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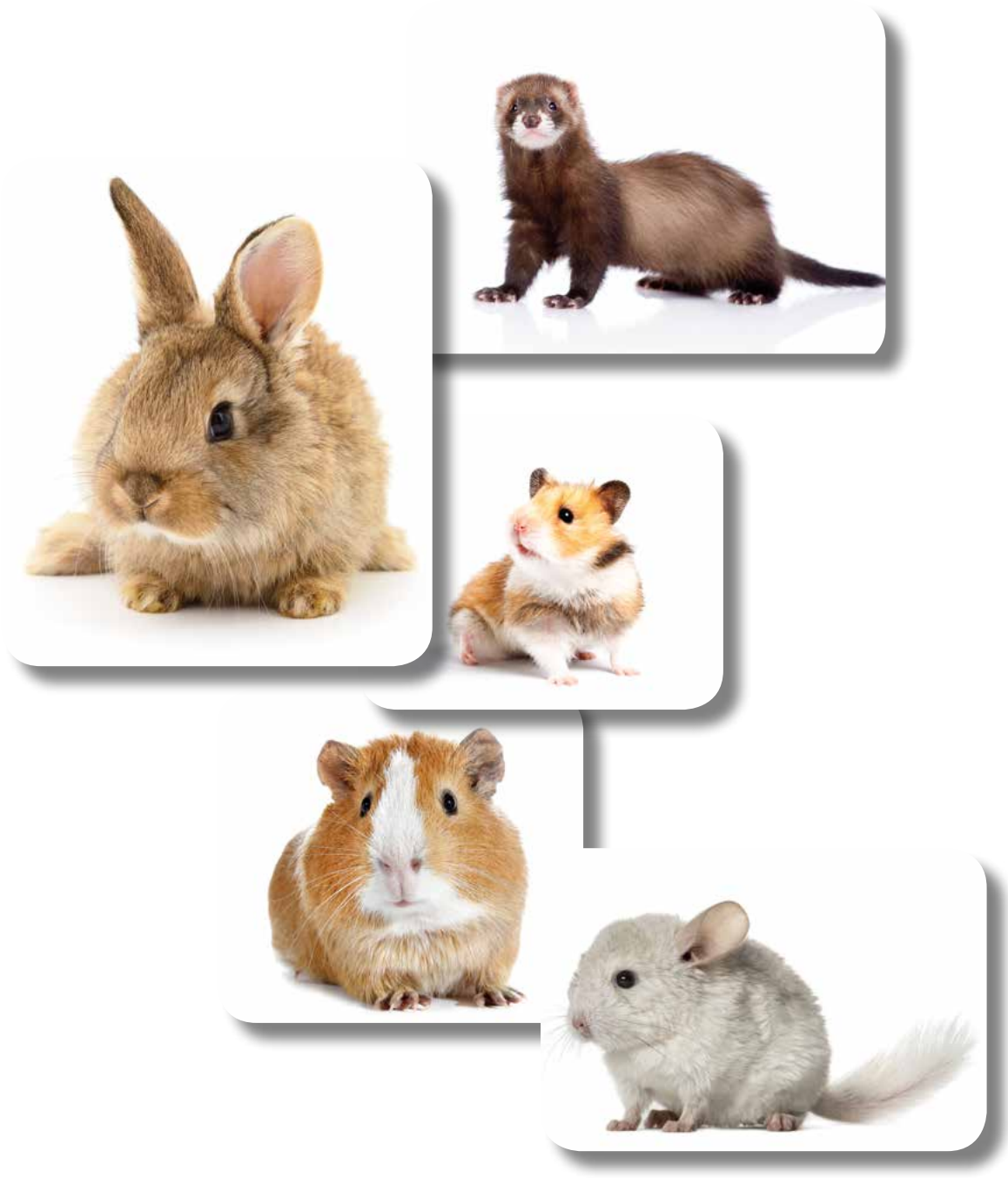
LABORATORY FOR CLINICAL DIAGNOSTICS



Laboratory Diagnostics in Small Mammals (small domestic animals)

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Contents

As of: January 2018

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Introduction

This guide addresses the particularities of laboratory testing in small mammals (small domestic animals). In veterinary medicine, the term small mammal is used for rabbits, guinea pigs, rats, mice, hamsters, ferrets and the like. The following text particularly describes the specific characteristics of animal species like rabbits, guinea pigs, chinchillas, degus, hamsters and ferrets.

Knowledge of laboratory diagnostics in small mammals does not yet cover the same range as in dogs and cats.
To broaden the horizon in this field of laboratory diagnostics, Laboklin conducts studies and partly establishes proprietary reference values for clinical-chemical as well as haematological examinations.

Measurement of clinical-chemical parameters is not subject to species-specific particularities and can thus be performed for every species – if requested also for species that are not listed on our submission form for small mammals. The submission form indicates those parameters that are of diagnostic interest for this target group. Determination of further measurement values is possible.
In addition to the automatic measurement and depending on the species, blood counts can be complemented by manual microscopic examination.

The following is a summary of the current knowledge in the autumn of 2017, which, according to expectations, will change and extend over the next few years.

Fig. 1: small lithium heparin tube (orange top)

Fig. 2: small tube for serum (white top)

Fig. 3: small EDTA tube (red top)

Important information on pre-analytics

Preparation

Unlike dogs and cats, do not fast small herbivores before taking a blood sample.

As small mammals are usually flight animals, the susceptibility to stress of this species is significantly higher than in dogs and cats. This is why it is of particular importance to have all the equipment required for collecting blood laid out in advance to keep the duration of manipulation as short as possible.

Due to the size of the animal, occasionally only small amounts of blood can be expected during sampling. The needle cone can therefore be removed before taking the sample to avoid coagulation in the cone during blood collection.

Sample material

Because the blood quantity is often very small, lithium heparin tubes **(Fig. 1)**, are especially suitable for sampling, as they can be used for doing a blood count as well as for determining a wide range of blood chemical parameters. Determination of T4 and fT4 from heparin plasma is also possible.

Fig. 4: blood smear

As an alternative to serum **(cf. Fig. 2)** and EDTA blood **(cf. Fig. 3),** 1 ml of heparin blood is sufficient for creating a domestic animal profile with blood count. In addition to the blood sample, it is beneficial to always send in a blood smear which was immediately prepared in the practice **(Fig. 4 and Fig. 5)**; this helps to counteract the negative impact on the cell morphology during transport.

Fig. 5: transport tube for slides

In any case, it is important to use small test tubes. Especially with plasma or serum which you have already centrifuged it is necessary to select a test vessel for the supernatant removed by pipette which suits the size of the sample and does not contain any additives or pellets.

Firstly, additives such as anticoagulants are interfering factors during pre-analysis and secondly, pellets in the test tube result in having to work with even less (than the already little amount of) material during examination.
If only little sample volume could be obtained and the material might not be sufficient for all the desired parameters, we recommended noting down the priority of the parameters to be measured directly on the submission form.

Puncture sites

A puncture site recommended for many small mammals is the Vena saphena lateralis. Other possible puncture sites are indicated in the following table.

	Vena auricularis	Vena cephalica	Vena jugularis	Vena saphena lat.
Rabbit	X	X	difficult to access due to the dewlap	X laterally on the lower leg
Guinea pig		X	difficult to access	X caudally on the lower leg
Chinchilla		X	X	X laterally on the lower leg
Degu				X
Ferret		X	X	X dorsally directly above the tarsal joint

Species-specific particularities when interpreting laboratory test results

Laboratory-relevant particularities of different small mammal species at a glance

	Blood count	Blood chemistry	Miscellaneous
Rabbit	- physiologically lymphocytic blood count (up to 81%) - bacterial infections lead to a pseudo left shift (shift from lymphocytic to granulocytic blood count) - rarely leukocytosis and occurrence of banded neutrophil granulocytes - „pseudo-eosinophilic" granulocytes (neutrophil granulocytes with small granules) - rarely eosinophilic granulocytes (up to 1%) - short lifespan of erythrocytes leads to increased occurrence of polychromasia, anisocytosis and reticulocytes	- most sensitive hepatic enzyme is GLDH - ALT levels rise in case of severe liver cell damage and chronic processes - AP activity in numerous tissues (intestinal mucosa, kidneys, bones, liver, placenta), no cortico-sensitive isoenzyme, age-related - urea does not depend on food intake (as it does in carnivores), isolated increase can indicate gastrointestinal bleeding - alimentary hypercalcaemia - synthesis of bilirubin limited (due to low biliverdin reductase activity), more than 70% of the bile pigments are made up of biliverdin	- mostly renal calcium excretion - high concentrations of crystals in the urine, even in clinically healthy animals → always evaluate in connection with clinical picture

