



Congestive heart failure in rabbits

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The rise in life expectancy of pet rabbits increases the risk of developing a cardiovascular disease. Signs appear gradually. Heart disease is often detected only at a late stage only.

Life expectancy of pet rabbits is up to 10-12 years for the smaller breeds. It is accompanied by an increase of circulatory diseases, of heart problems, and arteriosclerosis. The causes often are a diet too rich in fat or lack of exercise, but heart disease have also been observed in active

rabbits or rabbits involved in show jumping competition (Kaninhop, Figure 1).

Cardiovascular diseases are difficult to detect in rabbits. They may be asymptomatic or show fatigue and intolerance to exercise. Other signs are nasal discharge, a deep cough and snoring

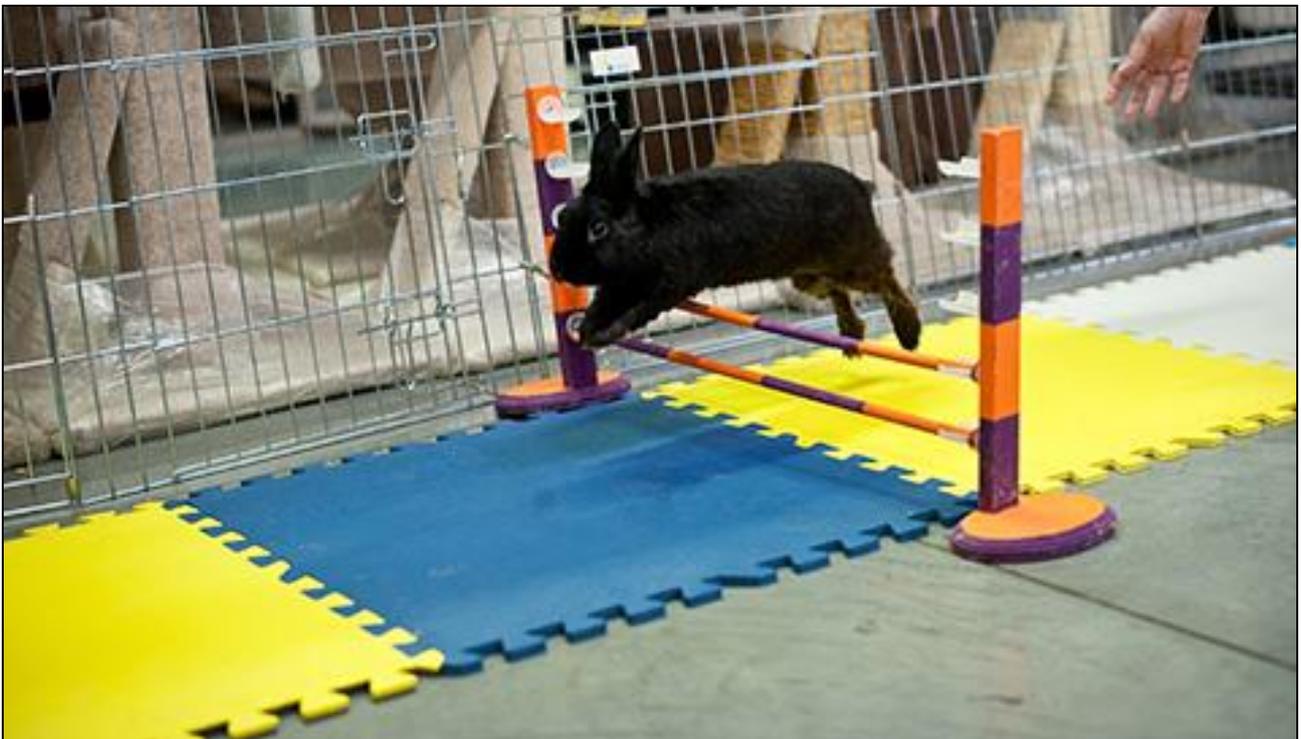


Figure 1: An athletic rabbit, actively participating in show jumping, can also develop heart disease (Picture courtesy of Sylvie Tjoei).

when the animal sleeps. An increase of the breathing frequency, a decrease of tidal volume (polypnea) and respiratory distress (dyspnea) result from a decreased blood flow as well as poor oxygenation of body tissues (hypoxia), due to lung compression caused by interstitial edema or pleural effusion (presence of fluids in the pleural cavity).

Anatomy of the rabbit heart

The size of the rabbit heart is relatively small in relation to the size of its body, and in comparison with that of other animals (Figure 2). It is placed high in the chest – between the lungs and near the sternum, protected by the pericardium. This double-walled sac consists of a deep layer (visceral pericardium) and a superficial layer (parietal pericardium) between which lies the pericardial cavity filled with fluid. The sliding

of the sheets relative to each other allows the movement of the heart. The pericardial fluid, in turn, protects the heart against shocks. The membrane of the pericardium is attached to the diaphragm, which helps keep the heart and major blood vessels in position in the thorax.

