Zaitsev *et al. Animal Diseases* (2024) 4:38
https://doi.org/10.1186/s44149-024-00143-w

Animal Diseases

ORIGINAL ARTICLE

Open Access

Mineral imbalance and cardiovascular disease in animals of the canine (*Canidae*) and feline (*Felidae*) families: a study in Russian zoos

Sergei Yu. Zaitsev[1,2*], Marina V. Stepanova[2,3] and Larisa F. Sotnikova[2,4]

Abstract

It is important to consider the full spectrum of complex interactions between mineral elements and biologically active substances to evaluate the development of cardiovascular disease (CVD) in animals, in addition to the classical physiological approach. This study aimed to assess changes in mineral element levels in wild and exotic animals in relation to their cardiovascular diseases. A total of 171 animals, including 128 healthy and 43 sick animals from three Russian zoos, were sampled and analyzed. For the first time, species from the canine (nine) and feline (seven) families from Moscow, Ivanovo, and Yaroslavl zoos in the Central Federal District of Russia were selected. A total of 108 samples from canines and 63 samples from feline animals were collected. Mineral element measurements were conducted on 1026 samples *via* a "Kvant-2A" atomic absorption spectrometer from Russia. Correlation and regression analyses were performed. CVDs were found in 10.1% of the studied animals, with a high percentage of heart muscle pathologies noted (25.8% of all CVDs). Iron (Fe) accumulated in canine and feline fur at approximately 208 and 203 mg/kg, with variations of 72.8% and 80.9%, respectively. A significant decrease in Fe and an increase in cadmium (Cd) during CVD were observed (correlations $r = 0.25$ and $r = 0.16$, respectively). The dysregulation of Fe homeostasis, increased absorption, and accumulation of Fe in the reticuloendothelial system are discussed. Finally, the mineral elements absorbed by canine and feline fur can be ranked in descending order: Fe > Zn > Cu > Pb > Cd > As.

Keywords Cardiovascular diseases, Canine family, Feline family, Mineral elements, Iron

Communicated by Zhixin Lei.

*Correspondence:
Sergei Yu. Zaitsev
s.y.zaitsev@mail.ru
[1] Federal Research Center for Animal Husbandry Named After Academy Member L.K. Ernst, Dubrovitsy, Moscow Region, Russia
[2] Research Laboratory of Ophthalmology, Oncology and Biochemistry of Animals, Federal State Budgetary Educational Institution of Higher Education "Russian Biotechnological University (ROSBIOTECH)", Volokolamsk Highway, 11, Moscow 125080, Russia
[3] Department of Bioecology and Biological Safety, Federal State Budgetary Educational Institution of Higher Education "Russian Biotechnological University (ROSBIOTECH)", Volokolamsk Highway, 11, Moscow 125080, Russia
[4] Department of Diseases of Small Domestic and Exotic Animals, Federal State Budgetary Educational Institution of Higher Education "Russian Biotechnological University (ROSBIOTECH)", Volokolamsk Highway, 11, Moscow 125080, Russia

Introduction

The welfare of domestic (Zhao et al. 2024; Vilmis et al. 2023) and wild (Berg et al. 2020; Stepanova et al. 2023) animals, especially zoos and aquariums, is considered by leading researchers to be a primary factor in all of their activities. In wild and exotic animals kept in large cities (Stepanova et al. 2023), the manifestation of cardiovascular diseases (CVDs) has not been studied in detail. A sedentary life in captivity, excessive and unbalanced diets, poor, and spoiled food, and contact with other animals and humans lead to the appearance of animal diseases (such as CVDs) that, in the wild, are most likely not recorded in these animals (Alshinetsky 2013; Balakirev et al. 2017; López-Alonso et al. 2007; Stepanova et al. 2023). However, the major efforts of veterinarians are now concentrated in the field of animal oncology because of its enormous prevalence in animals and enormous global veterinary oncology market, which "stands about US 260 million in 2023, and is estimated to reach US 800 million by 2033-end" (https://www.factmr.com/report/veterinary-oncology-market). For example, Andrade F.H. reported that "Mammary tumors of female dogs have greatly increased in recent years, thus demanding rapid diagnosis and effective treatment in order to determine the animal survival" (Andrade et al. 2010).

Diseases of the heart, kidneys, lungs and other organs cause serious damage to zoological collections, which consists of the death of animals, decreased productivity, culling, and increased treatment costs (Staroverova et al. 2021). These diseases can be caused by disorders of the levels and metabolism of the key mineral elements (MEs) essential for the animals (Fe, Zn and Cu) or some toxic MEs (Pb, Cd and As) (Stepanova et al. 2019). For example, in many regions of the Central Federal District (Russia), iron in the environment (especially in the soil and water of natural reservoirs) is present at concentrations above the maximum permissible levels (Staroverova et al. 2021; Vilmis et al. 2023). Excessive ME intake into the body can lead to the development of diseases of various etiologies, including CVDs (Stepanova et al. 2019).

The study of the elemental status of wild and exotic animals (in zoos in Russia and foreign countries) in connection with their pathological conditions is of a point nature and considers a narrow range of ME accumulation by internal organs, which does not allow for a comprehensive lifetime assessment of the status and timely adjustment of the diet (Stepanova 2021a). For a more objective assessment of the condition of animals, including rare animals, it is necessary to use noninvasive methods for taking and assessing the chemical composition of biosubstrates, which allows the development of individual programs for the prevention and correction of elementoses. These requirements are met by the study of the microelement composition of fur, which does not require special equipment for storage and transportation and can be stored for almost unlimited time without losing its information value. Animal fur ("hair cover ") serves as one of the objective indicators of an animal's adaptability to environmental conditions. Fur is the second most metabolically active tissue of the body, and its microelement status corresponds to a certain period of element accumulation and not to the moment of sampling (Stepanova 2021a). Moreover, the concentration of chemical elements in fur is significantly greater than that in physiological fluids traditionally used for clinical and biochemical analyses, which makes it possible to significantly expand the set of chemical elements available for analytical determination (Stepanova 2021b; Skalny 2021).

A study by Bayurov L.I. was conducted to determine the possibility of using the fur of wild and exotic animals as diagnostic information material for determining cardiovascular diseases (Bayurov et al. 2022). The skin is the largest and most extensive organ of the body, making up 12% to 24% of the dog's body weight, depending on its species, size and age. Most of the outer layer of a dog's skin is covered with hair, which provides effective protection to the body from the effects of adverse environmental factors, forming a barrier. Importantly, the condition of the dog's skin and coat can serve as a reliable criterion for the general health of the animal (Bayurov et al. 2022).

It is necessary to analyze the relationship between changes in the variety of MEs during the development of cardiovascular diseases since their mutual influence on accumulation has been proven. There are a number of works indicating a change in the microelement composition of biological environments during various diseases, including cardiovascular diseases. For example, a reliable increase in Pb content has been established in animals with cardiovascular disease, which has a negative effect on health (Kim et al. 2014) and is associated with pronounced toxicity of the metal to a number of systems and organs (Flora et al. 2012). The effects of lead on the mother's body and the development of congenital heart defects in newborns have been established (Liu et al. 2015), which are associated with the ability of MEs to disrupt the regulatory mechanisms of DNA methylation (Montrose et al. 2017; Sanchez et al. 2017). Today, MEs are highly important for the vital activity of biochemical metabolism in animals (Avtsyn et al. 1991). They are interconnected by their action with biologically active substances (vitamins and hormones) (Boev et al. 2002) and form strong complexes with enzymes (Shaikhiev et al. 2015); therefore, they play a significant role in a number of physiological processes, such as reproduction (Stankovsky et al. 2000), growth and development, the formation of bone tissue (Ca and P), hematopoiesis (Fe,

Zn and Cu), tissue respiration (Fe and Cu), photosynthesis (Cu and Mg), and the metabolism of proteins (Fe, Ca, Cu and Co), carbohydrates (Zn and Cr), etc. (Shaikhiev et al. 2015; Stepanova 2021a; Zaitsev 2017).

Iron (Fe) is an essential micronutrient for humans and animals and plays a major role in metabolic processes in endothermic animals. This ME is one of the most abundant elements on earth (Grigoriev 2009). Studies have shown that the concentration of Fe in the tissues of different bird and mammal species can be influenced by the type of diet and the biological characteristics of the species (Drozdova et al. 2017).

Most iron is present in the hemoglobin of erythroid cells (> 2 g) or the myoglobin of muscles (approximately 300 mg) as heme. The macrophages in the spleen, liver and bone marrow maintain a transient fraction of iron (at the level of 600 mg), whereas excess metal is stored in the liver parenchyma as ferritin (approximately 1,000 mg). All other cellular iron-containing proteins and enzymes are estimated to bind a total of approximately 8 mg of iron. Iron levels in the body are maintained by consuming approximately 1–2 mg of Fe daily from food to compensate for the loss of the same amount (Stepanova 2021a).

Iron homeostasis is ensured primarily by the regulation of its absorption and the body's limited ability to excrete it, as summarized in Fig. 1.