	Blood count	Blood chemistry	Miscellaneous
Guinea pig	- physiologically lymphocytic blood count - bacterial infections lead to a pseudo left shift - rarely leukocytosis and occurrence of banded neutrophil granulocytes - less but bigger erythrocytes than in other animal species - „Foa-Kurloff cells“ in the peripheral blood (mononuclear leukocytes with inclusion bodies, particularly high number during gestation) - lymphomas: pronounced lymphocytosis (leukaemic form)	- urea does not depend on food intake (as it does in carnivores), isolated increase can indicate gastrointestinal bleeding - alimentary hypercalcaemia - increase in ALT activity only if liver cells are severely damaged	- mostly renal calcium excretion - tendency to form urinary calculi (especially satin guinea pigs) - high concentrations of crystals in the urine, even in clinically healthy animals → always evaluate in connection with clinical picture
Chinchilla	- physiologically lymphocytic blood count - lymphocytes up to 94% of the total leukocyte count - bacterial infections lead to a pseudo left shift - rarely leukocytosis and occurrence of banded neutrophil granulocytes	- urea does not depend on food intake (as it does in carnivores), isolated increase can indicate gastrointestinal bleeding - alimentary hypercalcaemia - physiologically high bilirubin level (up to 6.46 µmol/l)	- hypercalcaemia leads to soft tissue calcification, (contrary to the other small herbivores) calcium is excreted through the intestines
Degu	- physiologically lymphocytic blood count	- urea does not depend on food intake (as it does in carnivores), isolated increase can indicate gastrointestinal bleeding	- strong tendency towards diabetes with cataract formation - different insulin structure with low insulin effect - difficulties with the adjustment of the diabetes
Ferret	- lymphocytic and granulocytic blood count possible, 50:50 with a tendency towards the lymphocytic blood count - physiologically higher haematocrit than in other domestic animals (up to 0.7 l/l) - no blood groups can be determined - increases in anaemia (causes: often hyperoestrogenism and gastrointestinal bleeding)	- urea concentration in the serum depends on food intake (as in dogs and cats) - creatinine has a very low sensitivity, increase in creatinine = renal damage - ALT: liver-specific, elevated in case of acute hepatopathy - AST: non-liver-specific (also occurs in muscles), elevated in case of chronic hepatopathy	- seasonal alopecia (depending on the rut) - be careful when shaving, fur might take several months to grow again - blood sampling under isoflurane anaesthesia results in a decrease of all haematological parameters

Haematological analysis

Physiologically, rabbits, guinea pigs, chinchillas, degus and other small mammals have a lymphocytic blood count (up to 94% lymphocytes in chinchillas). This means lymphocytes are dominant in healthy animals. In ferrets, the amounts of lymphocytes and neutrophil granulocytes are more or less the same.

In small mammals, acute bacterial infections and inflammations predominantly manifest themselves through a so-called pseudo left shift, which means a shift from a lymphocytic to a granulocytic blood count without an increase in banded neutrophil granulocytes. Leukocytes and banded neutrophil granulocytes can hardly be observed. In rabbits, eosinophilic granulocytes are very rare and cannot be used for the diagnosis of parasitic diseases or intolerances. However, an increase can be seen in case of tissue injury. Eosinophilic granulocytes can be found more often in guinea pigs; they occur, for example, more frequently in connection with mite infestation.

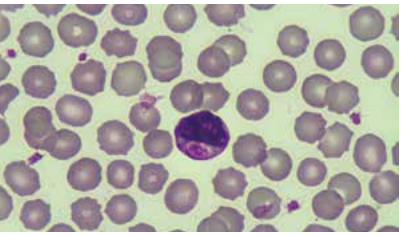

Fig. 6: Foa-Kurloff cells guinea pig

A peculiarity of the guinea pig is the presence of so-called “Foa-Kurloff cells” **(Fig. 6)**. These are mainly lymphocytes (mononuclear leukocytes) which have reddish inclusion bodies of up to 9 µm in size. Knowing about these cells avoids confusion with intracellular pathogen structures. A particularly high number is observed during gestation. This type of cell is presumed to be the equivalent of the natural killer cells of other mammals.

In ferrets, the physiologically higher haematocrit (up to 70%) should not be mistaken as a sign of dehydration. In the differential diagnosis of anaemic ferrets, gastric ulcers or hyperoestrogenism should be considered as a possible cause.

In rabbits, regenerative anaemia **(Fig. 7)** can be caused, amongst others, by a bleeding adenocarcinoma of the uterus, bladder and renal calculi or traumata; non regenerative anaemia is predominantly caused by chronic renal insufficiency, chronic infections or lymphosarcoma.

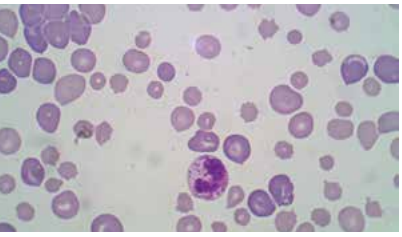

Fig. 7: regenerative anaemia rabbit

Lymphomas are often aleukaemic in rabbits, chinchillas and ferrets. However, in guinea pigs, a severe leukocytosis with profound lymphocytosis, caused by lymphatic disease, must be distinguished from a leukocytosis of different origin. This is done by evaluating the morphological structure of the lymphocytes using a fresh blood smear.

Blood chemical analyses

The domestic animal profile gives you a solid overview of the particular metabolic status of the patient’s liver, kidneys and electrolyte balance.

Liver metabolism

Liver metabolism plays an important role in routine diagnostics.
The liver function should always be monitored by examination of enzyme activity and substrate formation.

For the diagnosis of hepatic diseases, the activity of the enzymes ALT and GLDH is the most significant indicator. Acute hepatopathy or even short periods of anorexia lead to a substantial increase in GLDH activity. Chronic and severe liver damages result in a release and thus an increase in ALT. Initially, it is always GLDH that rises, followed by ALT and AST.

In the liver metabolism, AST is a rather unspecific parameter, as it can also be found in muscles. It is therefore always useful to also evaluate an increase in AST in combination with the CK.

AP and γ-GT are not liver-specific and very slow to react and are thus of minor importance in small mammals. It should be noted that AP is influenced by various parameters (age, gestation, bone diseases).

The metabolic status of the liver should always be seen in connection with the substrates glucose, albumin, urea, bilirubin and bile acids to distinguish between pre-, intra- or post-hepatic states of bile secretion disorders.

Kidney metabolism

Herbivorous small mammals only ingest little protein with their food, which is why the concentration of urea in the blood does not depend on food intake as it does in carnivorous or insectivorous small mammals.
Serum creatinine concentration is influenced by muscle mass and physical activity and therefore also increases in case of muscle damage or a catabolic metabolism. An isolated increase in urea is often caused by gastrointestinal bleeding, tissue damage, fever or certain medications such as glucocorticoids, tetracyclines and furosemide.

If both urea and creatinine are elevated at the same time, it can be due to different aetiologies:

- prerenal azotaemia: dehydration, hypovolaemia, insufficient renal blood circulation, low blood pressure
- renal azotaemia: acute and chronic renal insufficiency
- postrenal azotaemia: obstruction of the efferent urinary tract

Sugar metabolism

Physiologically, herbivorous small mammals never have an empty stomach and therefore show higher glucose levels compared to carnivores.

In herbivores, especially in caecotrophic animals, determination of the fasting glucose level is nearly impossible. In addition to determining the glucose level, it is thus necessary to revert to alternative parameters when diagnosing diabetes mellitus. Except for the degu, diabetes mellitus only occurs very rarely in small mammals.

If diabetes mellitus is suspected, it is recommended to repeatedly determine the serum glucose level, to test the urine several times for glucosuria and additionally determine the fructosamine level (physiologically, this can be up to 527 µmol/l in rabbits due to the slow carbohydrate metabolism and the active lipid metabolism). If high values are measured several times and the corresponding symptoms are present, the suspicion is confirmed after excluding the differential diagnoses.

Differential diagnoses for hyperglycaemia:

- stress hyperglycaemia (rather slight increase in small herbivores)
- periods of starvation and anorexia (especially rabbits form considerable amounts of carbohydrates)
- ileus
- obstructions in the gastrointestinal tract (terminal)
- hyperthermia
- hepatic lipidosis
- renal insufficiency, cystitis
- ovarian cysts in guinea pigs

Hypoglycaemia is very rare and is more of pre-analytical nature. An exception to this is a high glucose consumption in case of sepsis or tumours.

Electrolyte metabolism

The absorption of calcium in herbivorous small mammals depends on the food intake and is independent of vitamin D. It is also not based on need. Considerable fluctuations of serum levels are physiological.

In rabbits, up to 60% of the present calcium is excreted through the urinary tract (compared to < 2% in most other domestic animals). This explains the more frequent formation of urinary gravel and uroliths in this species. If the calcium serum level remains high for a longer period of time, irreversible calcification of organs may also occur (particularly kidneys, liver, vascular walls, muscles).

Calcium levels of more than 4.2 mmol/l support the diagnosis of hypercalcaemia.

Guinea pigs and degus also excrete excess calcium through the kidneys with the consequence of uroliths forming; in chinchillas, however, hypercalcaemia manifests itself in soft tissue calcifications.

Urinalysis

In small mammals, too, assessing the urinary status, including sediment, plays an important role in the diagnosis of urinary tract diseases – particularly in rabbits, guinea pigs and ferrets.
Urine has an intense yellow colour. In small herbivores, a slightly red discolouration of the urine is often misinterpreted as haematuria by their owners. Many times, it is due to food pigments, such as porphyrins, or oxidation products of other substances which result in a darkening of the urine.
The urinary status quickly indicates a possible cause for colour changes. If haematuria is confirmed, an adenocarcinoma in the uterus of unneutered female rabbits represents an important differential diagnosis for urolithiasis and inflammatory diseases of the lower urinary tract.

In herbivorous small mammals, the smell of the urine is always aromatic. A pungent odour normally indicates an infection, a fruity smell a ketosis.

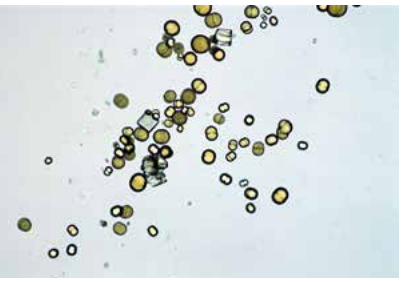

Fig. 8:
calcium carbonate crystals (round) and calcium oxalate crystals (square)

Different additional substances lead to a clouding of the urine. These substances may include crystals, mucus, pus, blood, epithelia and bacteria.
In rabbits and guinea pigs, the precipitation of calcium carbonate and calcium oxalate crystals **(Fig. 8)** is based on nutrition. A high number of these crystals with no further concretions being present has no relevance when symptoms are missing.
Because of the different metabolic situation, ferrets, as carnivores, tend to form more struvite crystals.