The axis of the heart runs along the ventral chest, slightly deviating to the left side. The heart shape is conical, the wider part or base is directed towards the front of the thorax while the apex (bottom tip) is directed to the spine and slightly to the left.

Internal structure of the heart

The rabbit heart is composed of 4 chambers:

- Two auricles – right and left, chambers with fine walls that are localized in the cranial portion of the heart. These

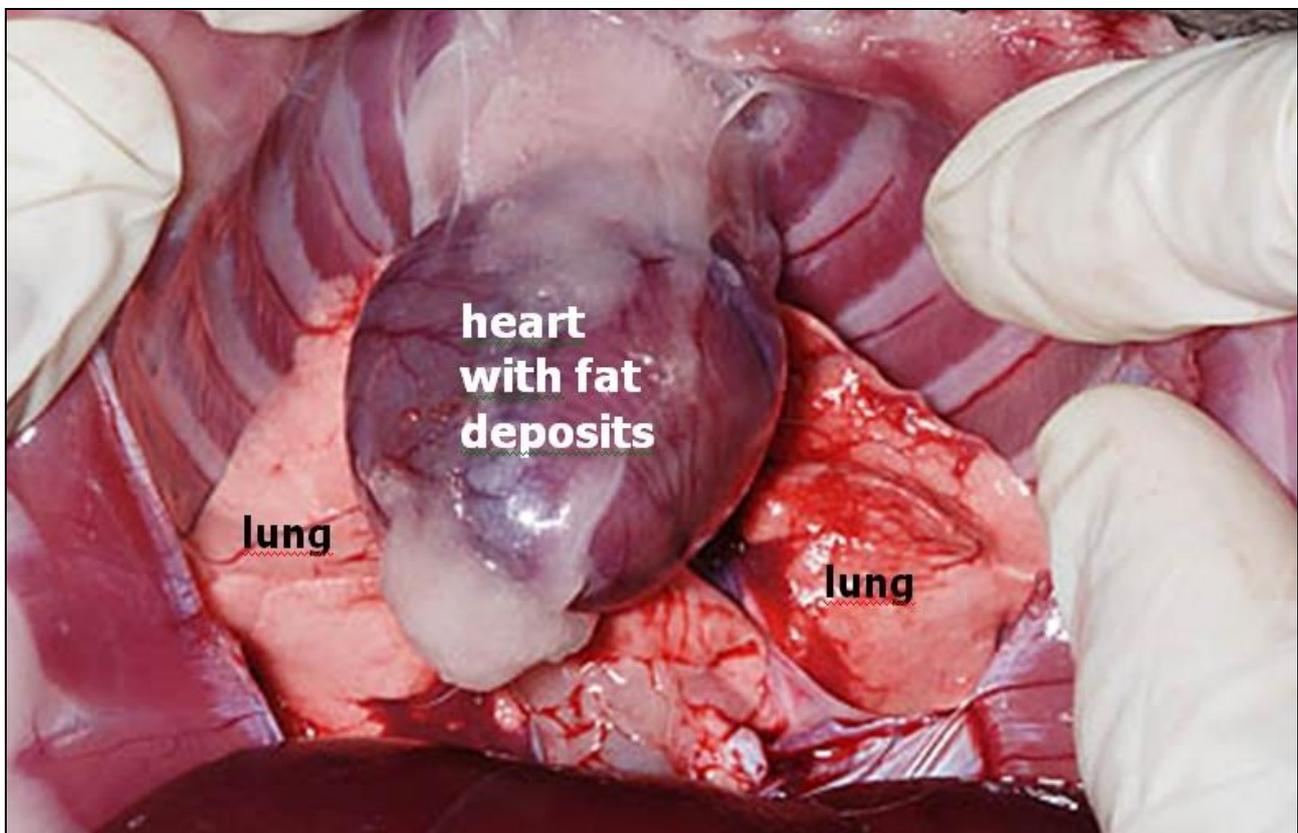


Figure 2: Anatomy of healthy lungs (Picture courtesy of Akira Yamanouchi).

chambers get the venous blood from:

- The cranial and caudal *vena cava* (one of two large veins returning blood from distant parts of the body to the right side of the heart) and the coronary sinus (veins that receive blood from the heart itself) transport the blood into the right auricle.
- The right and left pulmonary veins, which transport oxygenated blood from the lungs and connect to the heart on the dorsal side of the left auricle.
- Two ventricles with a thick, muscular wall; they form the muscular caudal portion of the rabbit heart. The left ventricle is larger than the right one. They are separated by the interventricular septum. Their walls (endocardium) have muscular ridges. The wall of the right ventricle is thicker than that of the right auricle and forms the conical apical portion, without reaching the apex. Ventricles pump blood out of the auricle into the bloodstream via the two aortic arches, the brachiocephalic trunk (left ventricle) and the pulmonary trunk (right ventricle)

Auricles and ventricles are separated by the inter-auricular and interventricular septa and by valves, which are held in place by tendons:

- On the right side, the tricuspid valve has 3 leaflets in most animals. In rabbits, it is formed of two leaflets only. When the right ventricle does not work normally or when the tricuspid valve is defective, the blood pressure increases, resulting in fluid accumulation in the tissues of the body, mainly in the abdomen and lower limbs
- On the left side, the bicuspid valve or mitral valve is formed by 2 leaflets. When the left ventricle is no longer able to

pump blood from the auricle or when the mitral valve does not function properly, blood will accumulate in the lungs (left heart failure). These become congested, leading to the formation of pulmonary edema (fluid accumulation). Oxygen uptake and its transportation from the lungs to the heart are impaired, resulting in fatigue. This is often accompanied by respiratory distress (dyspnea).

