

## Health problems in geriatric rats

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**The past decade has seen an exponential increase in the number of rodents kept as pets.**

Rats, in particular, are considered one of the best pet rodents due to their relatively large size, calm and social nature, low tendency to bite and relative intelligence (Lennox and Bauck, 2012).



**Figure 1.** Chromodacryorrhea in a rat. Porphyrin staining around the eye is a non-specific sign of stress that may indicate an underlying disease or a painful state, warranting further investigations. Image: Wendy Bament.

They can be excellent children's pets if handled from a young age and kept in social pairs or groups, and their natural inquisitiveness and dexterity make them fascinating pets that can respond well to training and human interaction. A survey showed approximately 100,000 rats are kept as pets in the UK ([www.pfma.org.uk/pet-population-2014](http://www.pfma.org.uk/pet-population-2014)).

Rodent owners are increasingly expecting high-quality veterinary care for these much-valued pet animals. The lifespan of a domestic rat is approximately two-and-a-half years to three years (Brown and Donnelly, 2012) and improved preventive and interventional health care is certainly leading to increasing numbers of geriatric pets.

The aged rat is susceptible to various diseases, many of which are analogous to geriatric canine

and feline ones (Haines, 2010). Rodents have been long used as models of human diseases in biomedical research, so there is a large amount of information available to the practitioner that is clinically applicable, in some cases, to pet rodents.

Many recommendations are also often based on empirical doses extrapolated from other species and/or anecdotal reports. These considerations need to be reiterated and the pet owner made aware of the potential risks involved in treating an often compromised geriatric individual.

It is also always important to remember rats are prey animals and do not tend to show evident signs of pain or disease. It is often difficult for owners to identify clear evidence of a problem, therefore these animals are sometimes presented very sick and in the latest stage of a disease process.

In humans, physical performance declines with increasing age and laboratory studies have shown age-related declines in physical function in many rodent species as well, including rats. Performance may predict longevity in rats (Carter et al, 2002); however, a declined performance in an older individual has to be distinguished clearly from reduced performance due to disease.

## **Common diseases of geriatric patients**

### **Red tears (chromodacryorrhea)**

In rats, porphyrin staining around the eye is a non-specific sign of stress that may indicate an underlying disease or a painful state (**Figure 1**; Miller, 2011).

Normally, the lacrimal secretions produced by the Harderian gland help in ocular lubrication and pheromone-mediated behaviours. These secretions fluoresce under UV light, but are removed during routine grooming. In stressed or debilitated rodents, they dry around the eyes and external nares, giving the false appearance of bleeding from the eyes or nose. Clinical evaluation in these cases is warranted.

### **Renal disease**

Chronic progressive nephrosis (CPN) is probably the most common disease of aged rats (Percy and Barthold, 2007). CPN is more commonly seen in males, with an incidence as high as 75%.

It is important to consider any changes in the daily husbandry routine, as renal disease is common in aged rats, but gross lesions can be seen in animals as young as six months of age in some strains (Haines, 2010).



**Figure 2.** *Mycoplasma pulmonis* is considered the most important infectious agent responsible for life-persistent, chronic respiratory disease in rats. Progression to broncho-pulmonary disease can occur.

Weight loss and lethargy are common, but non-specific, symptoms of affected animals. Proteinuria is also frequently reported in these cases and tends to worsen with age. Normal urine production is approximately 5.5ml/100g bodyweight and water consumption is 8ml/100g to 12ml/100g bodyweight in healthy rats. A free-catch urine sample can be easily obtained and examined for abnormalities.

Baseline values have been reported for rats (Haines, 2010). Obtaining a blood sample may be important to demonstrate increase blood urea nitrogen and creatinine levels, and decreased serum albumin/globulin ratio.

Differential diagnoses should include chronic bacterial pyelonephritis, hydronephrosis, ischaemic injury and toxic nephrosis (Haines, 2010). Diet and housing seem to have an important role in incidence and progression of chronic renal disease. Overfeeding seems to result in prolonged increased renal blood flow and glomerular filtration rate (Gumprecht et al, 1993).

Caloric restriction (25% to 30% reduction relative to ad libitum feeding; Keenan et al, 1995a), feeding a low protein diet (4% to 7%) and limiting the source of dietary protein seem to reduce incidence and severity of renal disease (Brown and Donnelly, 2012).

Prevention of overfeeding and obesity in pet rats may help to delay the onset and severity of this disease. Treatment is merely supportive. Dietary changes and fluid therapy may help to alleviate the symptoms for a relatively short period of time. Angiotensin-converting enzyme inhibitors have been suggested in cases of associated hypertension (Leenen et al, 1999).