In case of urinary symptoms, orthopaedic conditions and neurological disorders should also be cleared up for differential diagnostic purposes.

Faecal analysis

Faecal analysis is always recommended in case of diseases of the digestive organs, such as anorexia, weight loss, diarrhoea, tympany or constipation. Here, parasitic diseases as well as bacterial and mycological infections can be cleared up.

Always make sure to have sufficient sample volume. For a bacteriological/mycological or parasitological examination, it is recommendable to have at least a cherry-sized amount of faeces each, and for coproantigen detection such as giardia EIA at least a pea-sized amount of faeces.

Endoparasites will be discussed in more detail later.

Diagnosis of endocrinological diseases

The diagnosis of endocrinological diseases proves more difficult than in dogs and cats. In routine diagnostics of small mammals, it is most notably the function tests that have not yet become established, and single hormone measurements are often difficult or cannot be interpreted. This is why the patient's clinical picture is often of particular importance for diagnosis and therapeutic decision-making.
Heparin plasma or serum is usually needed for laboratory diagnostics of endocrinological diseases. The volume depends on the range of individual parameters to be determined. Specific features will be dealt with in more detail below.
The listed differential diagnosis exclusively refers to laboratory analyses and does by no means replace a complete clinical as well as further, imaging diagnostics.

Hypothyroidism in rabbits and guinea pigs

So far, only individual case descriptions of hypothyroidism in rabbits and guinea pigs can be found in literature.
However, it has to be noted that herbivorous small mammals are very sensitive to being fed with crucifers (= Brassica, e. g. cabbage, kohlrabi, broccoli, radish leaves, napa cabbage). These plants contain goitre-producing substances which limit the dietary intake of iodine. If cabbages are fed excessively or even exclusively, it will result in goitre formation.

Clinic/Cardinal symptoms:
The affected animals rarely develop symptoms of hypotheroidism. Here, a thorough anamnesis is of vital importance.

Laboratory diagnostics:
- determination of T4
- 250 µl of heparin plasma or centrifuged serum

Differential diagnosis:
- Cytological examination of masses in the neck area; especially in guinea pigs a lymphoma needs to be considered.

Therapy monitoring:
- Monitoring is done by repeating the determination of T4.

Hyperthyroidism in guinea pigs

Hyperthyroidism in guinea pigs is caused by hyperplasia, adenoma and adenocarcinoma of the thyroid gland. According to a study by Laboklin, the median age of affected animals is approximately 5 years.

Clinic/Cardinal symptoms:
The clinical picture can be compared to feline hyperthyroidism and is associated with progressive weight loss with initially stable or increased appetite. Masses can often be palpated ventrally on the neck. Additionally, the animals display behavioural problems such as restlessness, exaggerated startle response, hyperactivity, abnormal lying positions, segregation from conspecifics. As the course of the disease progresses, there are further symptoms such as polydipsia/polyuria, alopecia – starting from the inguinal area with a tendency to spread over the entire body –, inappetence, chronic smeary diarrhoea and cardiac problems due to progressive damage to the myocardium and the reductions in mobility associated with it.

Laboratory diagnostics

- determination of T4
- 250 µl of heparin plasma or centrifuged serum
- T4 within the reference range does not exclude hyperthyroidism (initial and final stage of the disease)
- Fine needle aspiration of the masses; it is not possible to state the dignity of a thyroid tumour during the cytological examination.

Differential diagnosis:

- clinical-chemical examination (diagnostic assessment of kidney values, fructosamines, proteins, electrolytes)
- urinalysis (to exclude cystitis, loss of protein)
- faecal examination in case of diarrhoea
- cytological examination to distinguish from malign lymphoma, sialocele, abscess, cervical lymphadenitis

Therapy monitoring:

- Monitoring is done by repeating the determination of T4 as well as urea and creatinine.

Diabetes mellitus in small mammals

Occasionally, diabetes mellitus occurs in small mammals. The aetiology is different in the individual species.

Rabbit

As rabbits, especially when under stress or in times of starvation, can form enormous amounts of carbohydrates and never have an empty stomach, they generally have higher glucose levels (up to 400 mg/dl).
Diabetes mellitus is caused by a dysfunction in insulin secretion due to hypergranulation of the β-cells.

Clinic/Cardinal symptoms:
Affected rabbits display polydipsia/polyuria and, as a result, a certain filthiness. Despite polyphagia, the animals lose weight as the disease progresses. The development of cataracts is controversial.

Laboratory diagnostics:

- hyperglycaemia
- increase in fructosamines > 527 µmol/l
- glucosuria

Differential diagnosis:

- clinical-chemical examination (particularly kidney values)
- blood count/differential blood count to exclude inflammation/sepsis
- urinalysis to exclude cystitis

Therapy monitoring:

- fructosamines and protein
- determination of the urine glucose level

Guinea pig

Diabetes mellitus mainly occurs in animals under the age of 3.

Clinic/Cardinal symptoms:
Guinea pigs initially suffer from obesity, which can become cachexia in the late stage. In addition, they often display polydipsia, polyuria and bilateral cataracts.

Laboratory diagnostics:
- hyperglycaemia
- fructosamines > 271 µmol/l
- glucosuria

Differential diagnosis:
- clinical-chemical examination (particularly kidney values)
- blood count/differential blood count to exclude inflammation/sepsis
- T4 to exclude hyperthyroidism
- ACTH stimulation test to exclude hyperadrenocorticism in polydipsia/polyuria
- urinalysis

Therapy monitoring:
- fructosamines and protein
- determination of the urine glucose level

Degu

In this species, diabetes mellitus often occurs spontaneously, if a very carbohydrate-rich diet is being fed and the animals become obese. It seems to be an insulin-independent form (type 2 diabetes) and is presumably associated with islet cell amyloidosis.
Similar to dogs, degus have a high aldose reductase activity in the lens. This leads to early cataract development in both eyes, if a high glucose level persists for a longer period of time.

Clinic/Cardinal symptoms:
- unspecific: lethargy, reduced general condition
- polyphagia with subsequent emaciation, polydipsia/polyuria
- bilaterally sudden appearance of cataracts

Laboratory diagnostics:
- repeatedly serum glucose and urinalysis for glucosuria
- Measurement of fructosamine concentration is possible, but difficult to interpret owing to a lack of studies.

Differential diagnosis:
- clinical-chemical examination (particularly kidney values)
- blood count/differential blood count to exclude inflammation/sepsis
- urinalysis to exclude cystitis

Therapy monitoring**:**
- determination of the urine glucose level

Ferret

Primary diabetes mellitus with β-cell atrophy is rare in ferrets. In this species, the underlying cause for diabetes mellitus is often aggressive pancreatic surgery after insulinoma or feeding with high glycaemic index and subsequent insulin resistance.

Clinic/Cardinal symptoms:
Symptoms are similar to those of dogs and cats:

- lethargy
- polydipsia/polyuria
- weight loss
- ataxia
- hyperglycaemia, hypercholesterolaemia, hypochloraemia
- glucosuria, ketonuria
- diabetic ketoacidosis with hypokalaemia, hyponatraemia and ketosis

Laboratory diagnostics:

- fructosamines > 201 µmol/l
- glucosuria

Differential diagnosis:

- clinical-chemical examination (particularly kidney values)
- blood count/differential blood count to exclude inflammation/sepsis
- urinalysis to exclude cystitis

Therapy monitoring:

- fructosamines and protein
- determination of the urine glucose level

Insulinoma in ferrets

Insulinoma is one of the most frequently diagnosed tumour diseases in ferrets. It is derived from pancreatic β-cells and leads to multiple nodules, but rarely to the formation of metastases in regional lymph nodes, liver and spleen. A genetic component is assumed.

Clinic/Cardinal symptoms:
Symptoms evolving as a result of the developing hypoglycaemia (intermittent, slowly progressive course) are:

- lethargy, increased need for sleep
- nausea and ptyalism, vomiting
- scratching at the mouth
- weight loss
- ataxia, weakness of the hind legs, tremor
- seizures and coma

Laboratory diagnostics:

- fasting glucose: < 3.2 mmol/l; if the glucose level lies within the reference range despite a strong suspicion, the ferret can be nil by mouth under observation for another 3-4 hours and glucose measurement can then be repeated.
- insulin determination additionally confirms the diagnosis: increased insulin levels if hypoglycaemia is present.
- CAVE: Insulin values within or even lower than the reference range do not necessarily exclude the presence of an insulinoma, as some tumours only intermittently produce insulin.
- For the determination of insulin it is imperative to send in the **centrifuged serum cooled** or frozen!

Differential diagnosis:

- clinical-chemical examination (particularly kidney and liver values, electrolytes)
- blood count/differential blood count to exclude inflammation/sepsis
- adrenal profile (if symptoms are unclear at the onset of the disease to exclude beginning hyperadrenocorticism)
- antibodies against distemper, parvovirus pathogen detection (PCR)

Therapy monitoring:

- The aim is freedom from symptoms, not normoglycaemia.

Hyperadrenocorticism

Cushing's disease in guinea pigs

Hyperadrenocorticism is extremely rare in guinea pigs, but needs to be considered depending on the symptoms. So far, only a few pathohistologically confirmed cases exist in literature.
It should be noted that basal plasma cortisol levels in the blood are significantly higher than in dogs and cats due to a higher frequency of pulsatile release of ACTH.

Clinic/Cardinal symptoms:

- bilateral alopecia (flanks, ventral abdomen)
- apathy
- polydipsia/polyuria
- polyphagia
- weight loss
- bilateral exophthalmos
- nervousness
- muscular atrophy

Laboratory diagnostics:
Diagnosis is carried out via **blood test** or saliva test by doing an ACTH stimulation test. After collecting the baseline cortisol sample, 20 IU ACTH (Synacthen Depot®) are applied intramuscularly, and the stimulated sample is collected 4 hours post applicationem.
A dexamethasone suppression test by means of a blood test can also be used for diagnosis. However, a higher dosage of dexamethasone is needed before cortisol in the plasma is suppressed (1 mg/kg i.v., i.p.).