Approximately 4 mg of Fe is contained in the circulation bound to Tf, which is 0.1% of the total amount of the element in the body. Most of these MEs in the body are located in the erythroid compartment of the bone marrow and in mature erythrocytes, which are contained in the heme portion of hemoglobin (Stepanova 2021a). The reticuloendothelial macrophages of the spleen, which remove Fe from senescent erythrocytes, provide it for the synthesis of new erythrocytes. Tf delivers iron to developing erythroid precursors as well as to other sites of ME utilization. Liver hepatocytes store Fe in ferritin membranes. During pregnancy, Me is transported to the fetus through the placenta. The distribution of Fe in the body changes with iron deficiency and iron overload (Pacyna et al. 2001).

Fe is a component of respiratory pigments (hemoglobin and myoglobin) and is contained in cellular enzymes (catalase, peroxidase, and cytochromes). A major amount of Fe is found in hemoglobin (hemoglobin Fe), whereas myoglobin iron makes up 10–15% of the total amount of Me; the Fe reserve is in the liver, spleen, and bone marrow (20% total); the Fe in the oxidases and cytochrome enzymes (10–15%); and the Fe in the blood plasma is no more than 0.1%. The most important Fe-containing protein is hemoglobin, the formation of which is influenced by Cu, Co, vitamin B12, pyridoxine, and other factors (Zaitsev 2017). The amount of Fe in the blood and serum of birds is 28.6–35.8 μmol/L (Antipov 2010).

The purpose of this study was to evaluate the features of some ME level changes related to cardiovascular diseases in wild and exotic animals of the canine and feline families.

Results

The "nosological profile" of the most common diseases

A multisided view of CVD occurrence in animals is possible only if all complex interactions between MEs and biologically active substances are taken into account in addition to the classical physiological "picture". A treatment was carried out on 43 heads of wild animals (25.1% of the studied animals). The diagnosis was established on the basis of the individual records of individuals, pathological-anatomical reports and veterinary procedures. On the basis of the "nosological profile", the most common diseases are summarized in Fig. 2.

On the basis of the "nosological profile" of noncommunicable diseases, diseases of the digestive and musculoskeletal systems, which are detected in 25.6% and 21.6% of all cases, respectively, are found most often in canine and feline families (kept at zoological institutions). The diseases of the cardiovascular and reproductive systems are in the middle of the row: 10.1% in both cases. The least frequently observed diseases are nervous system and hearing organ diseases, accounting for 1.5% and 0.3%, respectively. Among CVD cases, the highest percentage of pathologies of the heart muscle was noted during animal autopsy.

The levels of key mineral elements in animal *fur* species from the canine and feline families

In addition, the ME levels adsorbed by animal fur can be presented in the following descending order: Fe > Zn > Cu > Pb > Cd > As (Tables 1 and 2).

In the canine (feline) family, Fe accumulated in fur at about 208 (203) mg/kg, indicating the importance of Fe (Tables 1 and 2). When data from fur farms in the Moscow region were compared, an increase in the concentration of Fe in the fur of the sample was noted a few times (Balakirev et al. 2017; Staroverova 2011). The variability of the Fe content in the fur of the studied animals was 41.7%. During the correlation analysis of the obtained data (Tables 1 and 2), a direct connection was established, indicating synergism or antagonism in ME accumulation in comparison to Fe (Table 3).

During the correlation analysis of the obtained data (Table 3), the particular positive correlation coefficients (from very strong to moderate) between Fe and other MEs were calculated, indicating synergism in the accumulation of the following MEs: Cu, Cd (0.28, 0.66) for

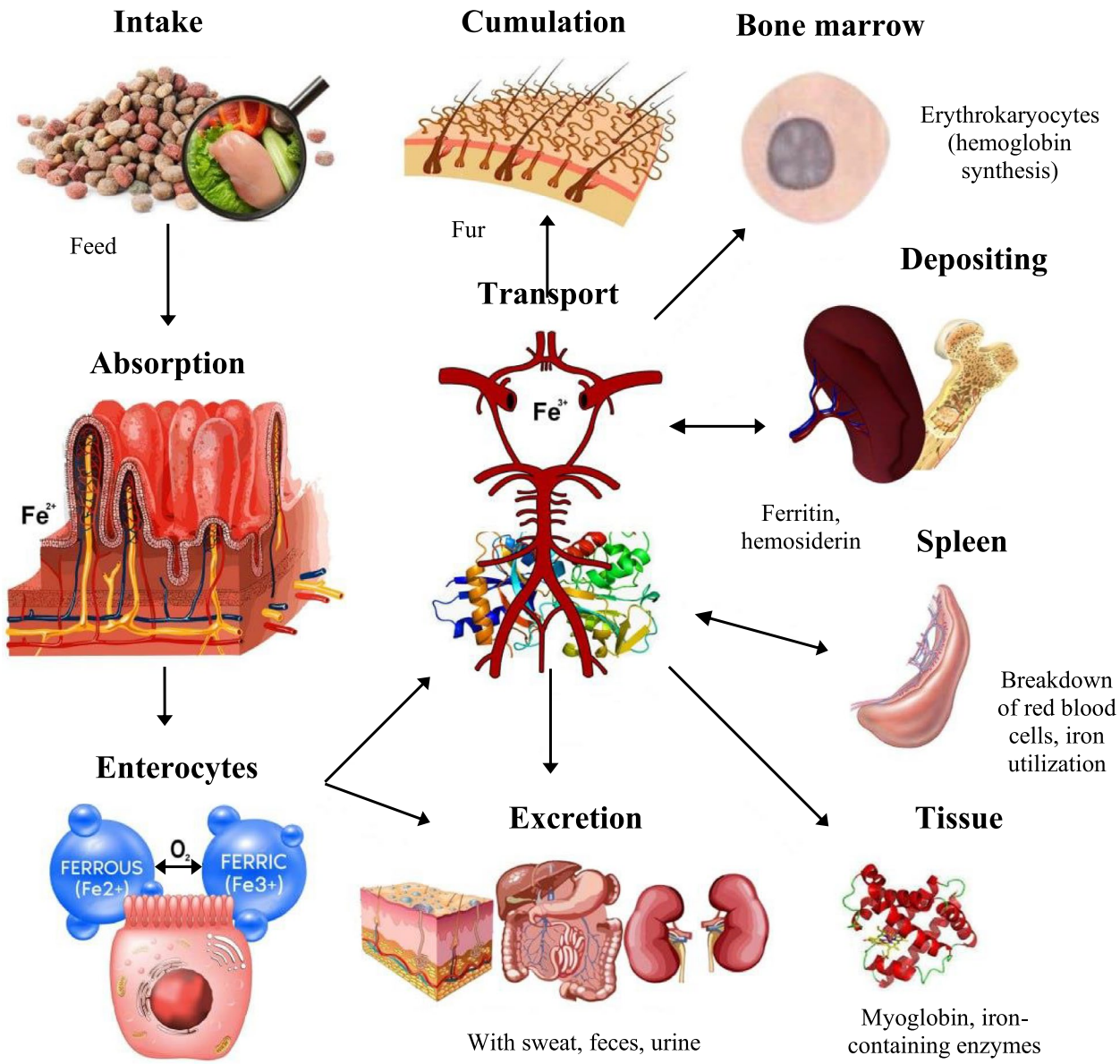

Fig. 1 A general scheme of iron accumulation in various tissues

Vulpes vulpes; Pb, As (0.43, 0.54) for *Vulpes (Fennecus) zerda*; Cu, Pb, Cd (0.94, 0.77, 0.38) for *Alopex lagopus var. dom.*; Cu (0.76) for *Canis familiaris*; Zn, Cu, As (0.83, 0.77, 0.88) for *Canis lupus tundrorum*; Cu, As (1.00, 0.87) for *Nyctereutes procyonoides*; Cd, As (0.66, 0.96) *Felis (Lynx) lynx*; Cu, Pb, Cd (0.82, 0.45, 0.84) for *Puma (Felis) concolor*; Zn, As (0.71, 0.50) *Uncia (Panthera) uncial*; Zn, Cu, Pb.