Valves can also be found at the connection site of blood vessels with the heart.

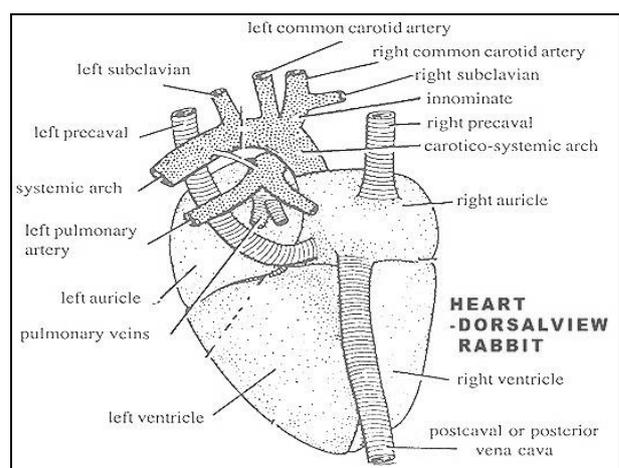
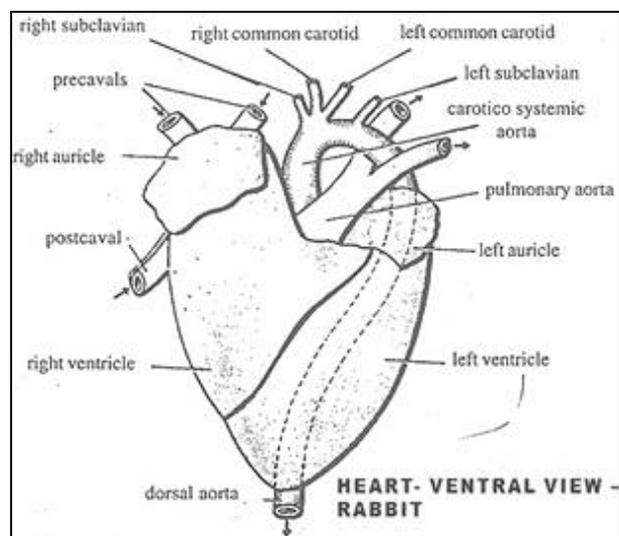


Figure 3: General ventral and dorsal views of the rabbit heart (Modern Text Book of Zoology: Vertebrates, R. L. Kotpal).

Physiological characteristics

Physiological characteristics differentiate the rabbit heart from that of other animals:

- The pulmonary artery and its branches are very muscular.
- The coronary arteries, which depart from the aorta and supply blood to the heart itself, are reduced in number. When compressed, myocardial ischemia develops due to poor collateral blood circulation.
- The aortic nerve has no chemoreceptors, only pressure-sensitive receptors, also called baroreceptors. Sensory nerves are thus not activated by chemical molecules, but only by the pressure of blood. Any modification of the blood pressure induces a reflex mechanism that allows the adaptation to changes (in blood pressure) by dilating or contracting blood vessels in the body.

Functioning of the heart

The heartbeat has two major steps: the contraction phase (systole) and the relaxation phase (diastole). The heart rhythm is initiated in a group of highly specialized muscle cells located in the inner wall of the right auricle: the sinoatrial node. The generated electrical pulse is transmitted to the auricles and to the ventricles via the atrioventricular bundle and Purkinje fibers. As a result, they contract.

When the auricles are filled with blood (deoxygenated in the right auricle and oxygenated in the left auricle), they contract to push the blood into the ventricles. When the latter are filled with blood, they contract and push the blood into the body of the animal.

Heart rate varies according to the size of the rabbit; it is faster for smaller breeds (180 to 250 beats/minute) than larger breeds.

Heart diseases in rabbits

Heart disease is mainly observed in rabbits older than 4 years, but, depending on the cause, it may also affect younger rabbits.

Heart problems can also be acquired during life. Infection by viruses (coronavirus), toxin-producing bacteria (*Clostridium piliformis*, *E. coli*, *Pasteurella multocida*) or protozoa (*E. cuniculi*) can cause myopathy, cardiomyopathy or endocarditis.

Deficiencies of nutrients, minerals (calcium, phosphorus) or vitamins can also cause heart disease in the long term. A deficiency in vitamin D or E (less than 23.2 $\mu\text{mol/L}$ in the blood serum) may cause abnormal mineralization in blood vessels or muscle weakness respectively.