Our research has shown that **cortisol** can also be determined from **saliva samples.** The collection of saliva samples for cortisol determination is a less stressful way of sampling for the guinea pig.
Sampling is carried out using a Salivette® **(Fig. 9).** This requires the collection system to remain between the molars and the buccal mucosa for 5 minutes so that the roll of synthetic fibres inside the Salivette® is completely saturated. Saliva can be collected by centrifugation with at least 1000 g for 2 minutes.

Fig. 9: Salivette®, Sarstedt

Differential diagnosis:

- determination of T4 to exclude hyperthyroidism
- determination of fructosamines and glucose in polydipsia/polyuria to exclude diabetes mellitus

Therapy monitoring:

- ACTH stimulation test (reference point: adequate baseline cortisol concentration and appropriate stimulating properties)

Hyperadrenocorticism in ferrets

In ferrets, hyperadrenocorticism develops due to a hyperfunction of the adrenal cortex. Aetiologically, castration (loss of the negative feedback of gonadal steroids → high concentration of gonadotropins lead to constant stimulation of the adrenal cortex), a genetic predisposition and exclusively keeping the ferrets indoors seem to play a role. 85% of the ferrets only have one enlarged adrenal gland (without atrophy of the contralateral side), in 15% both adrenal glands are affected. Histologically, hyperplasia, adenoma or adenocarcinoma can be present.
Classic hyperadrenocorticism in ferrets cannot be compared to Cushing's disease in dogs. As the pathology is different from those in dogs, the affected adrenal cortex of the ferret does not secrete high concentrations of cortisol but of sex hormones. In the zona reticularis, oestradiol, 17-hydroxyprogesterone and androstenedione are increasingly produced. If clinical symptoms are present, an increase in at least one of these hormones can generally be seen.

Clinic/Cardinal symptoms:

- behavioural changes (aggression)
- odour development due to increased secretion of the sebaceous glands
- symmetric alopecia and hair loss at the base of the tail (violet gland)
- neutered female ferrets with vulvar swelling (DD: residual ovarian tissue)
- Dysuria in male ferrets; adrenal androgens can cause the formation of periosteal and periurethral cysts.
- return of sexual behaviour, changes in sexual behaviour
- polydipsia/polyuria

Laboratory diagnostics:

- increase in plasma concentrations of androstenedione, 17-hydroxyprogesterone and oestradiol (most frequently it is 17-hydroxyprogesterone that is increased, followed by oestradiol, less often androstenedione)
- pathohistological examination of masses on the adrenal glands

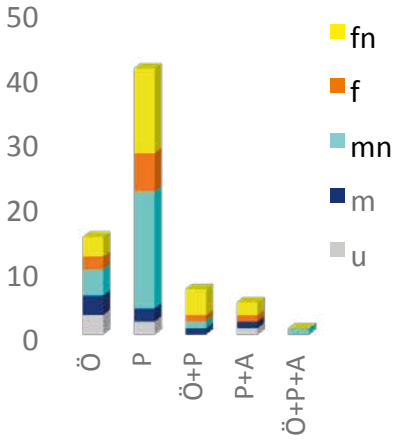

Fig. 10: The Laboklin adrenal cortex profile measures oestradiol (O), 17-OH-progesterone (P) and androstenedione (A).

In an evaluation (n = 192), the suspicion of a disease of the adrenal cortex was confirmed through increased hormone levels in 35% of the ferrets. 66.7% of the positive animals were neutered (24 x mn = male neutered, 22 x fn = female neutered). In the adrenal cortex profile it was progesterone that was most often increased, followed by oestradiol and oestradiol in conjunction with progesterone. Exclusive increases of androstenedione were not detected.

Differential diagnosis:

- determination of oestradiol as well as a complete blood count to exclude hyperoestrogenism in unneutered female ferrets
- ultrasound examination for presence of residual ovarian tissue in neutered female ferrets; incompletely neutered female ferrets can exhibit plasma concentrations of the hormones mentioned above at a similar level to ferrets with hyperadrenocorticism.
- In the differential diagnosis of male ferrets with dysuria, urethral concretions also need to be considered.

Therapy monitoring:

- Monitoring of the diverging parameters of the adrenal cortex profile previously determined

Hyperoestrogenism in ferrets

Hyperoestrogenism is often associated with oestrogen toxicosis or pro-oestrus anaemia. As the female ferret is an induced ovulator, the lack of ovulation/copulation can result in heat or permanent rut persisting for almost half a year. Already after a month, the bone marrow is influenced by the permanently elevated level of oestrogen.
Hyperoestrogenism can further be caused by a disease of the adrenal cortex in neutered male and female ferrets as well as by remaining residual ovarian tissue.

Clinic/Cardinal symptoms:

- significant vulvar swelling with and without vaginal discharge
- bilateral alopecia

Laboratory diagnostics:

- oestradiol
- aregenerative anaemia and pancytopenia
- reduced detection of reticulocytes
- further haematologic changes: normochromic or macrocytic, hypochromic anaemia, thrombocytopenia, later on also pancytopenia

Differential diagnosis:

- adrenal cortex profile to exclude hyperadrenocorticism

Therapy monitoring:

- blood count
- oestradiol

Diagnosis of infectious agents

Bacteria

A bacteriological examination is indicated if a bacterial infection is suspected and an antibiotic should be used. One of the common bacterial infections is, for example, the upper respiratory disease in rabbits – a mixed infection with *Bordetella bronchiseptica* and *Pasteurella multocida,* particularly with respiratory symptoms.

For the cultivation of bacteria, a swab with transport medium is required. Some types of bacteria can also be detected using PCR; here, suitable material is a swab without transport medium. Storage and transport can be done at room temperature.

The cultivation of bacteria from pus often fails, since pre-damaged or phagocytised bacterias grow poorly. Swabbing the inside of the abscess capsule should therefore be preferred. Examination of anaerobic bacterias, which may be involved in abscesses, must be requested separately on the submission form.

Liquids from sterile locations are best stored at room temperature, non-sterile liquids, such as collected urine, should better be cooled.

Detection of pathogens and antibodies in bacterial infections

Pathogen	Species	Cardinal symptom	Method	Sample material
Bordetella bronchiseptica	rabbit, guinea pig, mouse, hamster, ferret	respiratory symptoms	PCR [1] cultural examination [2]	[1] swab without medium [2] swab with transport medium
Chlamydia	most small mammals	respiratory symptoms, conjunctivitis, keratitis	PCR	swab without medium
Francisella tularensis (tularaemia)	rabbit, hare, mouse	acute course: septicaemia and death within 2 weeks chronic course: emaciation and ulcerated skin lesions	PCR	swab without transport medium or lymph node aspiration, tissue (especially spleen, liver, lung, kidney)
Helicobacter spp.	ferret	gastritis	PCR	vomitus, gastric lavage/ biopsy
Leptospira	rat, mouse	mostly subclinical	PCR	urine + EDTA blood
Mycoplasma pulmonis	rat, mouse	respiratory symptoms, pyometra, metritis	PCR	swab without medium
Pasteurella multocida	rabbit, guinea pig	respiratory symptoms, infections of the genital organs	PCR [3] (toxin producing in rabbits) cultural examination [2]	[3] swab without transport medium or BAL fluid, tissue (lung) [2] swab with transport medium

Pathogen	Species	Cardinal symptom	Method	Sample material
Salmonella	all	diarrhoea, often inapparent	cultural examination PCR	faeces
Treponema paraluiscuniculi (rabbit syphilis)	rabbit	swelling, nodules and scab on genital and head area	PCR [4] antibody detection by means of haemagglutination test [5]	[4] scabs, swab without transport medium (genital tract) [5] serum

Antibiogram and antibiotics

For the targeted treatment of a bacterial infection, it is important to know the resistance pattern of the bacteria. It is recommended that an antibiogram be performed.

At Laboklin, the antibiograms are performed by means of microdilution in accordance with CLSI guidelines (Clinical and Laboratory Standards Institute). Since the beginning of 2017, we have compiled our own panel of antibiotics to be tested for rabbits and rodents, which corresponds to the current state of scientific progress. It should, however, be borne in mind that not every active substance in the antibiogram can be used at random, as for example rabbits and guinea pigs respond more sensitively to certain antibiotics than mice and rats.

Generally, only few medicinal products are approved for rabbits and rodents. For the reclassification of unauthorised antibiotics for small mammals, the legal requirements must be observed. Added to this is the fact that rabbits are legally regarded as food-producing animals. To still be able to use antibiotics, an animal owner statement needs to be issued in which the use of the rabbit for food production is excluded. Otherwise, only those medicinal products shall be used or reclassified whose active substances are listed in Table 1 of the Regulation on Maximum Residue Limits (EU) No. 37/2010.

Rabbits and rodents can be divided in two groups: **herbivores** (rabbit, guinea pig, chinchilla, degu) and **granivores** (rat, mouse, hamster, gerbil). Their sensitivity to certain medications depends on the digestive physiology.

Herbivores are most sensitive because of their mainly gram-positive intestinal flora. Antibiotics which are primarily effective against gram-positive bacteria damage the intestinal flora and cause enteritis and enterotoxaemia. They should therefore be used with care in rabbits and should completely be avoided in guinea pigs, chinchillas and degus. Only in exceptional cases and with strict indication they may be administered parenterally to rabbits. Oral administration is contraindicated and can lead to life-threatening diarrhoea. These antibiotics include **p**enicillins, **l**incomycin, **a**mpicillin, **a**moxicillin, **c**ephalosporins, **c**lindamycin and **e**rythromycin (= PLACE rule). Additional administration of lactobacilli for the intestinal flora is recommended.