In contrast, during the correlation analysis of the obtained data (Table 3), the particular negative correlation coefficients (from very strong to moderate) between Fe and other MEs were calculated, indicating antagonism in the accumulation of the following MEs: As (-0.35) for *Vulpes vulpes*; Zn, Cu (-0.89, -0.54) for *Vulpes (Fennecus) zerda*; Zn (-0.74) for *Alopex lagopus var. dom.*; Pb, As (-0.88, -0.25) for *Canis familiaris*; Pb, Cd (-0.83, -0.39) for *Canis lupus tundrorum*; Cu (-0.34) for *Canis lupus*; Zn (-0.97) for *Nyctereutes procyonoides*; Zn, As (-0.82, -0.88) for *Puma (Felis) concolor*; Cu, Pb (-0.60, -0.94) *Uncia (Panthera) uncial*; Cu, As (-0.91, -0.43) for *Panthera tigris altaica*; and Cu, As (-0.71, -0.60) for *Panthera.*

Importantly, the correlation coefficients between Fe and other MEs (as an average for all the studied animal species of the canine family) are as follows: Zn (0.26), Cu

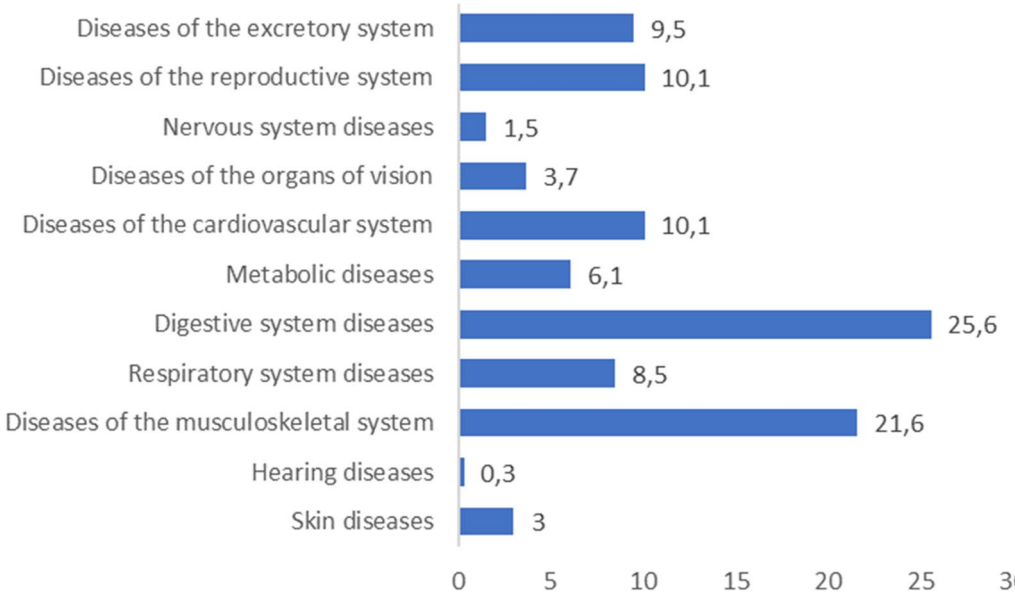

Fig. 2 "Nosological profile" of noncommunicable diseases (right) in animals kept in Russian zoological institutions: type of disease (right), number of animals with these diseases (left in %)

Table 1 ME contents in the fur of the animals of the canine family

Animal species (subspecies)	ME concentration, mg/kg					
	Zn	Cu	Fe	Pb	Cd	As
Vulpes vulpes	122.85±11.01	5.11± 0.81**	259.58±27.09***	6.27±1.54*	0.49±0.14*	0.19±0.08
Vulpes (Fennecus) zerda	151.75±8.79	18.79±3.59**	211.71±8.49***	5.12±0.77*	0.01*	0.40±0.07
Alopex lagopus var. dom	84.50±29.71	6.46±1.48**	105.91±4.15***	0.05±0.01*	0.03±0.00*	0.24±0.02
Canis familiaris	73.08±4.89	6.92±0.23**	73.25±2.18***	6.02±0.61*	0.15±0.05*	0.003±0.000
Canis lupus tundrorum	67.84±2.15	12.88±1.73**	265.18±4.12***	13.21±2.69*	0.03±0.00*	0.80±0.08
Canis lupus	95.96±9.74	9.48±3.64**	273.24±58.29***	7.26±1.11*	0.17±0.04*	0.43±0.06
Nyctereutes procyonoides	59.33±1.33	8.17±2.56**	116.68±2.68***	0.01*	0.57±0.00*	0.002±0.001

Reliability was calculated for each element between all species of animals studied on the basis of the Kruskal–Wallis criterion * $p < 0.001$; ** $p < 0.01$; *** $p < 0.05$

Table 2 ME contents in the fur of the animals of the feline family

Animal species (subspecies)	ME concentration, mg/kg					
	Zn	Cu	Fe	Pb	Cd	As
Felis (Lynx) lynx	51.54±3.21	4.26±1.92***	134.81±16.99*	0.85±0.19*	0.04±0.01**	0.30±0.02***
Puma (Felis) concolor	68.49±6.19	9.90±5.15***	267.02±18.73*	12.07±3.98*	0.22±0.13**	0.08±0.01***
Uncia (Panthera) uncial	17.34±3.21	2.52±0.65***	248.35±16.21*	9.11±1.13*	0.01**	0.33±0.06***
Panthera pardus orientalis	49.33±12.15	5.60±1.63***	216.10±36.91*	6.22±1.32*	1.10±0.52**	0.21±0.02***
Panthera tigris altaica	77.29±16.28	14.41±2.41***	309.68±31.09*	2.41±0.17*	0.17±0.03**	1.16±0.19***
Pantera leo var. alba	84.05±7.96	4.64±1.58***	295.15±19.24*	3.22±0.12*	0.01**	0.88±0.06***
Panthera leo	44.44±4.93	5.56±1.47***	116.94±11.65*	0.01*	0.21±0.02**	0.49±0.05***

Reliability was calculated for each element between all species of animals studied on the basis of the Kruskal–Wallis criterion * $p < 0.005$; ** $p < 0.01$; *** $p < 0.001$

Table 3 Correlation analysis of the joint accumulation of the studied MEs in the fur of the animals in the canine and feline families (kept at the zoo) in comparison to that in the Fe

Animal species	Zn	Cu	Pb	Cd	As
Vulpes vulpes	0.14	0.28	-0.01	**0.66***	-0.35
Vulpes (Fennecus) zerda	**-0.89***	-0.54	0.43	–[#]	0.54
Alopex lagopus var. dom	**-0.74***	**0.94***	**0.77***	0.38	-0.02
Canis familiaris	0.14	**0.76***	**-0.88***	-0.19	-0.25
Canis lupus tundrorum	**0.83***	0.77	**-0.83***	-0.39	**0.88***
Canis lupus	-0.10	-0.34	0.08	0.24	0.21
Nyctereutes procyonoides	-0.97	1.00	–[#]	–[#]	0.87
Felis (Lynx) lynx	0.07	0.07	-0.05	**0.66***	**0.96***
Puma (Felis) concolor	**-0.82***	**0.82***	0.45	0.84	**-0.88***
Uncia (Panthera) uncial	0.71	-0.60	-0.94	–[#]	0.50
Panthera pardus orientalis	**0.68***	0.53	0.50	0.45	-0.20
Panthera tigris altaica	0.40	**-0.91***	-0.13	**0.76***	-0.43
Pantera leo var. alba	0.77	0.71	**0.89***	–[#]	0.54
Panthera leo	-0.14	-0.71	–[#]	0.64	-0.60

Reliability is indicated on the basis of the basis of the calculation of the Spearman rank correlation coefficient * $p < 0.05$; "–[#]" traces the ME amount of one of the elements that do not make it possible to calculate the correlation coefficient

(-0.02), Pb (-0.17), Cd (0.24), and As (0.43). The correlation coefficients between Fe and the other MEs (as averages for all the studied animal species of the feline family) were as follows: Zn (0.17), Cu (0.06), Pb (0.08), Cd (0.26), and As (0.09). Thus, correlation analysis of the obtained data (Table 3) is more effective for the use of particular animal species but does not include all the studied animal species of the canine or feline family.

Since iron is one of the most important mineral nutrients involved in biological processes (e.g., heme synthesis, iron-dependent catalytic reactions, DNA synthesis, and mitochondrial respiration) (Abbaspour et al. 2014), its metabolism is extremely complicated and requires sufficient attention.

Currently, there is no information about the background and normal levels of iron content in animal fur; therefore, to assess the concentration of elements in "biosubstrates", centile scales are compiled on the basis of the abovementioned information (Table 4, Figs. 3 and 4).

Centile scales of Fe accumulation in the *fur* of the studied animals

On the basis of the obtained gradation scales, the ME content in the fur of the examined animals was assessed. The average level of ME accumulation in the canine samples was 50.5%, and that in the feline samples was 48.5%. Deviations in content are observed in felines in the direction of decreasing content: 25.7% versus 21.3%, and in canines, they are in equal proportions: 24.7% versus 24.8% (Fig. 3).

Table 4 Centile scales of Fe accumulation in the fur of the canine and feline families[a]

Centile scales	Estimation of corridor values	Canine family	Feline family
< 5%	Very low	≤ 3.20	≤ 1.77
5–10%	Low	3.21- 3.97	1.78—2.32
10–25%	Below average	3.98—83.94	2.33—34.41
25–75%	Average	83.95—211.32	34.42—330.70
75–90%	Above average	211.33—527.13	330.71—473.33
90–95%	High	527.14—832.41	473.34—487.97
> 95%	Very high	≥ 832.42	≥ 487.98

[a] mg/kg

For all the studied canine and feline samples, the iron levels were as follows: high concentrations, in 6.1–9.7% of the samples; above average, in 15.1–15.2% of the samples; averag, in 48.5–50.5% of the samples; below average, in 11.8–15.2% of the samples; low, in 4.5–7.5% of the samples; and very low, in 5.4–6.0% of the samples.

The deviations of the 1st degree (group I) from the average values of the healthy animal group N are taken to be values below 25 and above 75 centiles, 2nd degree: below 10 and above 90, 3rd degree: below 5 and above 95 and 4th degree: below 3 and above 97 centiles. In general, deviation of the 1st degree can be compared with the concept of "predisease" (group I), and deviations of the 2nd, 3rd and 4th degrees can be compared with the concept of "disease" (groups II, III and IV).