## **Respiratory disease**



**Figure 3.** Severe case of chronic respiratory disease in a rat that developed pulmonary abscesses.

The main concern with the respiratory tract in aged rats is bacterial infections, mainly caused by *Mycoplasma pulmonis*. This Gram-positive bacterium is ubiquitous in pet rodents and is considered to be the most important infectious agent responsible for life-persistent, chronic respiratory disease in rats (Goodman, 2009; Graham and Schoeb, 2011). It can be transmitted horizontally, via aerosol and direct contact, and vertically, in utero or from the doe to the offspring at birth (Graham and Schoeb, 2011).

*M. pulmonis* colonises the respiratory epithelium, nasal passages and middle ear, but can also affect the rat's reproductive tract. Progression to broncho-pulmonary disease can occur and the infection persists for life (**Figures 2 and 3**). Sendai virus is a paramyxovirus frequently encountered concomitantly with mycoplasmal infections. Sendai virus can exacerbate clinical signs due to mycoplasmosis because of its marked tropism for the respiratory tract, including the nasal cavities (Schoeb, 2000).

Many other pathogens may be responsible for respiratory tract disease in rats. *Streptococcus pneumoniae*, *Corynebacterium kutscheri*, cilia-associated respiratory bacillus and rat coronaviruses need to be considered in the differential diagnoses (Goodman, 2009; Graham and Schoeb, 2011), as well as mycotic and environmental causes.

Many respiratory infections are multifactorial, necessitating thorough investigations to achieve a

definitive diagnosis and for an early and more efficacious treatment. It must be stressed to the owners treatment is usually not curative and can only alleviate symptoms.

The use of particular antibiotics (beta-lactams, macrolides, lincosamides and aminoglycosides) via the oral, parenteral route, or via nebulisation can cause dysbiosis and fatal enterotoxaemia (especially in hamsters and gerbils). It does so also infrequently in rats and can be explored in particular cases (Kling, 2011).

Enrofloxacin and doxycycline in combination have also been successfully used in the management of micoplasmosis in rats.

Nebulisation can be useful in delivering antimicrobials, bronchodilators and mucolytics when able to produce particles small enough (3µm) to reach the alveoli (Mayer, 2008). In many rodents, the cardiac muscle fibres surround major branches of the pulmonary veins extending into the lung tissue. This allows infectious agents to spread from the heart, through the pulmonary veins, into the lungs (Kling, 2011).

Laboratory studies using rats as animal models of human disease (Hardy et al, 2002; Yildirim et al, 2010) and reports of clinical experience in pet patients (Knafo, 2014) have suggested use of sildenafil may have promising results in the management of chronic respiratory disease in pet rats.

## Neoplasia



**Figure 4.** Mammary tumours are extremely common, especially in female rats, and can be found anywhere from the axilla to the perianal area due to the extensive mammary tissue present in rodents.

Mammary tumours are common in older female rats (**Figure 4**). Benign fibroadenomas are over-represented (80% to 90%). Genetic factors, diet and environment seem to play a role.

Reduction of food intake (80% of ad libitum feeding) has been reported to reduce the incidence of these neoplasia (Tucker, 1979). Prolactin levels in rats with mammary tumours have been reported as 25 times higher than in six-month-old virgin females (Percy and Barthold, 2007).

Pituitary adenomas are commonly encountered in aged male and female rats. Neurologic signs, such as depression, unresponsiveness, anorexia (pituitary cachexia), ataxia, head tilt, circling and seizures may be seen in affected animals (**Figures 5 and 6**). It has been suggested prolactin-producing pituitary tumours may be associated with a higher incidence of mammary fibroadenomas (Sandusky et al, 1988).

Mortality is usually associated with increased intracranial pressure and compression atrophy of surrounding brain tissue, leading to progressive health deterioration (Orr, 2009).

## **Central nervous system degenerative changes**

Hindlimb weakness, altered motor function, abnormal tail movements, ataxia and paresis may indicate a degenerative disease of the spinal roots (radiculoneuropathy) associated with atrophy of the lumbar and hindlimb muscles (Witt and Johnson, 1990). This condition may be seen in 75% to 90% of older rats (older than 24 months; Haines, 2010).

Oral and/or parenteral B vitamins have been shown to attenuate inflammatory and neuropathic pain in laboratory animals (Haines, 2010). Age-related peripheral or CNS changes, neurogenic muscular atrophy and primary age-related muscular changes can all occur, but are often very difficult to distinguish (Brown and Donnelly, 2012).