When using eye medicines or with the local application of ointments on the skin, it must also be kept in mind that they can be taken up orally, for example, while grooming. Accordingly, for treating the eye, active substances should be preferred which are also well-tolerated orally. If this is not possible, eye medicine should be used in the form of drops or gels and a cone collar should be used when applying skin ointments.

Due to their digestive tract, antibiotics are better tolerated by Myomorpha than by herbivores. The hamster is an exception to this as it also reacts sensitively to certain antibiotics.

The following table will provide you with tips on those antibiotics that are tested in our antibiogram (as of 10/2017) but which cannot be used or only used under certain conditions due to medical reasons. For each active substance those species are specified for which a dosage exists in literature. Contraindications such as gestation, young animals in growth, impaired hepatic or renal function will not be treated in detail here.

Characteristics of antibiosis in rabbits and rodents

	Antibiotic	Can be used for the following species	Comments
β-laktam-antibiotics	Penicillin	mouse, rat, gerbil	do not apply to rabbits, guinea pigs, chinchillas and hamsters
	Ampicillin	mouse, rat, gerbil, (rabbit)	do not apply to guinea pigs, chinchillas and hamsters rabbits: only parenterally upon strict indication (rabbit syphilis)
	Amoxicillin	mouse, rat, (rabbit)	do not apply to guinea pigs, chinchillas and hamsters rabbits: only parenterally upon strict indication (rabbit syphilis)
	Amoxicillin/ clavulanate	mouse, rat	do not apply to rabbits, guinea pigs, chinchillas and hamsters
Cephalosporins	Cephalexin	mouse, rat, gerbil, (rabbit, guinea pig, hamster)	apply extremely cautiously to rabbits and small rodents (especially guinea pigs, chinchillas, hamsters) (destruction of the intestinal flora, particularly in case of oral administration of high doses)
	Cefovecin	hamster, rat, gerbil	must not be used for small herbivores (e. g. guinea pigs, rabbits) according to the package insert of the medication; only parenteral administration
	Ceftiofur	rabbit	rabbits: in case of jaw abscesses for insertion in the bone after surgical treatment
	Ceftazidime	(rabbit)	under extreme caution in rabbits, only parenteral administration
Aminoglycosides	Gentamicin	rabbit, guinea pig, chinchilla, hamster, mouse, rat, gerbil	only parenteral administration rabbits: in case of jaw abscesses for insertion in the bone after surgical treatment
	Neomycin	hamster, mouse, rat, gerbil, (rabbit, guinea pig, chinchilla)	avoid administration to rabbits, guinea pigs and chinchillas.
	Tobramycin	rabbit	in case of jaw abscesses for insertion in the bone after surgical treatment or as implants in case of osteomyelitis
	Amikacin	rabbit, guinea pig, chinchilla, hamster, mouse, rat, gerbil	only parenteral administration rabbits: in case of jaw abscesses for insertion in the bone after surgical treatment
Macrolides	Erythromycin	rabbit, mouse, rat, (hamster)	particularly in case of mycoplasma do not apply to hamsters or only under extreme caution, risk of enteritis and enterotoxaemia (also in rabbits)
	Spiramycin	rabbit	do not apply to guinea pigs, chinchillas and hamsters
	Clarithromycin	mouse	currently no dosage available for other rodents
	Azithromycin	rabbit, guinea pig, rat, mouse	currently no dosage available for chinchillas, gerbils and hamsters
	Tylosin	mouse, rat, gerbil, (rabbit, guinea pig, chinchilla, hamster)	careful with rabbits, hamsters, guinea pigs and chinchillas
	Tilmicosin	rabbit	parenteral administration preferred

	Antibiotic	Can be used for the following species	Comments
Linco-samides	Clindamycin	rat, (rabbit)	careful with rabbits; parenteral administration preferred
Gyrase inhibitors	Pradofloxacin	rabbit, hamster, mouse, rat	currently no dosage available for guinea pigs, chinchillas and gerbils
	Ofloxacin	rabbit	to be used as eye formulation
Tetracyclines	Tetracycline	mouse, rat, gerbil, (rabbit, guinea pig, chinchilla, hamster)	risk of diarrhoea especially after oral administration, particularly in rabbits, guinea pigs, chinchillas and hamsters
	Doxycycline	rabbit, guinea pig, chinchilla, hamster, mouse, rat, gerbil	no oral administration in rabbits, guinea pigs and chinchillas; risk of diarrhoea after oral administration in hamsters, mice, rats, gerbils

All other active substances contained in our antibiogram (as of autumn 2017) can be applied to rabbits, guinea pigs, chinchillas and the granivores mentioned above.

Viruses

Virus infections are either detected directly by using PCR or through the serological detection of antibodies by means of IFAT or a haemagglutination test.

The most important virus infections in rabbits are RHD (rabbit haemorrhagic disease) and myxomatosis. When RHD is suspected, the test specimens Laboklin has examined since 2016 were predominated by the previously rare RHDV2 while RHDV1 currently only plays a minor role. RHDV2 has widely spread throughout Germany and goes along with high morbidity and mortality rates. In ferrets, Aleutian disease, which is caused by a parvovirus and can also be detected using PCR by now, plays an important role. Because of recent developments, RHD and Aleutian disease will be dealt with again separately following the table with the overview on the detection of pathogens and antibodies in viral infectious diseases of small mammals.

The hamster polyomavirus infection presented in the end is proven by cytological and histological examination.

Detection of pathogens and antibodies in viral infections of small mammals

Pathogen	Species	Cardinal symptom	Method	Sample material
Distemper virus	ferret, raccoon	conjunctivitis, rhinitis, pneumonia, dermatitis with pruritus, diarrhoea, CNS symptoms	PCR	swab without transport medium, urine, liquor, EDTA blood (viraemia)
EBHSV (European Brown Hare Syndrome Virus)	hare	peracute deaths, weakness, apathy, loss of shyness, hind leg paralysis	PCR	faeces, tissue (especially liver)
Myxomavirus	rabbit	subcutaneous oedema in the facial and anogenital area, nodular skin tumours, severe conjunctivitis, respiratory problems, dysphagia	PCR [1] antibody detection using IFAT [2]	[1] swab without transport medium (conjunctiva, nose, pharynx), tissue (conjunctiva, lung, kidney) [2] serum

Pathogen	Species	Cardinal symptom	Method	Sample material
Orthopoxvirus (pox)	rabbit, guinea pig, rat, mouse	papules, pustules, ulcera	PCR	skin scabs
Parvovirus (Aleutian disease)	ferret, raccoon, mink	young animals: pneumonia adults: glomerulonephritis, arteritis, meningoencephalitis, hind leg paresis, fertility disorders	PCR	swab without transport medium (rectal swab), EDTA blood (viraemia), tissue (spleen, lymph nodes, bone marrow)
RHD virus 1+2	rabbit	peracute: asphyxiating seizures, shrill cries, epistaxis, sudden death acute: restlessness, apathy, haematuria, icterus	PCR	swab without transport medium (conjunctiva), urine, faeces, EDTA blood, bone marrow, tissue (liver)

RHD (Rabbit Haemorrhagic Disease)

The RHD virus is a calicivirus which causes haemorrhagic disease in rabbits with an acute/peracute course. Infections with RHDV1 mostly affect adult animals; in young animals only virus replication occurs without any clinical symptoms. Infections with RHDV2, however, also cause a clinical disease in young animals and nestlings. It seems that in recent years RHDV2 has replaced the classic RHDV1-strain in many countries (especially France, Germany, Great Britain). Depending on the virulence of the pathogen, mortality rates are 5-100%. Transmission occurs directly or indirectly (through biting insects as well as through contaminated material such as bedding, etc.). RHD virus is closely related to the calicivirus which causes European Brown Hare Syndrome (EBHS) in European hares. While hares are not susceptible to RHDV1, RHDV2 does lead to the disease in hares as well.

Clinic/Cardinal symptoms:

- peracute: convulsions, shrill cries, epistaxis, sudden death
- acute: restlessness, apathy, respiratory problems, fever, haematuria

Laboratory diagnostics:

- pathogen detection using PCR (swab without transport medium) including the differentiation between RHDV1 and RHDV2 from conjunctival swab, urine, faeces, EDTA blood or liver tissue (native)
- pathology: Acute necrotising hepatitis is typical!

Differential diagnosis:

- dissection to exclude other underlying diseases

Prophylaxis:

- Classic RHDV1 vaccines and combination vaccines (myxomatosis/RHDV) do not provide protection against RHDV2. Since December 2016, a new vaccine against RHDV2 has been available on the German market. The combination vaccine against RHDV1 and RHDV2 which is approved in France can only be obtained with a special permit in Germany.
- The small, non-enveloped viruses are very environmentally stable and remain infectious for up to 3 months.

Aleutian disease (parvovirus)

Aleutian disease (Aleutian mink disease) is caused by a parvovirus. The virus is related to the parvovirus in dogs and cats, but differs antigenetically from them and is the only species of the genus *Amdoparvovirus*. The non-enveloped, single-stranded DNA virus is extremely resistant. Minks, but also ferrets, raccoons, skunks and other Musteloidea may become infected.
Transmission occurs both directly and indirectly. The incubation period can take up to two years. Due to massive antibody production (hypergammaglobulinaemia), immune complexes are formed which deposit in organs and cause inflammation there. Clinically inapparent infections are possible. The formation of symptoms depends on the virus strain, but also on the age and genotype of the host (Aleutian minks are particularly susceptible).