Inadequate iron overload or deficiency is correlated with a wide range of cardiovascular diseases. Iron deficiency can impair cardiomyocyte mitochondrial function and energy supply, leading to cardiac dysfunction (von Haehling et al. 2019). Excess iron can also be toxic, producing hydroxyl radicals through Haber–Weiss–Fenton reactions, causing oxidative damage to cellular components such as lipids, proteins and DNA (Galaris et al. 2019). Moreover, iron-mediated cell death, namely, ferroptosis, has recently been reported to cause cardiomyocyte damage and to play an important role in cardiovascular diseases (Wu et al. 2021; Li et al. 2021). Deviations of degree I (26.9–30.4%) and degree II (10.6–17.2%) are most often observed in the sample. Degrees III and IV deviation from the healthy animals (group N) were noted in 2.2–4.5% and 3.2–6.0% of the individuals, respectively (Fig. 4).

To establish the relationships between the contents of microelements in samples of animal biological media and general morbidity, correlation and regression analyses were carried out during the study period, the results of which are

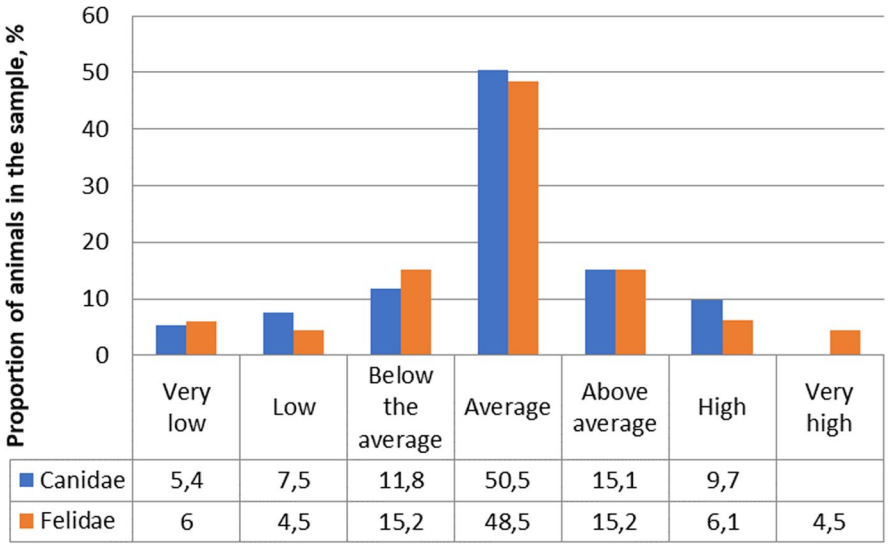

Fig. 3 Fe contents in the studied samples of animals

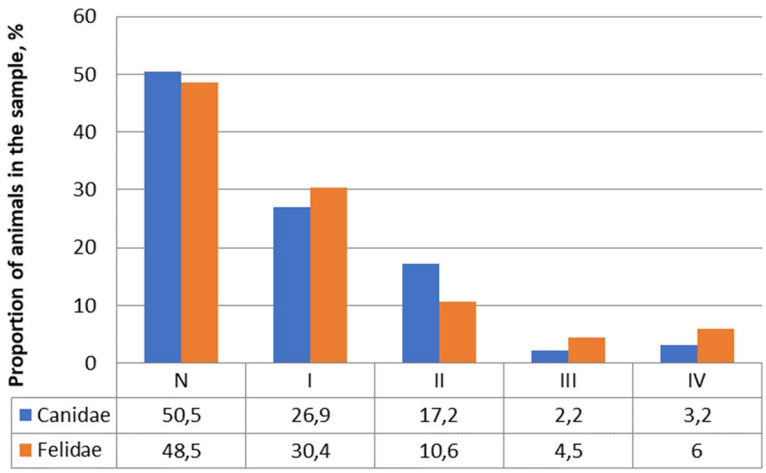

Fig. 4 Fe contents (percentages) in animal fur

presented in Tables 2 and 3. The diagnosis was established on the basis of the study of individual medical cards of animals and the pathological reports of veterinary procedures.

The following correlations between the ME content in samples of integument derivatives and the overall incidence of cardiovascular disease (with the proven role of environmental factors) were observed: 0.25, 0.32, -0.01, 0.19, 0.61 and 0.16 mg/kg for the Fe, Cu, Zn, Cd, Pb and As levels, respectively.

Relationship between Fe accumulation and diseases of the cardiovascular system

A reliable relationship between Fe accumulation and diseases of the cardiovascular system has been established, which corresponds to data from the literature (Abbaspour et al. 2014; Li 2021). The following ME contents in animals have been observed, taking into account previous cardiovascular disease: 142±55, 18.7±3.5, 128±12, 6.88±1.02, 5.01±0.68, and 0.340±0.121 mg/kg for Fe, Cu, Zn, Cd, Pb and As, respectively.

A significant decrease in iron levels occurs during the development of cardiovascular diseases. Dysregulation of Fe homeostasis, increased uptake and ME accumulation in the reticuloendothelial system leads to the removal of the element from the blood into the cells of the reticuloendothelial system following a decrease in the availability of iron for erythroid progenitor cells and iron-limited erythropoiesis (Weiss et al. 2005).

The acute phase protein hepcidin plays a key role in the development of anemia because it inhibits intestinal Fe absorption. In addition, there is a simultaneous increase in iron uptake by macrophages and a blockade of iron export from macrophages, mainly to the bone marrow. As a result, the concentration of iron in the blood decreases, which slows erythropoiesis and causes anemia (Roy et al. 2005). However, such a decrease in the serum iron concentration can sometimes be beneficial because it makes iron less available to microorganisms, inhibiting their growth (Bogun 2015).

A significant increase in Pb content was revealed in animals with damage to the cardiovascular system. The influence of lead on the maternal body and the development of congenital heart anomalies in newborns has been established (Liu et al. 2015).

The sample revealed a significant increase in cadmium content in animals with diseases of the cardiovascular and circulatory systems. The hematopoietic system is one of the targets of the toxic effects of Cd. An increase in the level of xenobiotics in the blood is caused by a decrease in the hemoglobin concentration (Chen et al. 2015) and increases the likelihood of developing iron deficiency anemia (Shah et al. 2011; Suh et al. 2016). Experiments have shown that exposure to cadmium is accompanied by a shift in the blood count toward myelopoiesis (Zhang et al. 2018), as well as hemolysis and insufficient production of erythropoietin (Semenova et al. 2020; Horiguchi et al. 2011).

There is evidence of chronic and acute exposure to As in the etiology of cancer, cardiovascular disease (hypertension and atherosclerosis), neurological disorders, gastrointestinal disorders, liver and kidney diseases, reproductive health effects, skin changes and other health disorders. The role of antioxidant defense systems against arsenic toxicity has also been discussed (Jomova et al. 2011).

Discussion

Dysregulation of Fe homeostasis

Dysregulation of Fe homeostasis and increased uptake and accumulation of ME in the reticuloendothelial system lead to the removal of the element from the blood into the cells of the reticuloendothelial system following a decrease in the availability of iron to erythroid progenitor cells and iron-limited erythropoiesis (Weiss et al. 2005). The acute phase protein hepcidin plays a key role in the development of anemia because it inhibits Fe absorption in the intestine. In addition, there is an increase in iron uptake by macrophages and a block in iron export from macrophages, mainly to the bone marrow. As a result, the concentration of iron in the blood decreases (with a normal total amount of iron in the body), which slows erythropoiesis and causes anemia (Roy et al. 2005). However, sometimes such a decrease in the concentration of iron in the serum can be beneficial, since it makes iron less available to microorganisms, inhibiting their growth (Bogun 2015). The iron level in the body is maintained by daily absorption of Fe with food to restore the loss of a similar amount of ME due to exfoliation of the mucous membrane and skin cells, bleeding and other losses.

The most common cause of iron deficiency is improper or unbalanced nutrition due to a limited set of products in the diet and a decrease in the ability of the intestine to absorb iron. Helminths have a negative effect on digestive processes, making it difficult, among other things, to absorb iron.

Iron deficiency can also be caused by the following factors:

- active growth;
- pregnancy (fetal needs);
- impaired absorption;
- blood loss;
- Drugs for the treatment of gastrointestinal diseases (antacids, proton pump inhibitors, H2 blockers).

Moreover, some substances weaken the absorption of Fe^{3+}:

- antibiotics;
- bran;
- vegetable phytofibers.

Iron intake into the body depends on the components of the animal's diet: absorption of feed of animal origin and organic acids improves whereas absorption of plant origin worsens (for example, owing to the presence of fiber). In mammals, the absorption of microelements occurs mainly in the duodenum, predominantly in the bivalent form. Enterocytes secrete mucosal apotransferin into the intestinal lumen, which is loaded with iron and then penetrates into the enterocyte. After penetrating the cell, transferrin transfers iron to its plasma analog. In the cytosol of the enterocyte, a certain amount of iron is included in phyritin, but most of it is lost when the cells of the mucous membrane are desquamated, and only a small part passes into the blood plasma. Before Fe is incorporated into ferritin or transferrin, ferrous iron is oxidized to ferric iron.

