures unknown. As a high starch and low fibre diet has been implicated with a fall in hindgut pH and caecal floral dysbiosis, a high fibre diet is likely to play a protective role.

Eimeria species; hepatic form - Eimeria steidae).	dysentery although hyperacute cases may die first. Hepatic form—more common. Retarded growth, swollen abdomen, liver palpably enlarged. Usually no diarrhoea. Oöcysts demonstrable in faeces or bile with hepatic form. Hepatic form at necropsy reveals swollen liver, and disseminated micro-abscesses with pus tracking along bile ducts.	environmental contamination of sporulated oocysts after more than two days in the environment. Mainly occurs in weanling rabbits, infected from doe or from other weaners in floor pens. Will not transmit in rabbits in grid floored cages (no transmission by coprophagy as oöcysts are not sporulated). Various coccidiostats are effective e.g. sulphaquinoxaline 0.1% in drinking water for one-two weeks or .025% in food for prophylaxis. Increase frequency of pen cleaning or place in cages to prevent transmission. Avoid mixing weaners from different litters.
Encephalitozoonosis (Encephalitozoon cuniculi - protozoan, previously Nosema cuniculi)	Causes nephritis and encephalitis, mainly in young rabbits. Affected rabbits are stunted, may have swollen skulls, nervous signs, and enlarged kidneys with white cortical foci and pitted surface. Confirmed histologically (Goodpasture's stained sections of kidney and brain) or serologically.	No treatment. Control by removing carrier does which produce affected litters or by serological testing. Generally difficult to eradicate other than by complete replacement with S.P.F. stock. This is a common infection in laboratory animal colonies but clinical cases are generally very few. Has been suspected of being zoonotic but evidence for this is uncertain. Diagnosis of this agent with histopathology using polarised light effectively shows the spores as bifringent.
Mite infestations - Ear mite - Psoroptes cuniculi Fur mite - Cheyletiella parasitovorax	Ear mites - brown accumulation in ear canals; inflammation, pruritis, and crusting of ears and adjacent skin. Fur mites - no signs or alopecia, reddened hairless scaly patches over back and head.	Spread by direct contact. Adult mites survive off host for one week or more. Treat with topical insecticides e.g. 0.5-1.0% mallathion, insecticidal ear drops, ivermectin orally or by injection at 400 μg/Kg (e.g. 0.8% sheep oral formulation in drinking water diluted one in 1000) and repeat weekly for four weeks, or exposure to dichlorvos strips.
Vitamin D toxicity	Loss of body weight despite normal appetite; high protein levels in urine; at necropsy, metastatic calcification of proximal aorta, lung arterioles, and renal cortex, with severe nephritis.	Rabbits do not seem to have a strict need for Vitamin D. Dietary levels over 3,000 iu/kg are toxic.
Vertebral trauma	Partial or complete posterior paresis with full bladder and urine overflow. Vertebral luxation or fracture on X-ray.	May be due to struggling while being handled or in a restraint box, but also often self inflicted possibly due to startling. Osteoporosis due to prolonged cage confinement with no exercise is a major cause of vertebral fracture.
Sore hocks (pododermatitis)	Pressure sores with scabs or secondary infection on the ventral surface of hock joint.	Occurs in caged rabbits, particularly large fully grown rabbits and with rough or uneven wire floors. Woven wire floors are worst. Cage floors of stamped out sheet stainless steel or plastic are preferable. Place affected rabbits in cages with soft bedding floor until healed, then give a solid surface in cage to sit on. Topical treatment and systemic antibiotic if required.
Gastric furballs	Loss of body weight and loss of feed intake and faecal output. May be palpable or visible on X-rays.	Paraffin and laxatives may be effective, otherwise surgical removal. Provide diet with at least 14% crude fibre and supplement with lucerne hay regularly.

Euthanasia methods			
Techniques	Recommended	Acceptable with reservations	Not acceptable
Chemical			
Inhalant	None recommended	Halothane [b] Enflurane [bd] Nitrous oxide [b]	Chloroform [bcef] Carbon dioxide [cf]
Injectable	Pentobarbitone sodium i/v or i/p 60mg/kg	Ketamine with a premedicant such as acetylpromazine or xylazine	Ketamine alone [c]
Physical	None recommended	Stunning and dislocation [af] Captive bolt [afg] Neck dislocation or [a] Decapitation (only if anaesthetised first)[ag]	Neck dislocation without anaesthesia [cf] Decapitation [cfg]

[a] Training required
[b] Occupational Health and Safety issues
[c] Inhumane
[d] Expensive
[e] Hazardous to health of operator
[f] Aesthetically unpleasant
[g] Requires specialised equipment

From Reilly (1993)

Other diseases

Venereal spirochaetosis is occasionally seen and responds well to penicillin. Ringworm, although not generally considered to be a disease of rabbits, does occur, particular in weaner rabbits. The lesions are rarely crusty and are usually circular alopecic areas with exposed and slightly inflamed pink skin.

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