Clinic/Cardinal symptoms:

- young animals: pneumonia
- adults: glomerulonephritis, arteritis, meningoencephalitis, hind leg paralysis, fertility disorders

Laboratory diagnostics:

- pathogen detection using PCR (swab without transport medium) from rectal swab samples, EDTA blood (viraemia) or tissue (spleen, lymph nodes, bone marrow)
- protein electrophoresis (hypergammaglobulinaemia)

Differential diagnosis**:**

- clinical-chemical examination including blood count

Prophylaxis:
Canine parvovirus vaccines do **not** provide protection against an infection with Aleutian mink disease virus. There is currently no appropriate vaccine available.

Hamster polyomavirus infection

The structure and biology of hamster polyomavirus is similar to polyomavirus of mice. It is assumed that the European hamster (C. cricetus) is the natural host of this virus.
Hamster polyomavirus causes a multisystemic, persistent infection. Excretion and transmission of the virus mainly takes place through urine. Additionally, the virus has an oncogenic effect.
In epizootic hamster colonies, hamster polyomavirus causes transmissible lymphoma. Up to 80% of the young hamsters can be affected. In colonies in which the virus is enzootic, the incidence of lymphoma declines in young hamsters, presumably because they are protected by maternal antibodies. The number of skin tumours (trichoepithelioma) induced by hamster polyomavirus (HaPyV), in contrast, increases in older hamsters.

Symptoms:
HaPyV lymphoma:

- young animals affected
- emaciation
- palpable masses in the abdomen
- swelling of the axillary and neck lymph nodes

HaPyV skin tumours/trichoepithelioma:

- older animals affected
- masses in the facial area and the limbs; however, masses can occur anywhere on the body

Laboratory diagnostics:
Diagnosis is made cytologically/histologically. Information on sampling can be found on page 28f.
HaPyV lymphoma:

- cytological or histological examination:
  generally lymphoid cell population, in exceptional cases also erythroblastic, reticulo-sarcomatoid and myeloid types

HaPyV skin tumours/trichoepithelioma:

- histological examination
- possibly detection of intranuclear HaPyV crystalloids in keratinised epithelial cells

Differential diagnosis:

- histological examination for the diagnostic clarification of other processes, such as transmissible ileal hyperplasia or tumours (e. g. sarcoma)

Fungi

Particularly if changes in the skin or diarrhoea are present in small mammals, fungal infections must be considered.

In case of skin changes like alopecia, scales and scab formation, the examination for dermatophytes is indicated. For the detection of dermatophytes it is best to send in scabs and hair with roots from the periphery of the skin lesion. Samples can be sent in clean paper bags or wrapped in aluminium foil.

With diarrhoea, diagnosis of fungi is done during the faecal analysis.

Cyniclomyces guttulatus

Cyniclomyces guttulatus is a rather apathogenic yeast which can multiply exponentially in rabbits, guinea pigs, chinchillas and degus due to incorrect feeding, dental diseases and parasites and can cause diarrhoea. The level of *Cyniclomyces guttulatus* can be determined semi-quantitatively in the parasitological faecal analysis.

Dermatophytoses in small mammals

Recent studies have proven that especially guinea pigs can also be asymptomatic carriers of dermatophytes, while this is hardly the case in rabbits. Overall, dermatophytoses appear to be significantly more frequent in guinea pigs than in rabbits.

Particularly if guinea pigs are new at somebody's home, their owner should be informed about the zoonotic potential. A preliminary mycological evaluation should be taken into consideration, especially if there are children in the household.

Dermatophytoses play the most important role. Lately, especially the Trichophyton species *Arthroderma benhamiae*, the teleomorph of *Trichophyton mentagrophytes,* which was previously rare in German-speaking countries, is often detected in guinea pigs (Fig. 11). *Arthroderma benhamiae,* too, is a zoonotic agent that can cause severely inflamed skin infections in humans.

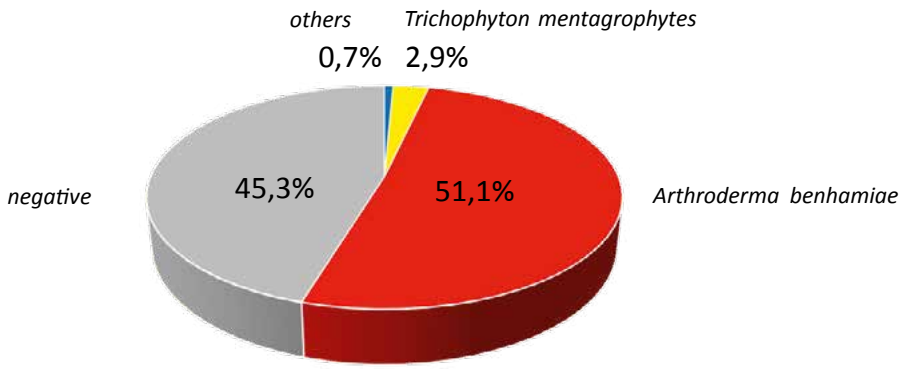

Fig. 11: Dermatophyte examination in guinea pigs by means of culture and PCR. For some time, in guinea pigs mostly the dermatophyte *Arthroderma benhamiae* has been isolated. *Arthroderma benhamiae* represents the teleomorph form of *Trichophyton mentagrophytes* but shows different growth characteristics in culture. In contrast, *Trichophyton mentagrophytes* is detected considerably less often than before.

Clinic/Cardinal symptoms:

- alopecia, formation of scabs and scales
- changes in the skin, mostly in the head area (especially mouth and ears), but can also spread over the back and limbs

Laboratory diagnostics:

- Microscopic and cultural examination: from skin, hair, scales (best sent in a paper bag). It is advisable to perform an additional parasitological evaluation, since ectoparasites represent the most important differential diagnosis of dermatophytes (especially rabbits: *Cheyletiella parasitovorax)*.
- Dermatophytes PCR is a helpful supplement to conventional diagnostics using fungal cultures. The time to make a diagnosis can be shortened (2-4 working days) which allows for early antimycotic treatment. The following zoonotic agents are reliably detected: *Microsporum canis, Microsporum gypseum, Microsporum persicolor, Trichophyton species of Arthroderma benhamiae, Trichophyton mentagrophytes* and *Trichophyton equinum*.
  Following a positive PCR result, it is possible to differentiate the species!

Differential diagnosis:

- mycological examination
- parasitological examination
- cytological and histological examination

Therapy monitoring:

- microscopic and cultural examination
- PCR is not suitable for immediate therapy monitoring as killed dermatophytes are detected as well.

Parasites

Systemic endoparasitoses

Encephalitozoon cuniculi

The unicellular pathogen *Encephalitozoon cuniculi* occurs globally in all mammals and birds, but only in rabbits it represents an important infectious disease with clinical manifestation. Other mammals (including humans) can develop symptoms in case of severe immunosuppression.

Clinic/Cardinal symptoms:
Clinically inapparent up to manifest forms of the disease possible!

- CNS symptoms (torticollis, nystagmus, paresis, etc.)
- renal symptoms (chronic renal insufficiency, non-regenerative anaemia, polydipsia/polyuria, etc.)
- eye symptoms (phacoclastic uveitis, cataract, and others)

Laboratory diagnostics:

- serology (serum):
  - antibody titre: IgG negative → encephalitozoonosis unlikely, differential diagnoses must be searched for! → re-test for IgM
  - antibody titre: positive → is proof of an infection, but does not state whether the infection is responsible for the symptoms. Encephalitozoonosis is likely to be the cause of the symptoms if differential diagnoses are excluded (see below).
  - If it can be avoided, serologically positive animals should not be kept together with encephalitozoon-free animals!
- pathogen detection using PCR (swab without transport medium):
  - In the urine: only a positive sample is proof of an infection as the spores are only excreted intermittently.
  - in lens material: very high sensitivity, good diagnostic agent in animals with phacoclastic uveitis
  - dissection material (kidney, CNS)

Differential diagnosis:

- clinical-chemical examination including blood count
- bacterial examination (*Pasteurella multocida* and others; swab with medium)
- urinalysis

Therapy monitoring:

- Serological monitoring (decrease of antibody titre), but pathogen elimination is impossible!

Toxoplasma gondii

The cat is the only definitive host and carrier of *Toxoplasma gondii,* all other mammals and human beings are intermediate hosts. In the intermediate hosts, tissue cysts are formed. Small mammals get infected by taking up oocytes from the environment through contaminated herbage or water and the infection generally progresses without any symptoms. In rare cases, it can lead to diseases. Small mammals do not play a role in human toxoplasma infections.

Clinic/Cardinal symptoms:

- respiratory symptoms
- conjunctivitis
- hind leg paresis
- seizures

Laboratory diagnostics:

- pathogen detection using PCR (swab without transport medium) from tissue samples or liquor
- antibody detection using IFAT (EDTA plasma, heparin plasma, serum)

Differential diagnosis:

- clinical-chemical examination (especially liver, kidney, electrolytes, glucose) including blood count
- bacteriological examination (swab with medium)

Therapy monitoring:

- serological monitoring using IFAT

Endoparasites in the intestinal tract

Endoparasites are detected by parasitological examination of faeces using flotation and sedimentation processes and subsequent microscopic examination. Here, the level of the yeast *Cyniclomyces guttulatus,* which, as described above (see page 22), may also cause diarrhoea, can be determined semi-quantitatively, too.

Due to intermittent shedding of parasite stages, it is recommended to examine faeces from 3 days.