When comparing the data on the level of trace element concentration in the fur of red foxes with the data on fur farms in the Moscow Region, an increase in the concentration of all MEs in the fur coat of the sample was noted: Zn by 9.4; Cu by 4.6; Fe by 49.9; Pb by 33.0; Cd by 24.6; and As by 16.9 times (Staroverova et al. 2011). Differences

in the accumulation of pollutants may be associated with the age characteristics of the objects under study: the authors studied the characteristics of ME accumulation in the biosubstrates of foxes in the Moscow Region selected for analysis were only individuals under 12 months of age, whereas we studied the elemental status of the fur of adult sexually mature individuals over 3 years of age. When comparing the data from arctic foxes with those from fur farms in the Moscow Region, an increase in the concentration of the following MEs in the fur coat of the sample was noted: Zn by 5.3; Cu by 4.3; Fe by 14.1; and Cd by 2.1 and As by 24.0 times (Staroverova et al. 2011). The Pb levels in the compared samples did not differ. Differences in the accumulation of pollutants may be associated with the age characteristics of the objects under study: the authors studied the characteristics of the accumulation of MEs in the biosubstrates of arctic foxes in the Moscow region selected for analysis were only individuals under 12 months of age, and we studied the elemental status of the fur of adult sexually mature individuals over 2 years of age.

The average level of zinc accumulation in the studied sample of wolves was 174.03±48.04 mg/kg, that of copper was 9.74±2.13 mg/kg, that of iron was 237.07±26.35 mg/kg, that of lead was 11.79±3.03 mg/kg, that of cadmium was 0.19±0.09 mg/kg and that of arsenic was 0.39±0.06 mg/kg. The Cu content in wolf fur is 1.51 times greater than that in the liver of this animal species living in Croatia (Berglund et al. 2011). The average level of zinc accumulation in the studied sample of European wolves was 103.42±31.84 (73.86–132.48) mg/kg, that of copper was 4.69±1.98 (0.13–9.39) mg/kg, that of iron was 415.37±36.48 (133.69–702.85) mg/kg, that of lead was 8.22±1.47 (4.71–11.24) mg/kg, that of cadmium was 0.58±0.07 (0–1.31) mg/kg, and that of arsenic was 0.09±0.01 (133.0004–0.18) mg/kg. When the results obtained in this study were compared with the data on the elemental composition of wolf fur from natural habitats, an increase in the concentration was established: Zn, 20.4; Cu, 1.96; Pb, 4.22; and Cd, 1.98, a decrease in As of 7.33 times. Differences in the level of accumulation of elements are associated with the maintenance of the studied wolves in conditions of the greatest anthropogenic pollution under the conditions of regional centers and a megalopolis (Bondarev 2012).

No reliable literature data were found on other studied animal species from zoological institutions (available to us).

Comparison of cardiovascular disease incidence in domestic and wild animals

Among domestic animals, the largest proportion of the development of cardiovascular diseases was observed in dogs—65.5% (from 64.9% to 66.2% depending on the year of the study). In cats, CVD accounts for 34.5% of cases (from 35.1% to 33.8% depending on the year of study) (Kuryatova et al. 2016). The proportion of dead animals is also greater in dogs than in cats: 39.7% (34.3% -46.8%) versus 36.3% (28.8%-43.7%) of cases. Chronic heart failure remains the leading cause of death in dogs.

In recent work (Lakhdhir S. et al. 2020), numerous methods have been used to study the development of myocarditis in dogs of various etiologies: "64 (presumed antemortem diagnosis) and 137 (postmortem diagnosis only) dogs" of various races were treated at U.S. tertiary care facilities (Lakhdhir S. et al. 2020). Importantly, "cardiac troponin I (cTnI) concentrations > 1.0 ng/ml can support a diagnosis of myocarditis in conjunction with other proposed diagnostic criteria" (Lakhdhir S. et al. 2020).

The share of cardiovascular diseases among diseases of noncommunicable etiology varies depending on the region and year of the study. For example, among cats in Moscow, the proportion of CVD in Korobova's studies ranged from 2–3% to 10–12% (Korobova 2023), whereas in Irkutsk, it was 35.5% (Sakharovsky et al. 2014). In dogs, the proportion of cardiovascular diseases ranged from 10.0% in Moscow to 15.6% in Tyumen (Kozlovskaya 2013). An analysis of CVD distribution (recorded among domestic animals) revealed that the highest percentage of incidence in dogs with valvular endocardiosis ranged from 39.2% in Blagoveshchensk to 55.4% in Tyumen and that of cardiomyopathy ranged from 32.4% to 38.3% (Kuryatova et al. 2016, Kovalenko et al. 2020).

In a recent work (Romito G. et al. 2023), "transient myocardial thickening (TMT)" in cats was studied. TMT is a poorly characterized clinical entity. In general, TMT most commonly occurs in young cats with "left atrial (LA) dilation and dysfunction" and increased "cTnI associated with congestive heart failure" (Romito G. et al. 2023). The authors reported that proper treatment typically leads to the "resolution of clinical, laboratory, and echocardiographic abnormalities in a relatively short period of time" (Romito G. et al. 2023).

Experimental evidence suggests that oxidative stress is involved in pathological vascular and valve calcification over a long period of time (Mercier et al. 2020; Cui et al. 2020), which is triggered by iron (which leads to calcification of blood vessels and valves). Previous studies have shown that intraleaflet hemorrhage is associated with the progression of valve calcification, and iron deposition is observed within calcified valves. Interestingly, iron deposition can also be found in noncalcified valves, suggesting that iron deposition occurs before calcium deposition at sites of valve calcification (Morvan et al. 2019). Valvular iron accumulation has been observed in calcified human aortic valves and is positively correlated with the degree

of calcification (Laguna-Fernandez et al. 2016). In addition, a significant decrease in the expression of the iron exporter was observed in differentiated cells induced by tumor necrosis factor-α and transforming growth factor-β, as well as in cells isolated from stenotic aortic valves. In the presence of ferrous sulfate, cells expressed increased amounts of ferritin subunits and exhibited the ability to proliferate (Laguna-Fernandez et al. 2016).

In addition, iron holotransferrin may promote aortic calcification through the activation of interleukin-24 (Kawada et al. 2018). Some indirect evidence supports a link between iron accumulation and the progression of atherosclerosis (Stanley et al. 2006; Cai et al. 2020). Congenital heart pathologies in dogs account for 2.5% to 9.8% of cases. (Kuryatova et al. 2016; Kozlovskaya et al. 2013). The incidence of myocarditis and myocardial infarction was 5.8% of all patients. The incidence of neoplasia in dogs ranges from 2.1–8.2% of the total number of affected dogs (Kuryatova et al. 2016; Kozlovskaya et al. 2013).

Among cardiovascular diseases in cats, the incidence of cardiomyopathy is the highest, ranging from 52.0% to 67.0% (Kuryatova et al. 2016; Cai et al. 2020). Congenital heart pathologies account for 16.2% of sick animals. The incidence rates were slightly lower for arterial hypertension (10.4%) and coronary heart disease (7.1%).

Dietary iron restriction also prevents the development of hypertension and renal fibrosis in mice with aldosterone/salt-induced hypertension (Li et al. 2021; Weiss et al. 2005; Roy et al. 2005; Bogun 2015). These data suggest that the dysregulation of iron metabolism may be an important independent risk factor for hypertension. However, detailed mechanistic information on the role of iron in systemic hypertension is lacking. Early studies confirmed that high levels of iron are mobilized into the coronary circulation after prolonged ischemia and that cardiac cytosolic iron levels are increased in ischemic rat hearts (Li et al. 2021). However, these results were not replicated for the other animals; further studies are needed to test the potential clinical implications of this therapeutic strategy.

Conclusion

The iron levels in the fur of the animals with cardiac issues were lower than those in the fur of the healthy animals in the present study. The other findings of our study were connected with the evaluation of the Fe levels in animals in comparison with the other ME levels because of the important interactions between the studied MEs (Fe, Zn, Cu, Pb, Cd and As). Thus, 108 and 63 samples from 171 animals were taken for analysis from canine (nine species) and feline (seven species) families, respectively, at Russian zoos. A total of 10.1% of all CVD cases occurred in the studied animals. Fe accumulated in canine and feline fur at approximately 208 and 203 mg/kg (variations of 72.8% and 80.9%, respectively). A direct correlation was established, indicating synergism in ME accumulation in fur among all the studied elements. A significant decrease in Fe and an increase in Cd by CVD were detected ($r = 0.25$ and $r = 0.16$, respectively, with $p < 0.05$). The dysregulation of Fe homeostasis and increased absorption and accumulation of Fe in the reticuloendothelial system are discussed. Finally, the MEs adsorbed by canine and feline fur can be arranged in the following descending order: Fe > Zn > Cu > Pb > Cd > As. Thus, the study revealed that iron levels in the fur of animals with heart problems were lower than those in healthy animals. This finding raises the possibility of direct correlations between iron deficiency and heart disease in animals.

Methods

Materials

There were 171 animals of the canine and feline families chosen (from the 1206 wild and exotic animals in total) for this study on the basis of a retrospective analysis of records entered in the animal registers. Moreover, only species of wild and exotic mammals of the canine and feline families were selected; these species were maintained at zoological institutions in areas with various "technogenic loads" in the Central Federal District (Moscow, Ivanovo and Yaroslavl zoos).