Stress, in particular that caused by an overpopulation of rabbits in a small space, causes an elevation of catecholamine's in the blood. These can trigger dysfunctions of the left ventricle.

Finally, the administration of certain drugs or anesthetic agents can lead to damage or necrosis of the cardiac tissue. These include doxorubicin, the repeated use of ketamine-xylazine mixture or the use of α -agonist detomidine

Heart disease can be classified into several categories:

- Congenital: Cardiac abnormalities may be congenital, e.g. defects of inter-auricular or ventricular septa have been observed in a handful of rabbits.
- Myopathies: diseases of the myocardium muscle lead to an increased volume of the heart and a decreased heart function. Diseases that cause an enlargement of the heart are relatively common compared to hypertrophic or restrictive cardiomyopathy.

- Congestive heart failure: leading a decreased level of oxygen in the blood.
- Tachycardia: abnormal heart beat.
- Pulmonary congestion: excessive accumulation of fluids in the lungs as a result of lung disease may lead to an impaired functioning of the heart.

Congestive heart failure in rabbits

The main causes for congestive heart failure are damages to the heart muscle as a result of an infectious disease or a dysfunction of the left ventricle. In rabbits, other causes have also been found such as living in a cage and lack of exercise, or a diet deficient in vitamins and nutrients. Other causes include:

- Deficiency bicuspid or mitral valve, of congenital origin, or caused by an infection (viral or bacterial)
- Diseases of the coronary vessels,
- Diseases of the myocardium, inflammation or cardiomyopathy,
- Anemia or a low level of red blood cells,
- Lung diseases, such as pneumonia.

Congestive heart failure is observed in all rabbits, regardless of size or gender. Some breeds seem, however, more susceptible, namely giant rabbit breeds like the French lop, Rexes, white New Zealand rabbits and those whose purebred parents were crossbred.

Clinical signs

Clinical signs develop slowly and are often overlooked because they are nonspecific of heart disease. They include a loss of appetite and refusal to eat, fatigue and intolerance to exercise. Digestive disorders may be present, such as a distended abdomen, production of hard, dry feces or diarrhea. As the disease progresses other signs appear, such as persistent cough, and signs of pain or aggression. The

respiratory rate increases, accompanied by audible respiration, dyspnea and mouth breathing.

Fluid accumulation in the abdomen (ascites), peripheral edema and liver enlargement (splenomegaly) is possible with a failure of the right heart side (arterial pulmonary hypertension and pressure overload of the right ventricle), often secondary to bronchi -pneumopathy.

At advanced stages of the disease, the heart is unable to pump enough blood throughout the body. The mucous membranes of the oral cavity or nostrils become cyanotic. Fluids accumulate around the heart and in the lungs (Figure 6). At this stage, it is congestive heart failure. Breathing is difficult and deep. Inhalation of air is noisy and more labored than the expiration. The nostrils are dilated. Breathing may become abdominal (diaphragmatic). Rabbits may take a characteristic body position at rest keeping their front part in the raised position (Figure 4). If respiration becomes difficult, the neck and head are extended upwards.

When congestive heart failure is acute, the rabbit can suffer from syncope, collapse and die.

Diagnosis

Diagnosis of heart disease is not easy. The medical history of the rabbit is often uneventful. At an early stage, the animal shows no clinical manifestations, except in cases of stress, anxiety or excitement. In advanced stages, heart disease is often overlooked because the signs are general, and not indicative.

When cardiac abnormalities are suspected, various tests help visualize the enlargement of the heart, a rapid heart rate, and/or the presence of pulmonary edema.



A



B

Figure 4: Rabbits enjoy resting on top of each other. Top picture (A) shows Babe resting on top of Otjie. This is typical of a close friendship, with the abdomen resting over the bottom rabbit. In the bottom picture (B), Belgian giant, Adar is resting over the Rex rabbit, Flora, keeping the front thoracic portion of his body in an elevated position, a possible sign of heart failure (Picture courtesy of Sylvie Tjoei (A) and MediRabbit.com (B).

A blood test helps to quickly detect abnormalities in electrolytes levels or parameters indicative of organ function.

Chest and abdomen radiographs provide valuable information about the shape and size of the heart and lungs, help detect heart failure, emphysema, the possible presence of pulmonary edema and visualize blood vessels (Figures 5, 6). It allows ruling out a neoplasm of the thymus or the

presence of metastases in the lung tissue. Yet this technique has its limitations. Pulmonary embolism (blood clots in the lungs) is not visible and requires additional diagnostic tools.