Rabbit	
Protozoa	
Eimeria spp.	frequently in rabbit breeding stocks, young animals particularly susceptible, sometimes high mortality
Giardia	very rare, detection preferably by MIFC or SAF method or the even more sensitive coproantigen ELISA
Nematodes	
Passalurus ambiguus	frequent, symptoms often only in profound infections, higher detection rate with anal tape test
Strongylida ***(Graphidium strigosum, Trichostrongylus retortaeformis)***	rare, especially in wild rabbits, infection in open-air enclosures/ outdoor housing or by feeding contaminated herbage from grasslands
Strongyloides spp.	very rare, especially in wild rabbits, infection in open-air enclosures/outdoor housing or by feeding contaminated herbage from grasslands
Trichuris leporis	very rare, especially in wild rabbits, infection in open-air enclosures/outdoor housing or by feeding contaminated herbage from grasslands
Tape worms	
family Anoplocephalidae	very rare; intermediate host: moss mites, which are ingested with the herbage
Trematodes	
Fasciola hepatica, Dicrocoelium dendriticum	of secondary importance, infection through herbage contaminated with metacercaria or through infected ants

Guinea pig	
Protozoa	
Eimeria caviae	more frequent in breeds than in companion animals, especially young animals are affected
Cryptosporidia	higher infection rates have been described for larger populations, of minor importance in pet keeping, detection preferably by coproantigen ELISA
Giardia	rare, usually no symptoms, detection preferably by MIFC or SAF method or the even more sensitive coproantigen ELISA
Trichomonads	physiological intestinal commensals, massive replication due to changes in the intestinal environment (e. g. dental diseases, feeding mistakes, parasites) or in case of immunosuppression → illness detection in the native smear of fresh faecal samples

Guinea pig	
Protozoa	
Entamoeba caviae	physiological intestinal commensals, massive replication due to changes in the intestinal environment (e. g. dental diseases, feeding mistakes, parasites) or in case of immunosuppression → illness
Balantidium coli	physiological intestinal commensals, massive replication due to changes in the intestinal environment (e. g. dental diseases, feeding mistakes, parasites) or in case of immunosuppression → illness
Nematodes	
Paraspidodera uncinata	occurs more often in larger populations or in outdoor housing, diarrhoea only in higher degree of infestation
Trichuris gracilis	occurrence more likely in wild guinea pigs
Tape worms	
Hymenolepis nana, Hymenolepis diminuta	very rare, infection through oral ingestion of eggs *(Hymenolepis nana)* or of intermediate hosts *(Hymenolepis nana, Hymenolepis diminuta)* like insects (fleas, beetles, mealworms, cockroaches)

Chinchilla	
Protozoa	
Eimeria chinchillae	rare
Cryptosporidia	rare detection preferably by coproantigen ELISA
Giardia	frequent, usually subclinical, symptoms particularly in young animals detection preferably by MIFC or SAF method or the even more sensitive coproantigen ELISA
Nematodes	
Oxyuridae, Trichostrongylids	only of importance in animals caught in the wild
Tape worms	
Hymenolepis nana	very rare, infection through oral ingestion of eggs or of intermediate hosts like insects (fleas, beetles, mealworms, cockroaches)

Ferret	
Protozoa	
Coccidia (Eimeria and Isospora)	rare, especially in young animals
Cryptosporidia	rare, especially in young and immunosuppressed animals detection preferably by coproantigen ELISA
Giardia	usually subclinical detection preferably by MIFC or SAF method or the even more sensitive coproantigen ELISA
Nematodes	
Toxocara cati, Toxascaris leonina, Ancyclostoma spp., Uncinaria spp., Capillaria spp.	infection more likely in animals kept outside or animals going for walks
Tape worms	
Taenia spp., Mesocestoides spp., Ariotaenia procyonis, Dipylidium caninum	rare
Trematoden	
----------	of no importance in pet keeping

In the **granivores hamster, rat, mouse and gerbil,** flagellates (Giardia, *Spironucleus muris,* trichomonads) and amoebae *(Entamoeba muris)* have no clinical relevance. However, in case of immunosuppression, stress, malnutrition or changes in the intestinal environment, these protozoa can multiply greatly and cause diseases. Trichomonads are detected in the native smear of fresh faecal samples, testing for giardia is done by MIFC or SAF method or the even more sensitive coproantigen ELISA. Other protozoa like cryptosporidia or *Eimeria spp.* are rarely detected and *Eimeria spp.* are only found in rats and mice. The coproantigen ELISA is used for the detection of cryptosporidia.

As nematodes, oxyuridae are often found. They can cause diarrhoea and itching in the anal area up to a rectal prolapse, but usually the infection is inapparent. *Syphacia obvelata* can be found in all granivores, *Syphacia muris* and *Aspiculuris tetraptera,* in contrast, can only be found in rats, mice and gerbils. *Syphacia mesocriceti* is important in hamsters, while *Dentostomella translucida* rarely occurs in hamsters and gerbils. Syphacia eggs can also be detected by doing a tape test. In rats and mice, *Trichuris muris, Heterakis spumosa, Nippostrongylus muris, Nematospiroides dubius* and *Strongyloides spp.* are very rarely detected.

The tape worms *Hymenolepis nana* and *Hymenolepis diminuta* can be found in all granivores. Infection occurs through oral ingestion of eggs *(H. nana)* or of intermediate hosts *(H. nana, H. diminuta)* like insects (fleas, beetles, mealworms, cockroaches). The tape worm *Catenotaenia spp.,* which uses feed and storage mites as „intermediate host", is rarely found in granivores.

Ectoparasites

In case of skin changes and itchiness, testing for ectoparasites is indicated. Fleas that are already clearly visible with the naked eye can rarely be found in the respective species. Lice very rarely occur in rabbits *(Haemodipsus ventricosus)* and rarely occur in guinea pigs, chinchillas and degus. These are lice from rats, mice *(Polyplax serrata* and *Polyplax spinulosa)* or rabbits. They are clearly visible in the fur, but can also be detected microscopically on hairs or by means of a tape test preparation.
The following table lists the possible occurrences and diagnostic methods for other ectoparasites.

Rabbit	
Cheyletiella parasitovorax	microscopical, tape test of skin/scales/hairs
Psoroptes cuniculi	otoscopy or microscopically from ear secretions/scabs rolled onto a slide with a cotton swab soaked in oil
Leporacarus gibbus	macroscopically visible, hair or tape test
***Ornithonyssus bacoti* (rare)**	macroscopically visible, tape test (best in the evening) or from the surrounding (bedding, bottom side of furnishings)
Demodex (very rare)	microscopical, deep skin scraping
Sarcoptes scabiei	microscopical, skin scraping *(Sarcoptes scabiei var. canis* by means of PCR)
***Notoedres cati var. cuniculi* (very rare)**	microscopical, skin scraping

Guinea pig	
***Trixacarus caviae* (sarcoptic mange)**	microscopical, skin scraping
Notoedres muris (rare)	microscopical, skin scraping
Chirodiscoides caviae (fur mite)	macroscopically visible, hair or tape test
Cheyletiella parasitovorax (rare)	tape test of skin/scales/hairs
Demodex (rare)	microscopical, deep skin scraping
Ornithonyssus bacoti (rare)	macroscopically visible, tape test (best in the evening) or from the surrounding (bedding, bottom side of furnishings)
Biting lice	macroscopically visible, hair/tape test
Sarcoptes scabiei	microscopical, skin scraping *(Sarcoptes scabiei var. canis* by means of PCR)

Chinchilla, Degu	
Ornithonyssus bacoti (rare)	macroscopically visible, tape test (best in the evening) or from the surrounding (bedding, bottom side of furnishings)

Ferret	
Otodectes cynotis	otoscopy or ear secretions rolled onto a slide with a cotton swab soaked in oil
Sarcoptes scabiei	microscopical, skin scraping *(Sarcoptes scabiei var. canis* by means of PCR)

In addition to fleas and lice, hair, fur and bloodfeeding mites can also be detected in **granivores**. The hair mites *Myocoptes musculinus* and *Myobia musculi* are found in mice and rarely in hamsters. Of the fur mites, *Radfordia affinis* is found in mice and *Radfordia ensifera* in rats. In all granivores considered here, the bloodfeeding mite *Ornithonyssus bacoti* can best be detected in a tape test in the evening or is found in the surroundings (bedding, bottom side of furnishings).

Sarcoptic mites are detected microscopically in skin scrapings. What needs to be considered are *Notoedres notoedres* in hamsters and rarely *Notoedres musculi* in mice, *Notoedres muris* in rats as well as *Trixacarus diversus* (syn. *Sarcoptes anacanthos)* in rats and hamsters. In deep skin scrapings, Demodex can microscopically be found in hamsters (and rarely in rats, mice and gerbils) as well as *Psorergates simplex* in mice and rarely *Psorergates rattus* in rats.

Cytological and histological examination

Sampling and test procedure

The cytological and histological examination is becoming more and more important in small mammals.
As rodents and rabbits are particularly sensitive regarding anaesthesia and surgical interventions, cytological diagnosis should, in some cases, be preferred over surgical extirpation with subsequent pathohistological examination.

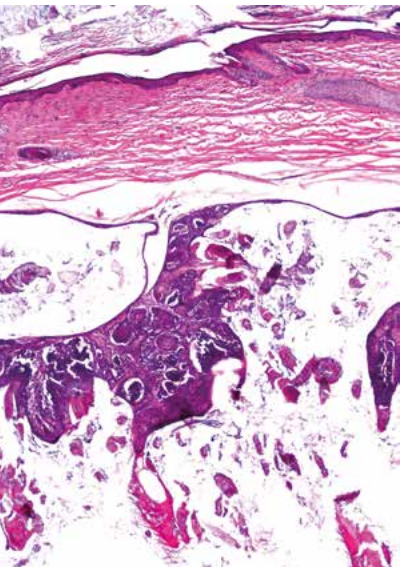

Fig. 12: trichofolliculoma guinea pig

Cytological examination is a micro-invasive intervention and provides results within a very short period of time. Here, fine needle aspiration is recommended. A syringe with an attached needle (G22 – G27) is used. During puncture, a vacuum is created and, if possible, the tissue to be examined should be punctured several times in different directions. Before removing the needle from the tissue, the vacuum must be released to avoid the material receding into the syringe. The material obtained is now carefully pressed onto a glass slide (or onto several slides) and streaked out depending on the consistency of the sample. More liquid sample material can be spread like a blood smear. If the material is viscous, it should be attempted to carefully spread the sample with the needle tip.
Since cytologically the morphology of the individual cell is assessed, it is important to spread the material in a thin layer. Thus, if too much material is available, it is recommended to spread it onto several glass slides. Fixation of the cells is achieved by air drying.