The work was carried out *via* a comprehensive approach involving a combination of modern environmental, biochemical and statistical methods in areas with different technogenic loads. In a highly urbanized metropolis — the city of Moscow, which is located in the Presnensky district of the Central District — the most industrially developed territory, where there are many industries (plants, factories, etc.) and business centers, in the Yaroslavl region, the Zavolzhsky district of the city of Yaroslavl was studied—a large industrial and transport center characterized by a high anthropogenic load on the atmosphere, surface water bodies and soil cover, with a developed oil refining, chemical, mechanical engineering and heat power complex (there is a waste incineration plant in the district) and the Frunzensky district of the city of Ivanovo — a regional center with a satisfactory environmental situation and a developed textile industry, poor environmental condition of natural water bodies.

Numerous samples from 128 healthy and 43 sick animals (171 total animals) from three Russian zoos were collected and studied.

In the canine family, a study of the ME content in the hair of 9 animal species (subspecies) was carried out: the "ordinary" fox *Vulpes vulpes* ($n = 18$), the fennec

fox *Vulpes (Fennecus) zerda* ($n=6$), the "silver" fox *Alopex lagopus var. dom.* ($n=12$), "Alaskan malamute" *Canis familiaris* ($n=12$), polar wolf – *Canis lupus tundrorum* ($n=6$), "ordinary" wolf – *Canis lupus* ($n=18$), black wolf – *Canis lupus pambasileus* ($n=12$), red wolf – *Cuon alpinus* ($n=9$), and raccoon dog – *Nyctereutes procyonoides* ($n=15$). In total, 108 samples were taken from canine animals in the family, and 648 ME measurements were performed.

In the feline family, seven species were studied: lynx – Felis (Lynx) lynx ($n=15$), puma – Puma (Felis) concolor ($n=9$), snow leopard (Irbis) – Uncia (Panthera) uncial ($n=6$), Far Eastern (Amur) leopard – Panthera pardus orientalis ($n=9$), Amur tiger – Panthera tigris altaica ($n=12$), lion (white variation) Pantera leo var. alba ($n=6$), and lion – Panthera leo ($n=6$). Sixty-three samples were taken, and 378 ME measurements were performed.

Noninvasive, stress-free methods of biomaterial selection were used in this work.

The selected animal species for the study were kept at many zoological institutions, including those under study. Some of these species are of commercial importance (common foxes and arctic foxes), others are conserved (fennec, wolf, snow leopard, Far Eastern (Amur) leopard, Amur tiger, lion), and some are invasive in certain territories of the Russian Federation (raccoon dog). All animals of the abovementioned species kept at the zoological institutions under study were examined. The sample is representative even at the scale of zoos, members of the European Association of Zoos and Aquaria (EAZA, https://www.eaza.net/about-us/eaza/), since 6.3%—19.7% of the samples of the zoo animal population of the studied species were selected.

A sample of fur weighing from 1 to 3 g was taken from a 1 cm^2 area of the animal's back skin located below the projection of the shoulder blades. The samples taken in this way were placed in special envelopes, which were then sealed and labeled with the animal's species, sex, year of birth, and date of sampling.

The fur was subsequently cleaned in the laboratory as follows.

1. The samples were placed in glass containers with a ground-in lid.
2. The samples were filled with acetone at a volume ratio of 1:3 (sample: acetone) with constant stirring for 10 min.
3. The fur was then incubated in acetone for 24 h.
4. After the fur was mechanically cleaned, the sample was repeatedly (several times) washed with distilled water and dried again for 12 h to determine the dry weight of the sample before analysis.

After preparation, the length of the hair formed in a certain age period was determined, reflecting the level of metabolic processes of chemical elements in a similar age interval, taking into account the date of sample collection. The hair collected from the animal, taking into account the established average regrowth rate, was divided into sections corresponding to distal regrowth for the winter and summer periods.

Distal regrowth for each area was calculated via the following formula:

$$L = S \times I,$$

where L is the distal distance measured from the hair root, mm;

S is the hair growth rate, mm/day;

I is the age period under study, days.

Fur samples were subjected to acid mineralization under elevated pressure. The following solutions were used in the study: concentrated nitric acid, an aqueous solution of at least 65% mass fraction, with a density of approximately 1.4 g/cm^3; concentrated hydrogen peroxide, an aqueous solution of at least 30% mass fraction; and concentrated hydrochloric acid, an aqueous solution of at least 30% mass fraction, with a density of approximately 1.15 g/cm^3 (Russian GOST 10929–76 https://docs.cntd.ru/document/1200017430). The duration of mineralization of the homogenized sample in the microwave devices ranged from 15–30 min, with increasing power from 100–1000 W. During sample mineralization in a heating block under elevated pressure, the sample was heated from room temperature to 300 °C for 190 min. After mineralization, the sample is cooled in a closed state to a temperature close to room temperature to reduce the pressure inside the vessel. Intermediate standard solutions of the elements are prepared by successive dilution of the stock solutions by 10 and 100 times using nitric acid with a mass fraction of 1%.

Standard solutions are prepared from intermediate solutions after their dilution with the same acid solution as the sample solutions. As a zero standard, a solution of nitric or hydrochloric acid with a mass fraction of 1% was used to dissolve samples and dilute standard comparison solutions in a given series of tests.

Preparation of the test solution. When dry ashing or acid extraction is used followed by ashing, the sol is dissolved in a crucible with nitric acid (1:1) by volume, which is calculated on the basis of 1–5 cm^3 of acid on the basis of the test, exclusively from the ash content of the product. The solution is brought to the state of wet salts through evaporation. The precipitate was dissolved in 15–20 cm^3 of nitric acid with a mass fraction of 1%, transferred to a 25 cm^3 measuring flask and brought to the mark with the same acid.

If the ash is not completely dissolved, the resulting solution with the precipitate is evaporated to wet salts, dissolved in a minimum volume of hydrochloric acid (1:1) by volume, boiled again to wet salts and dissolved in 15–20 cm^3 of hydrochloric acid with a mass fraction of 1%. The solution was quantitatively transferred to a 25 cm^3 measuring flask and brought to the mark with the same acid. If the sol still does not dissolve completely, the solution with the precipitate is brought to a volume of 30–40 cm^3 of hydrochloric acid with a mass fraction of 1% and heated in a water bath or electric stove at low heat for 0.5 h. Even after this complete dissolution did not occur, the solution was filtered through a filter prewashed with a solvent, the precipitate was washed and discarded, and the filtrate was transferred to a 50 cm^3 measuring flask and brought to the mark with the same acid. In this work, two main methods of atomic absorption spectrometry were used: electrothermal and flame methods (Stepanova 2021a).

The results of the analysis of each set are used to calculate the average concentrations of metals and other elements in the sample, as well as to determine the measurement error.

The obtained data on the actual concentration were converted into a mass fraction via formula (1):

$$w = \frac{aVd}{m} \quad (1)$$

where w is the mass fraction of the element being determined in the sample, mg/kg.

a is the actual concentration of the element being determined in the test solution, $mg/dm.^3$

V is the volume of the test solution, $cm^{3.}$

m is the sample weight, g.

d is the dilution factor.

Methods and instruments

The studies were carried out via a "Kvant-2A" atomic absorption spectrometer (Russia) according to the methods described in (Vilmis et al. 2023; Stepanova et al. 2023, 2019; Staroverova et al. 2021). The work was carried out on verified equipment in an accredited laboratory with daily calibration. Fur samples (1–3 g) of all types were taken from the whole body (Vilmis et al. 2023). All the samples were cleaned and degreased with acetone and water for two days. Then, wet acid ashing was carried out on an electric stove and then in a muffle furnace with a gradual increase in temperature from 250 °C to 450 °C with a half-hour exposure. The samples were assessed for the levels of the following microelements: Fe, Zn, Cu, Pb, Cd, and As. The correlation and regression analyses were carried out via MS Excel.

Three-dimensional echocardiography has been used primarily to assess and visualize cardiovascular diseases in animals (Mitrokhina 2022).

The obtained results were processed statistically. The arithmetic mean values (M), average errors (m) and standard deviations (δ) were determined. To identify statistically significant differences in the compared groups and the contingency between the features and the nature of the distribution of compatibility data, the nonparametric Shapiro–Wilk W criterion was used. To check the reliability of the differences between two samples, the Student and Fisher criteria were used, and several independent samples for one feature were compared via one-way variance analysis and nonparametric variance analysis via the Kruskal–Wallis criterion. To clarify the interdependence between two or more samples, regression analysis and Spearman's rank correlation coefficient were used. For all types of statistical analysis, a significance level of 0.05 was adopted. The databases used were "Microsoft Office Excel" 2010 and "Statistica" version 10.0 in the Windows XP environment (Stepanova 2021a).

Abbreviations

CVD	Cardiovascular disease
GOST	A normative legal document in Russia, in accordance with the requirements of which the standardization of production processes is carried out
MEs	Mineral elements

Acknowledgements

Not applicable.

Authors' contributions

Each author (M.V. Stepanova, L.F. Sotnikova, S.Yu. Zaitsev) has made substantial contributions to the conception and design of the work; the acquisition, analysis, and interpretation of data; has drafted the work or substantively revised it; has approved the submitted version and all substantially modified versions that involve the author's contribution to the study; has agreed both to be personally accountable for the author's own contributions and to ensure that questions related to the accuracy or integrity of any part of the work (even those in which the author was not personally involved), are appropriately investigated, resolved, and the resolution documented in the literature.