Electrocardiography (ECG) and ultrasound are important tools in the diagnosis of heart disease. The procedure is simple, painless, non-invasive, and allows the comparison of modifications of the

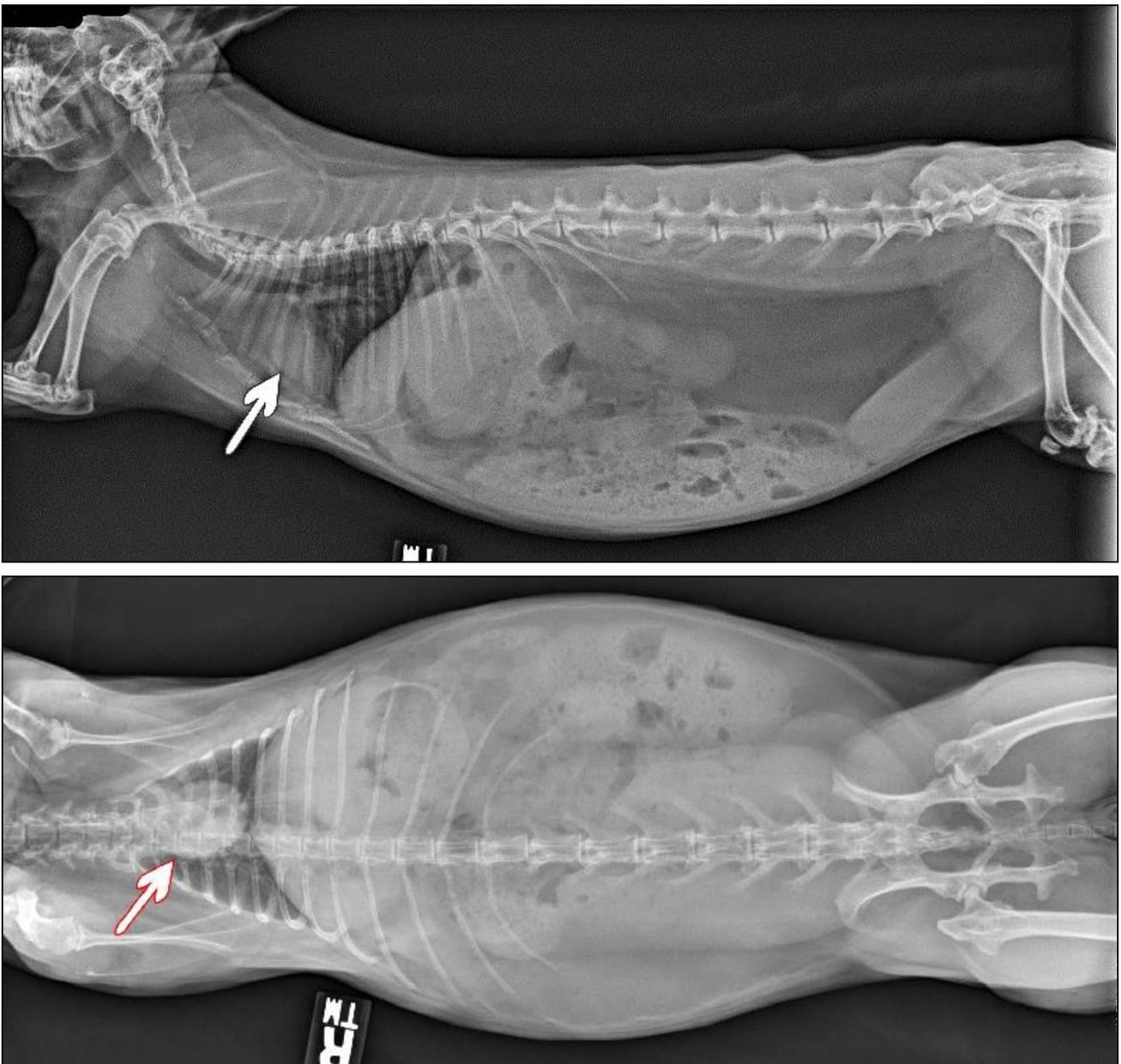


Figure 5: Lateral and ventral-dorsal x-rays of the thorax and abdomen of a healthy rabbit, showing the position of the heart, of blood vessels going to the heart and of the organs (Radiographs courtesy of Kim Chilson).