By using fine needle aspiration, it is possible to examine cutaneous and subcutaneous masses without too much stress for the animal. Thoracic and abdominal masses are accessible for diagnostic evaluation using fine needle aspiration under ultrasound guidance. Depending on the result of the fine needle aspiration, surgery may then be considered in accordance with the cytological cell count. It should be noted that cytological evidence is only provided in positive cases, which means that even if no tumour cells are found in the smear, a tumour process can still not be ruled out.

Histological examination serves to clarify an inflammatory process, a skin disease or to evaluate a tumour process including the determination of the dignity. To be able to obtain a meaningful evaluation, the size of the sample should not be less than 0.5 cm. Exceptions to this are, for example, biopsies of the gastric mucosa or Tru-cut-biopsies of internal organs. The formation of artefacts, such as squashing or electrocoagulation, for example due to thermal surgery, needs to be avoided. After surgical extirpation or after taking biopsy samples, the tissue needs to be fixed immediately (4% neutral buffered formaldehyde = 10% formalin). For the evaluation and diagnosis of the submitted samples, a preliminary clinical report and information on the original localisation of the tissue are also important.

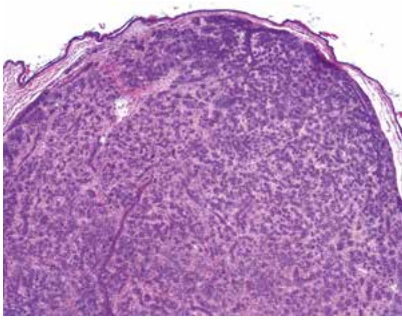

Fig. 13: trichoblastoma rabbit

Important areas of diagnosis

It is frequently **skin tumours** that are sent in for pathohistological examination, since they are clinically noticed as masses and can normally be surgically removed.
In guinea pigs, lipomas and trichofolliculomas are regularly diagnosed.
In rabbits, trichoblastomas are by far the most common benign epithelial skin tumours, and in rats, mammary tumours (particularly fibroadenomas) occur regularly. Through histological examination it is also possible to determine the dignity of the present neoplasia. Especially the growth pattern of the tumour compared to its surrounding is an important criterion which can only be evaluated histologically.

Uterus tumours have scarcely been described in small mammals. The only exception are rabbits, as endometrial adenocarcinomas are frequently seen in them.

A study conducted by Laboklin on changes in the uterus of guinea pigs found that this species shows a wide range of additional masses in cervix and uterus:

- polyp/hyperplasia
- deciduoma
- cervical gland adenoma/carcinoma
- endometrial adenoma/carcinoma
- tumours of the smooth muscles (leiomyoma/leiosarcoma)
- malign mixed Müllerian tumour

Often, benign tumours are dominant. Furthermore, ovarian cysts are common in guinea pigs.

In hamsters, tumours which may occur when induced by hamster polyomavirus (see page 21) can be detected cytologically/histologically.

Dermatohistopathology has also gained in importance in small mammals. An infectious genesis, such as dermatophytosis, Malassezia dermatitis, ectoparasites and tumourous processes (for example: epitheliotropic lymphoma), can be clarified by histological examination.
As a particularity, sebaceous adenitis in rabbits needs to be mentioned, which, so far, can only be diagnosed by histological examination. Sebaceous adenitis in rabbits can also indicate a primarily internal disease or also a tumourous process.

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Our tests for small mammals

Haematology+Blood Chemistry Profiles

Compl. Blood Count EB,HB/0.5ml(+BS)
Leukogram EB/0.5ml(+BS)
Reticulocytes EB/0.5ml
Morphology EB/0.5ml+BS
Rodent Profile (Rab, GP, Rt, Ms, Ha) HP,S/0.5ml
+ Blood Count HB,EB/0.5ml
(urea, crea, protein, AST, ALT, GLDH, AP, γ-GT, CK, K, Na, Ca, Mg, bile acids, PO4, fructosamine)
Rodent Profile + T4 (Rab, GP) HP,S/0.5ml
(urea, crea, protein, AST, ALT, GLDH, AP, γ-GT, CK, K, Na, Ca, Mg, bile acids, PO4, fructosamine, T4)
Ferret Profile NaFB+S/0.5ml
(glucose, trigly, γ-GT, AST, CK, LDH, protein, albumin, globulin, urea, crea, Ca)

Single Determinations

ALT (GPT) EP,HP,S/0.5ml
Bile Acids S/0.5ml
Calcium S/0.5ml
Cholinesterase EP,HP,S/0.5ml
Fructosamine S/1ml

Liver

Serum Protein Electrophoresis S/1ml

Kidney / Urine

Urinalysis incl. Sediment H/5ml

Hormones / Vitamins

17 OH-Progesterone S/0.5ml
Cortisol S/0.5ml
Adrenal Profile S/0.7ml
(17-OH-progesterone, androstenedione, oestradiol
Testosterone S/0.5ml
Thyroxin T4 S/0.5ml
Free T4 (fT4) S/0.5ml
Vitamin D3 (25 OH) S/0.5ml!

Pathology

Histopathology
(tumour diagnostics, dermatohisto-pathology, organpathology, biopsies)

Cytology
(aspirates, impression smears, etc.)

Faeces

Profiles

Rodent Faecal Profile + Endoparasites
(bacteriology and mycology, salmonella, endoparasites)

Ferret Faecal Profile
(bacteriology and mycology, salmonella, endoparasites, Giardia sp. antigen EIA)

Parasitology

Endoparasites
(flotation and sedimentation)
Cryptosporidia-Ag (EIA)-Mammals
Giardia sp. Antigen (EIA)

Bacteriology

Swabs / Aspirates

Bacteriology & Mycology TM,GW
Bacteriology (aerobes) TM,GW
Mycology TM,GW
Detection of Anaerobes TM,GW

Skin / Hair

Bacteriology & Mycology HA,HT
Bacteriology (aerobes) HA,HT
Mycology HA,HT
(dermatophytes and yeasts)
Trichogram HA
Ectoparasites HA,HT

Single Determinations

Campylobacter
Clostridium-perfringens enterotoxin (Rab)
Mycobacteria
(microscopic detection of acid fast rods)
Salmonella
Yersinia

Special Microbiological Tests

Antibiogram
Antibiogram Anaerobes
Extended Antibiogram
Aromatogram
MRSA Differentiation
(in addition to bacteriological testing)
MRSP Differentiation
(in addition to bacteriological testing)
ESBL Differentiation
(in addition to bacteriological testing)

Serology

Infectious Diseases (Antibodies)

Cytomegalovirus* (Ms) S/0.5ml
E. cuniculi (Rab, GP) EP,HP,S/0.5ml
Hantavirus* (Rt, Ms) S/0.5ml
Lymphocytic Choriomeningitis Virus (LCMV)* (GP, Ms, Ha) S/0.5ml
Myxomavirus* (Rab) S/0.5ml
Sendai Virus* (Rab, GP, Rt, Ms, Ha) S/0.5ml
Toxoplasma gondii (IgG + IgM) (Rab, GP) EP,HP,S/0.5ml
Treponema paraluiscuniculi* (Rab) S/0.5ml

PCR Assays

Bordetella bronchiseptica (Rab) A
Chlamydia A
Dermatophytes (Rab, GP) HA,HT,K
Distemper Virus (Fr, raccoon) H,LQ,A,EB
EBHS-Virus (Hare) FA
Encephalitozoon cuniculi H,LQ
Francisella tularensis A,Ln
Helicobacter spp. (Fr) V
Leptospira H+EB
Mycoplasma pulmonis (Rt, Ms) A
Myxomavirus (Rab) A
Parvovirus (Aleutian mink disease) EB,A,FA
Pasteurella multocida (toxin producing) (Rab) A
Pox (Orthopoxvirus) (Rab, GP, Rt, Ms) K
RHDV 1+2 (Rab) A,EB,FA,H
Salmonella A,FA
Sarcoptes scabiei var. canis (Rab, GP, Fr) HT
Toxoplasma gondii (Rab, GP) LQ
Treponema paraluiscuniculi (Rab) K,A

PCR-Profiles

Respiratory Profile (Rab) A
(Bordetella bronchiseptica, chlamydia, toxin producing Pasteurella multocida)

Depending on the spread of the pathogen, tissue samples are also suitable for PCR.

A	swab (without medium for PCRs)	GP	guinea pig	HT	skin	Rab	rabbit
BAL	bronchoalveolar lavage	GW	tissue	K	scurf	Rt	rat
BS	blood smear	H	urine	Ln	lymph node	S	serum
EB	EDTA blood	HA	hairs	LQ	CSF	TM	swab with medium
EP	EDTA plasma	Ha	hamster	Ms	mouse	V	vomit
FA	faeces	HB	heparin blood	NaFB	sodium-fluorid blood	*	partner lab
Fr	ferret	HP	heparin plasma	PCR	polymerase chain reaction	!	cooled

www.LABOKLIN.com

D-97688 Bad Kissingen · Steubenstraße 4
Tel. +49 971 72020 · Fax +49 971 68546
info@laboklin.com

CH-4002 Basel · Postfach · Riehenring 173
Tel. +41 61 3196060 · Fax +41 61 3196065
labor.basel@laboklin.ch

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