## **Managing anaesthetic risks**

The risks associated with anaesthetising a healthy geriatric rat may be considered generally similar to those in younger patients. However, it is important to recognise the high incidence of underlying pathologies in animals such as rats can disguise signs of illness until late in the course of the disease.



**Figure 5.** Head tilt may be seen in rats with pituitary gland neoplasia.

If the animal is already sick and an anaesthetic procedure is necessary to treat a problem, this should be performed early in the disease process as the risks increase when the patient is sicker.

However, according to Brodbelt et al (2007; 2008a and 2008b), age per se – and not just the associated poor health status – is an important risk factor for anaesthetic-related deaths in dogs, cats and rabbits. This may be related to increased susceptibility to the depressant effects of anaesthetics used, hypothermia and subsequent prolonged recoveries.

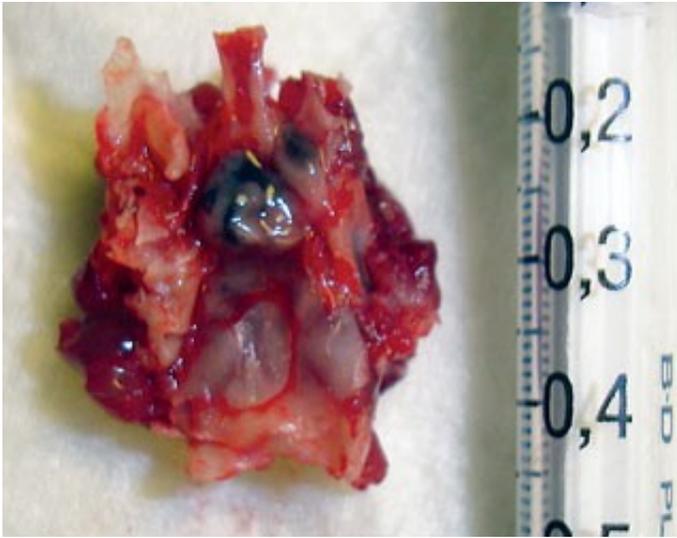
Several studies have been performed in laboratory settings to evaluate and compare the effects of different anaesthetics on a variety of functions in young and aged rats (Stratmann et al, 2010; Erasso et al, 2013), but an in depth review of these studies is beyond the scope of this article.

An understanding of the physiological changes associated with the ageing process, consideration and appropriate evaluation of the health status of the patient (for example, routine haematobiochemistry and/or urinalysis), careful monitoring during the anaesthetic procedure and appropriate care in the postanesthetic period until full recovery are necessary to reduce risks and increase the chances of a positive outcome.

## **General considerations**

Arthritis, neurologic and musculoskeletal diseases causing stiffness, abnormal gait and difficulty ambulating are commonly seen in geriatric rats.

In all these cases, it is important to modify the animal's environment to allow it easier access to food and water, reduce the effort when moving around and avoid slipping. More absorbent or additional bedding may be used and more frequent cage cleaning advised when increased urination occurs secondary to kidney disease. Supplemental heating may be necessary in certain cases, always making sure to avoid hyperthermia and burning.



**Figure 6.** Gross appearance of a large pituitary tumour in a female rat. Notice the reddish brown colouration with a haemorrhagic appearance.

Diet and longevity have long been studied in laboratory settings. Results have shown caloric intake may be the single most important factor influencing the incidence and severity of lesions and longevity (Keenan et al, 1995a and 1995b; Gumprecht et al, 1993). Overfeeding, on the other hand, may have adverse effects on the early development of many spontaneous tumours and degenerative diseases – for example, diet-induced obesity and diabetes – (Keenan et al, 2005; Mihaiu et al, 2010).

Drug dosages may need to be adjusted according to the specific disease identified. Do not use medicated water as rats will often avoid drinking when water tastes different, leading to dehydration and/or inappropriate dosing. Alternatively, some medication may be given mixed in juice, tinned fruit or yogurt. In the majority of cases, diseases are not treatable, but medical treatment and husbandry advice may be able to improve the quality of life of the affected animals.

Communication with the owner is essential in all these cases to allow understanding of the disease progress in the affected pet and to help in decision-making regarding the best care plan for the pet, including euthanasia when treatment is not available or no longer effective.

There is little information on optimum routine health care for geriatric rats to increase longevity and delay the onset of diseases. Ageing rats will probably be less active, sleep more, interact less, eat less often and show a gradual weight loss, but the rate of this progression is generally slow.

If significant changes occur (for example, behavioural changes, sudden weight loss, marked increased water intake) over days to a few weeks, especially when one single area/organ is affected, this should be regarded with suspicion and a health check and further investigations are warranted to rule out disease as a cause of the issues observed.

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