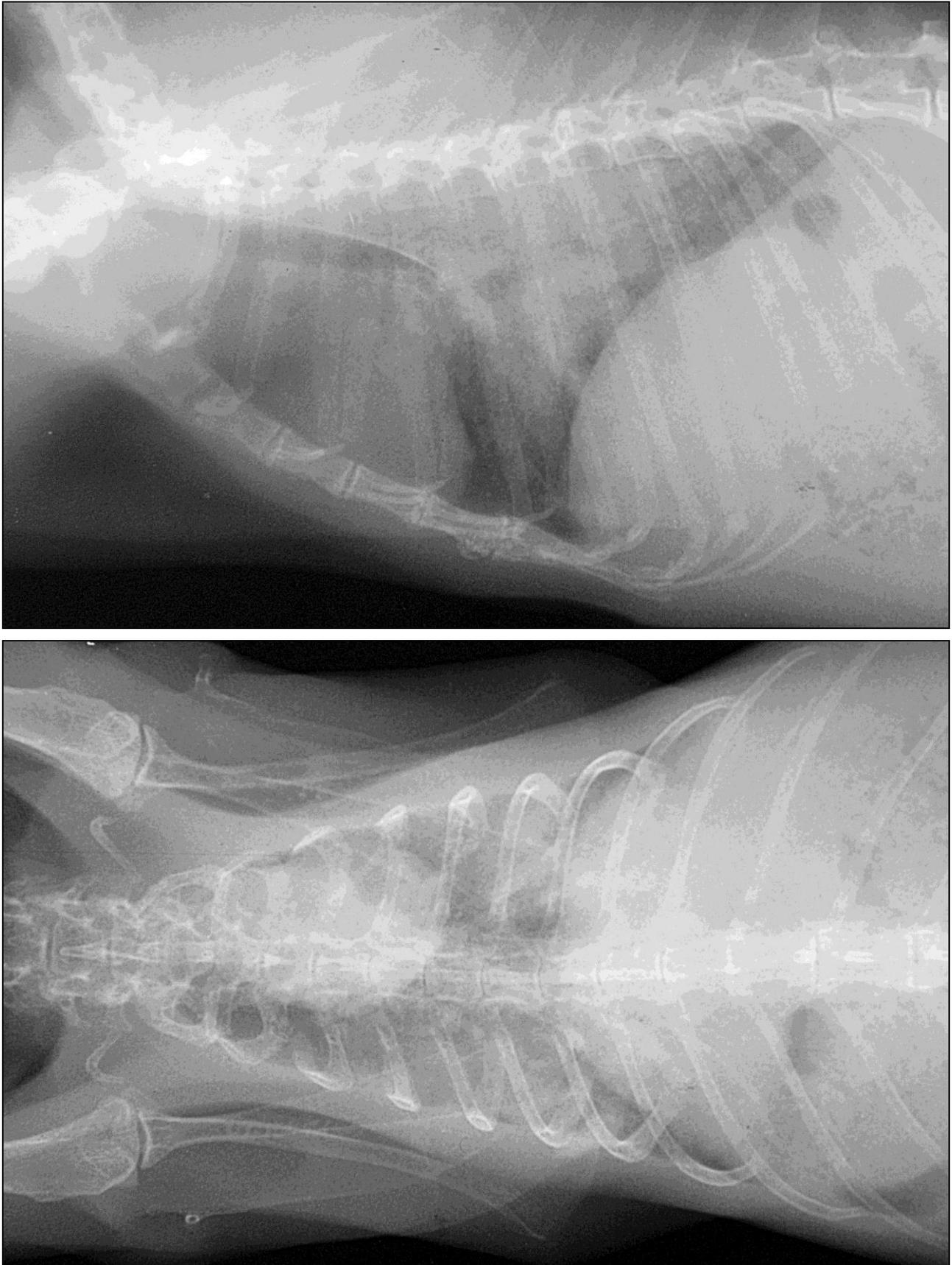


Figure 6: Lateral and dorso-ventral x-rays of the thorax of Babe, suggesting congestive heart failure: an enlarged heart touching the left chest wall and pulmonary edema. The rabbit died during the veterinary examination and attempts of resuscitation and oxygen administration failed. (Radiographs courtesy of Sylvie Tjoei).

electrical activity of the heart, by amplifying electrical pulses that pass through the heart. Electrocardiography is used to evaluate and monitor events such as pain in the chest, difficulty respiration, or arrhythmia.

The heart rate of a healthy rabbit has the shape of a sine. It excludes respiratory sinus arrhythmia (RSA), as there is no influence of breathing on the flow of sympathetic and *vagus* impulses to the sinoatrial node. Depending on the method used, a series of waves are obtained, which provide information on the pacemaker (electrical part which produces the pulse), nerve conduction and rhythm of heart. The different waves are called P, Q, R, S and T

and follow in alphabetical order:

- P wave of the electrocardiogram is associated with the atrial contraction,
- QRS series of waves is associated with ventricular contraction,
- P-Q or P-R interval gives a value for the time taken for the electrical impulse to travel from the auricle to the ventricle,
- T wave comes after the contraction.

Diseases or mineral deficiencies can lead to modifications of the values of the different waves:

- Abnormal P wave: right or left atrial hypertrophy, atrial premature beat, hyperkalemia.