Funding

The work was supported by the Ministry of Higher Education and Science of the Russian Federation (project code FSMF-2022–0003) at Russian Biotechnological University (ROSBIOTECH).

Data availability

The datasets used and analyzed during the current study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate

The experimental protocols concerning these animals were approved by the special scientific council of the "Russian Biotechnological University (ROSBIOTECH)" (April 9, 2024; protocol No. 4; Moscow). All experiments and conditions (animal care, feeding, biological material sampling, etc.) were performed in accordance with the applicable regulations: internationally recognized guidelines (the revised Animals (Scientific Procedures) Act 1986 in the UK and Directive 2010/63/EU in Europe) and the Statement of the ROSBIOTECH Ethical Committee (April 9, 2024; protocol No. 4; Moscow).
There are no human participants, human data or human tissue in this manuscript.

Consent for publication
Not applicable.

Competing interests
The author declares that they have no competing interests.

Received: 19 July 2024 Accepted: 2 October 2024
Published online: 22 October 2024

References

Abbaspour, N., R. Hurrell, and R. Kelishadi. 2014. Review on iron and its importance for human health. *Journal of Research in Medical Sciences: The Official Journal of Isfahan University of Medical Sciences.* 19 (2): 164–174.

Alshinetsky, MV. 2013. *Some diseases of the gastrointestinal tract of cats.* In: Current veterinary problems in zoos. Proc. international seminar; 2012 Nov. 19–23; Moscow Zoo, Russia. Moscow: Zoo Publ. (Russ.).

Andrade, F.H., F.C. Figueiroa, P.R. Bersano, D.Z. Bissacot, and N.S. Rocha. 2010. Malignant mammary tumor in female dogs: Environmental contaminants. *Diagnostic Pathology* 5 (1): 45. https://doi.org/10.1186/1746-1596-5-45.

Antipov, A.A. 2010. Physiological and biochemical features and effects of interactions in the assimilation and metabolism of nutrients in agricultural poultry (review). *Problems of Biology of Productive Animals.* 2: 5–43.

Avtsyn, PA, Zhavoronkov, AA, Rish, MA, and LS. Strochkova. 1991. *Human microelementoses: etiopathology, classification, organopathology.* Moscow:Medicine "USSR Academy of Medical Sciences".

Balakirev, NA, Maksimov, VI, Staroverova, IN, Balakirev, AN, and SYu. Zaitsev. 2017. The biological role of minerals in cellular fur animal farming. Moscow:Agricultural Technologies Publishing House.

Bayurov, L.I., and K.D. Mikheeva. 2022. Properties of dog hair and possible ways of its use. *Polythematic Network Electronic Scientific Journal of the Kuban State Agrarian University.* 176: 16–35. https://doi.org/10.21515/1990-4665-176-002. Russ.

Berg, C., H. Lerner, A. Butterworth, and C. Walzer. 2020. Editorial: Wildlife Welfare. *Frontiers in Veterinary Science.* 7: 576095. https://doi.org/10.3389/fvets.2020.576095.

Berglund, A.M., M.J. Koivula, and T. Eeva. 2011. Species- and age-related variation in metal exposure and accumulation of two passerine bird species. *Environmental Pollution.* 159: 2368–2374. https://doi.org/10.1016/j.envpol.2011.07.001.

Boev, V.M., A. Lestsova, and N.M. Amerzyanova. 2002. Hygienic assessment of the content of trace elements in drinking water and food products in the system of social and hygienic monitoring. *Hygiene and Sanitation.* 5: 71–73 Russ.

Bogun, L.V. 2015. Anemia of chronic disease. *Bulletin of KhNU named after. V.N. Karazin. Medical series.* 29: 81–87 Russ.

Bondarev, A.Y.A. 2012. Toxicants in the organisms of the wolf and some other mammals of the Altai Territory. *Bulletin of the Altai State Agrarian University.* 91 (5): 44–49 Russ.

Cai, J., M. Zhang, Y. Liu, H. Li, L. Shang, et al. 2020. Iron accumulation in macrophages promotes the formation of foam cells and the development of atherosclerosis. *Cell Biosci.* 10 (1): 137. https://doi.org/10.1186/s13578-020-00500-5.

Chen, X., H. Zhou, X. Li, Z. Wang, G. Zhu, et al. 2015. Effects of lead and cadmium coexposure on hemoglobin in a Chinese population. *Environmental Toxicology and Pharmacology.* 39 (2): 758–763. https://doi.org/10.1016/j.etap.2015.02.005.

Cui, L., Q. Zhou, X. Zheng, B. Sun, and S. Zhao. 2020. Mitoquinone attenuates vascular calcification by suppressing oxidative stress and reducing apoptosis of vascular smooth muscle cells via the Keap1/Nrf2 pathway. *Free Radical Biology and Medicine.* 161: 23–31. https://doi.org/10.1016/j.freeradbiomed.2020.09.028.

Drozdova, E.A., and E.S. Aleshina. 2017. Effect of iron nanoparticles on blood biochemistry and nonspecific immunity indicators of agricultural poultry. *Russian Journal of Immunology.* 11 (2): 303–305.

Flora, G., D. Gupta, and A. Tiwari. 2012. Toxicity of lead: A review with recent updates. *Interdisciplinary Toxicology.* 5 (2): 47–58. https://doi.org/10.2478/v10102-012-0009-2.

Galaris, D., A. Barbouti, and K. Pantopoulos. 2019. Iron homeostasis and oxidative stress An intimate relationship. *Biochimica et Biophysica Acta (BBA)-Molecular Cell Research* 1866 (12): 118535. https://doi.org/10.1016/j.bbamcr.2019.118535.

Grigoriev, AN. 2009. *Distribution of chemical elements in the upper part of the continental crust.* Ekaterinburg: Ural Branch of the Russian Academy of Sciences. (Russ.).

Horiguchi, H., E. Oguma, and F. Kayama. 2011. Cadmium induces anemia through interdependent progress of hemolysis, body iron accumulation, and insufficient erythropoietin production in rats. *Toxicological Sciences.* 122 (1): 198–210. https://doi.org/10.1093/toxsci/kfr100.

Jomova, K., Z. Jenisova, M. Feszterova, S. Baros, J. Liska, et al. 2011. Arsenic: Toxicity, oxidative stress and human disease. *Journal of Applied Toxicology* 31 (2): 95–107. https://doi.org/10.1002/jat.1649.

Kawada, S., Y. Nagasawa, M. Kawabe, H. Ohyama, A. Kida, et al. 2018. Iron-induced calcification in human aortic vascular smooth muscle cells through interleukin-24 (IL-24), with/without TNF-alpha. *Scientific Reports.* 8 (1): 658. https://doi.org/10.1038/s41598-017-19092-1.

Kim, J., Y. Lee, and M. Yang. 2014. Environmental exposure to lead (Pb) and variations in its susceptibility. *Journal of Environmental Science and Health, Part C* 32 (2): 159–185. https://doi.org/10.1080/10590501.2014.907461.

Korobova, V.V. 2023. Results of an electrocardiographic study of HCM in cats of different ages. *Bulletin "Biomedicine and Sociology"* 8 (1): 67–72. https://doi.org/10.26787/nydha-2618-8783-2023-8-1-67-72. Russ.

Kovalenko, A.A., and O.A. Stolbova. 2020. Dilated cardiomyopathy in dogs. *Bulletin of the Buryat State Agricultural Academy named after VR Filippova* 4 (61): 58–64. https://doi.org/10.34655/bgsha.2020.61.4.009. Russ.

Kozlovskaya, N.G. 2013. Breed predispositions of dogs and cats to cardiac diseases. *Russian Veterinary Journal. Small domestic and Wild Animals* 6: 32–35 Russ.

Kuryatova, EV, and OA. Zhulikova. 2016. The spread of cardiovascular diseases among dogs and cats in Blagoveshchensk, Amur region. In: *Problems of animal science, veterinary medicine and animal biology in the Far East.* : Collection of scientific papers; Gogulov VA, editor. 2016; Blagoveshchensk, Russia. Far Eastern State Agrarian University. 81–85. Blagoveshchensk: Far Eastern State Agrarian University (Russ.).

Laguna-Fernandez, A., M. Carracedo, G. Jeanson, E. Nagy, P. Eriksson, et al. 2016. Iron alters valvular interstitial cell function and is associated with calcification in aortic stenosis. *European Heart Journal.* 37 (47): 3532–3535. https://doi.org/10.1093/eurheartj/ehw122.

Lakhdhir, S., A. Viall, E. Alloway, B. Keene, K. Baumgartner, and J. Ward. 2020. Clinical presentation, cardiovascular findings, etiology, and outcome of myocarditis in dogs: 64 cases with presumptive antemortem diagnosis (26 confirmed postmortem) and 137 cases with postmortem diagnosis only (2004–2017). *Journal of Veterinary Cardiology.* 30: 44–56. https://doi.org/10.1016/j.jvc.2020.05.003.

Li, S., and X. Zhang. 2021. Iron in Cardiovascular Disease: Challenges and Potentials. *Frontiers in Cardiovascular Medicine* 8: 707138. https://doi.org/10.3389/fcvm.2021.707138.

Liu, Z., Y. Yu, X. Li, A. Wu, M. Mu, et al. 2015. Maternal lead exposure and risk of congenital heart defect occurrence in offspring. *Reproductive Toxicology.* 51: 1–6. https://doi.org/10.1016/j.reprotox.2014.11.002.

López-Alonso, M., M. Miranda, P. García-Partida, A. Mendez, C. Castillo, and J.L. Benedito. 2007. Toxic and trace metal concentrations in the liver and kidney of dogs. *Biological Trace Element Research.* 116: 185–202. https://doi.org/10.1007/BF02685930.

Mercier, N., S.C. Pawelzik, J. Pirault, M. Carracedo, O. Persson, et al. 2020. Semicarbazide-sensitive amine oxidase increases in calcific aortic valve stenosis and contributes to valvular interstitial cell calcification. *Oxidative Medicine and Cellular Longevity.* 20 (1): 127–132. https://doi.org/10.1590/1806-9061-2017-0604.

Mitrokhina, N.V. 2022. *Methods of Laboratory Diagnostics*. Moscow: Veterinary Center of Pathomorphology and Laboratory Diagnostics of Dr. Mitrokhina N.V.

Montrose, L., C. Faulk, J. Francis, and D.C. Dolinoy. 2017. Perinatal lead (Pb) exposure results in sex- and tissue-dependent alterations in the DNA methylation of murine IAP transposons in adults. *Environmental and Molecular Mutagenesis.* 58 (8): 540–550. https://doi.org/10.1002/em.22119.

Morvan, M., D. Arangalage, G. Franck, F. Perez, L. Cattan-Levy, et al. 2019. Relationship of iron deposition to calcium deposition in human aortic valve

leaflets. *Journal of the American College of Cardiology* 73 (9): 1043–1054. https://doi.org/10.1016/j.jacc.2018.12.042.
Pacyna, J.M., and E.G. Pacyna. 2001. An assessment of global and regional emissions of trace metals to the atmosphere from anthropogenic sources worldwide. *Environmental Science.* 9: 269–298. https://doi.org/10.1139/a01-012.
Romito, G., A. Elmi, C. Guglielmini, H. Poser, C. Valente, P. Castagna, C. Mazzoldi, and M. Cipone. 2023. Transient myocardial thickening: A retrospective analysis on etiological, clinical, laboratory, therapeutic, and outcome findings in 27 cats. *Journal of Veterinary Cardiology.* 50: 51–62. https://doi.org/10.1016/j.jvc.2023.09.001.
Roy, C.N., and N.C. Andrews. 2005. Anemia of inflammation: The hepcidin link. *Current Opinion in Hematology.* 12 (2): 107–111. https://doi.org/10.1097/00062752-200503000-00001.
Sakharovsky, AV, and C. Ludypov. 2014. Analysis of diagnostic studies of the cardiovascular system in cats in Irkutsk. In: *Fundamental and applied research in veterinary medicine and biotechnology: Materials of the International Scientific and Practical Conference dedicated to the 80th anniversary of the Irkutsk State Agricultural Academy and the 10th anniversary of the first graduation of veterinarians*; 2014 Nov 10–11; Irkutsk, Russia. 121–125. Moscow: Pero Publishing House. (Russ.).
Sanchez, O.F., J. Lee, N.Y.K. Hing, S.E. Kim, J.L. Freeman, and C. Yuan. 2017. Lead (Pb) exposure reduces global DNA methylation level by noncompetitive inhibition and alteration of DNMT expression. *Metallomics* 9 (2): 149–160. https://doi.org/10.1039/c6mt00198j.
Semenova, A.V., O.F. Chernova, M.V. Gorbacheva, and T.V. Perfilova. 2020. Species diagnostic characteristics of wool fibers of representatives of the camelid family, as criteria for identifying textile material. *Design and technology.* 76 (118): 49–57 Russ.
Shah, F., T.G. Kazi, H.I. Afridi, N. Kazi, and J.A. Baig. 2011. Evaluation of status of trace and toxic metals in biological samples (scalp hair, blood, and urine) of normal and anemic children of two age groups. *Biological Trace Element Research.* 141 (1–3): 131–149. https://doi.org/10.1007/s12011-010-8736-8.
Shaikhiev, I.G., and K.I. Shaikhieva. 2015. Keratin-containing poultry waste as sorption materials for removing pollutants from aquatic environments. 1. Extraction of metal ions. *Bulletin of the Technological University.* 18 (2): 445–449 Russ.
Skalny, A.A. 2021. Comparative assessment of the informativeness of determining the content of chemical elements in blood serum, hair (wool), organs and tissues of experimental animals. *Problems of Biological, Medical and Pharmaceutical Chemistry* 24 (11): 54–61 Russ.
Stankovsky, AP, and LN. Kantaeva. 2000. *Birds of the Omsk region.* Omsk: Publishing House "Omsk State Pedagogical University".
Stanley, N., N. Stadler, A.A. Woods, P.G. Bannon, and M.J. Davies. 2006. Concentrations of iron correlate with the extent of protein, but not lipid, oxidation in advanced human atherosclerotic lesions. *Free Radical Biology and Medicine.* 40 (9): 1636–1643. https://doi.org/10.1016/j.freeradbiomed.2005.12.031.
Staroverova, I.N., S.V. Pozyabin, V.I. Maksimov, SYu. Zaitsev, N.A. Balakirev, and A.A. Deltsov. 2021. Relationship of dielectric properties of the hair cover with its morphophysiological and biochemical characteristics in farmed fur-bearing animals. *Agricultural Biology.* 56 (4): 809–818 Russ.
Staroverova, IN. 2011. Features of the skin and hair cover of fur animals (minks, arctic foxes, foxes) in postnatal ontogenesis. D. Sc. Thesis, Moscow SAVMB (2021) (Russ.). Available online at: https://mgavm.ru/nauka/dissertatsionnye-sovety/d_35_2_023_01/.
Stepanova, M.V. 2021. Determination of the content of chemical elements in the feathers of the pink flamingo Phoenicopterus ruber roseus as a method for assessing the health status. *Bulletin of the APK of the Upper Volga region.* 53 (1): 44–51. https://doi.org/10.35694/YARCX.2021.53.1.008.
Stepanova, M.V., A.V. Timakov, and N.G. Yarlykov. 2019. Nosological profile of noncontagious diseases of wild animals in a zoo. *Veterinary doctor (Kazan).* 5: 45–53 Russ.
Stepanova, M.V., L.F. Sotnikova, and SYu. Zaitsev. 2023. Relationships between the Content of Micro- and Macroelements in Animal Samples and Diseases of Different Etiologies. *Animals* 13: 852. https://doi.org/10.3390/ani13050852.
Stepanova, MV. 2021a. *Content of heavy metals and arsenic in the environment and biosubstrates of wild and exotic birds and mammals in zoos*. D. Sc. Thesis, Moscow SAVMB (2021) 477 p. (Russ.). Available online at: https://mgavm.ru/nauka/dissertatsionnye-sovety/d_35_2_023_01/.
Suh, Y.J., J.E. Lee, D.H. Lee, H.G. Yi, M.H. Lee, et al. 2016. Prevalence and relationships of iron deficiency anemia with blood cadmium and vitamin D levels in Korean women. *Journal of Korean Medical Science* 31 (1): 25–32. https://doi.org/10.3346/jkms.2016.31.1.25.
Vilmis, DA, Sotnikova, LF, Melikova, YN, Stepanova, MV, Zaitsev, SYu, Kolomietch, SN, et al. 2023. Pathogenetic features and ways of correcting ophthalmopathies associated with paraneoplastic syndrome in animals. ROSBIOTECH, 84–119. Moscow: ROSBIOTECH.
von Haehling, S., N. Ebner, R. Evertz, and S.D. P. Ponikowski Anker. 2019. Iron deficiency in heart failure: An overview. *JACC Heart Fail.* 7 (1): 36–46. https://doi.org/10.1016/j.jchf.2018.07.015.
Weiss, G., and L.T. Goodnough. 2005. Anemia associated with chronic disease. *The New. England Journal of Medicine.* 352 (10): 1011–1023. https://doi.org/10.1056/NEJMra041809.
Wu, X., Y. Li, S. Zhang, and X. Zhou. 2021. Ferroptosis as a novel therapeutic target for cardiovascular disease. *Theranostics.* 11 (7): 3052–3059. https://doi.org/10.7150/thno.54113.
Zaitsev, SYu. 2017. *Biological chemistry: from biologically active substances to organs and tissues of animals*. Moscow:ZAO "Capital Print".
Zhang, T., J. Liu, J. Zhang, N. Zhang, X. Yang, et al. 2018. Effects of dietary zinc levels on growth performance, organ zinc content, and zinc retention in broiler chickens. *Rev. Bras. Cienc. Avic.* 20: 127–132. https://doi.org/10.1590/1806-9061-2017-0604.
Zhao, L., M. Cui, and FFu. Zhen. 2024. Focus on pet diseases. *Animal Diseases.* 4: 25. https://doi.org/10.1186/s44149-024-00132-z.

Publisher's Note