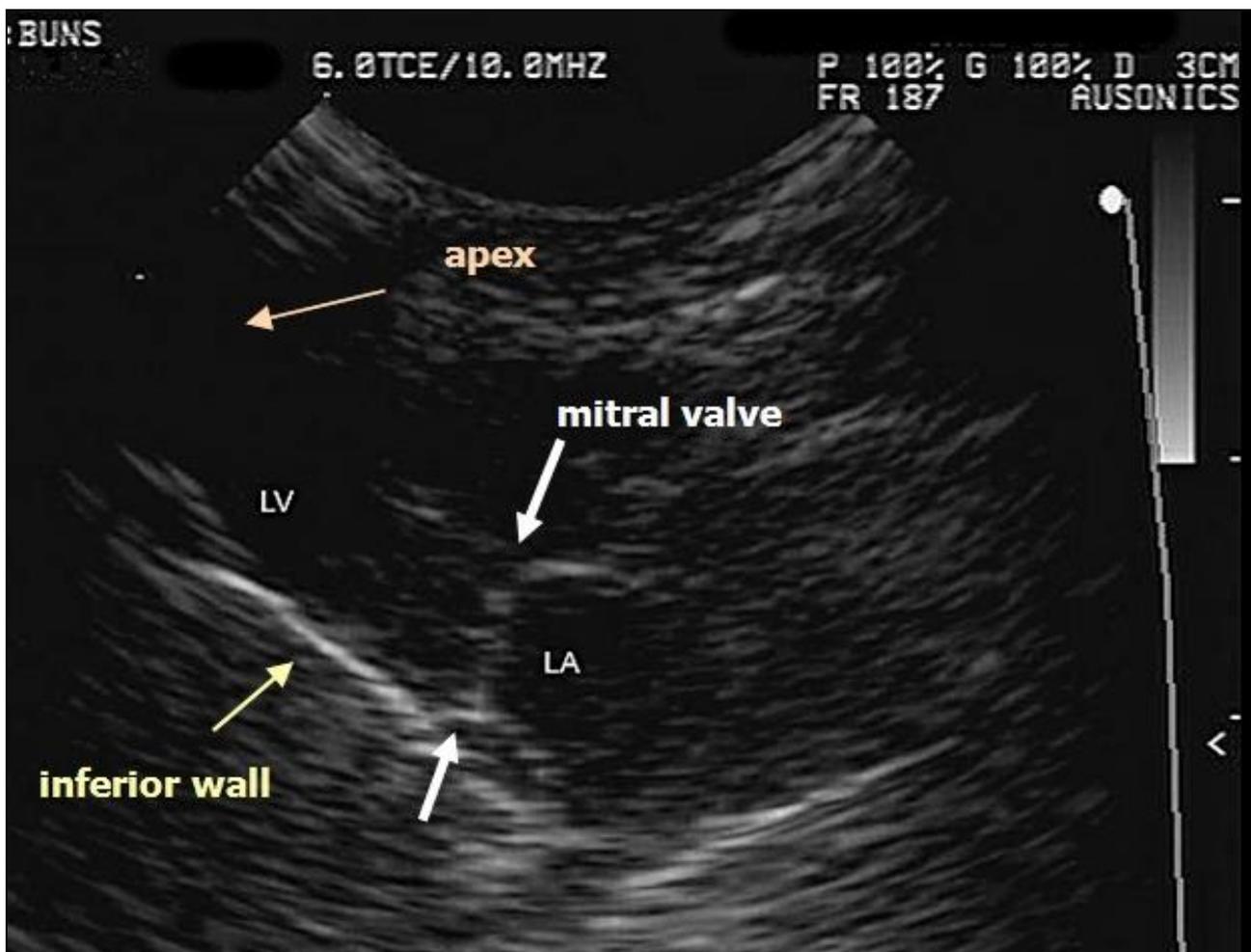


Figure 7: Para-sternal right view of the left ventricle in a healthy rabbit (Picture: Dr. Tom Chlebecek).

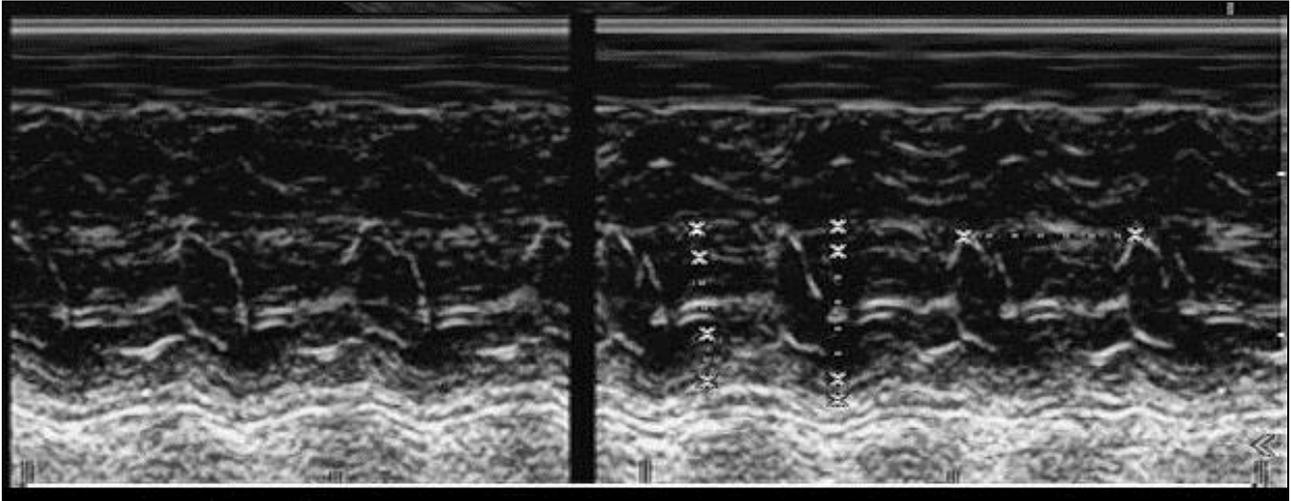


Figure 8: Echography in corresponding TM mode, with the mitral valve in line with the ultrasound beam (Picture: Dr. Tom Chlebecek).

P wave	Amplitude: 0.1 – 0.15 mv 0.04 – 0.12 Duration: 0.03 – 0.04 sec 0.01 – 0.05 sec
QRS interval	Duration: 0.015 – 0.04 sec 0.02 – 0.06 sec R-wave amplitude: 0.03 – 0-039 mV
Duration P – R	0.05 – 0.1 sec 0.04 – 0.08 sec
Duration Q – T	0.08 – 0.16 sec
R wave amplitude	Amplitude: 0.03 – 0.039 mV
T wave	Amplitude: 0.05 – 0.17 mV

Table 1: Electrocardiogram values in a healthy rabbit.

- Abnormal QRS interval: right or left bundle branch block, ventricular rhythm, hyperkalemia, among others.
- Abnormal Q-T duration: hypocalcemia, hypothyroidism, brain hemorrhages, congenital deformations, myocardial infarction, myocarditis.
- Abnormal T wave: hyperkalemia, hyperacute myocardial infarction and left

bundle branch block in case of a tall T wave; ischemia, age, stress, pericarditis, intraventricular conduction delay, electrolyte disturbance, in case of a small, flattened or inverted T wave.

These tests are not done routinely in rabbits. It is, therefore, imperative that the veterinarian analyzing the results is familiar with the particularities of rabbits in order to interpret the results correctly.

Treatment

Rabbits suffering from chronic heart failure can have a good quality of life, even if they are less active and rest often. If they do not suffer from severe respiratory distress, euthanasia is not indicated. The care of a rabbit with heart disease does, however, require special daily involvement of the owner of the rabbit.

Indeed, the treatment does not cure congestive heart disease, but stabilizes it when:

- Treating the underlying diseases, pneumonia or any other lung disease. A pleurocentesis may be useful in a rabbit

suffering from pleural effusion and severe dyspnea.

- Administering drugs that improve cardiac function and reduce pulmonary edema. The use of diuretics can relieve the retention of fluids and sodium. Nitrate based medications can reduce the pressure on the heart.
- Reducing stress in the living environment.
- Preventing weight gain or obesity.
- Supplying a healthy diet that includes pellets, good quality hay, fresh greenery and fresh or dried medicinal herbs. Nutrient deficiencies should be avoided.

Type of drugs	Doses	Way	Frequency
Anti-arrhythmic			
Lidocaine	0.5-1 mg/kg	PO	BID, SID
Anticholinergic			
Atropine (ineffective in many rabbits, as they possess atropinase)	0.05-0.5 mg/kg	SC, IM	Bolus
Glycopyrrolate	0.01-0.1 mg/kg	SC, IM, IV	Bolus
Beta blocker			
Atenolol	0.5-2 mg/kg	PO	SID
Diuretic			
Furosemide	0.3-4 mg/kg	PO, SC, IM, IV	BID, SID
Calcium-channel blockers			
Diltiazem	0.5-1 mg/kg	PO	BID, SID
Angiotensin-converting-enzyme			
Enalapril	0.1-0.5 mg/kg	PO	q24-48
Vasodilator			
Glyceryl nitrate		ointment	QID, BID

Table 2: Drugs administered to rabbits with heart failure. Some are not licensed for use in animals and/or rabbits (in alphabetical order).

Hawthorn may have beneficial effects on the heart, but its action is slow and takes a few weeks before stabilizing the congestive heart failure

Long-term control of heart failure includes the use of:

- Angiotensin-converting enzyme (ACE). They work to relax blood vessels, allowing blood to flow more easily. The heart can rest and, eventually, regain its normal size and ease breathing. Enalapril has a small advantage over other available drugs.
- Diuretics (furosemide). Increased excretion of sodium and fluids reduces the manifestations of congestive heart failure. The dose is based on the body weight. Indeed, excessive dosing leads to dehydration and potential kidney failure, while too low a dose brings no action or relief of symptoms. A side effect of diuretics administration is decreased blood potassium level.
- Inotropic agents (digoxin). They help stimulate a stronger pumping of the heart and increase the volume of blood pushed out of the left ventricle with each beat. In rabbits, these drugs are used to control sub-acute and chronic disorders of the myocardia, supraventricular arrhythmia or valve regurgitation (abnormal leaking of blood from the ventricle backward into the auricle during systole).

Regular medical monitoring of the rabbit is necessary when administering these drugs in order to verify the state of hydration, body weight, as well as serum levels of electrolytes, urea nitrogen and creatinine. Long-term prognosis remains uncertain.

If the rabbit is suffering from an acute heart failure, treatment includes administration of oxygen and rest in a quiet place.

Acknowledgements

In memory of Sagwa and Babe



Thank you to Sagwa and Babe, who died in just a few months apart from each other, from thymoma and severe heart failure respectively.

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