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Review

Secrets of the Astute Red Fox (*Vulpes vulpes*, Linnaeus, 1758): An Inside-Ecosystem Secret Agent Serving One Health

Andreia Garcês [1,2,*] and Isabel Pires [3]

1 INNO—Veterinary Laboratory, Rua Cândido de Sousa, 15, 4710-503 Braga, Portugal
2 Cooperativa de Ensino Superior Politécnico e Universitário, CRL-CESPU, Rua Central Dada Gandra, 1317, 4585-116 Gandra, Portugal
3 CECAV, University of Trás-os-Montes and Alto Douro, Quinta de Prados, 5000-801 Vila Real, Portugal; ipires@utad.pt
* Correspondence: andreiamvg@gmail.com; Tel.: +35-19-1851-0495

Abstract: An ecosystem's health is based on a delicate balance between human, nonhuman animal, and environmental health. Any factor that leads to an imbalance in one of the components results in disease. There are several bioindicators that allow us to evaluate the status of ecosystems. The red fox (*Vulpes vulpes*, Linnaeus, 1758) has the widest world distribution among mammals. It is highly adaptable, lives in rural and urban areas, and has a greatly diverse diet. Being susceptible to environmental pollution and zoonotic agents, red foxes may act as sentinels to detect environmental contaminants, climatic changes and to prevent and control outbreaks of emerging or re-emerging zoonosis. This paper aims to compile the latest information that is related to the red fox as a sentinel of human, animal, and environmental health.

Keywords: *Vulpes vulpes*; sentinel; bioindicator; health; contaminant; pollution; zoonosis; antibiotic resistance

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1. Introduction

The red fox (*Vulpes vulpes,* Linnaeus, 1758) is the medium-size canid with the widest world distribution [1]. This species is present throughout the northern hemisphere and regions of North Africa and has been introduced into Australia, where it is considered a plague [1,2]. It is listed as least concern by the International Union Conservation of Nature (IUCN), and in some countries is hunted by its fur and meat [1]. It is highly adaptable to local environmental conditions so that this animal can be found in urban, suburban, and rural areas. Red foxes live in small family groups and are more active at night [2]. They are opportunist predators who can adjust their diet to seasonal and local availability. Their heterogeneous diet can include fruits, invertebrates, small mammals, birds, and even rubbish [2,3]. Their main predators are large carnivores (e.g., wolves, bears), large birds of prey (e.g., golden eagles), and humans [2,4]. The major cause of the admission of these animals to wildlife rehabilitation centers is traffic accidents and poisoning [5,6]. Foxes also harbor a number of pathogens, including some zoonotic [2].

Because the red fox is one of the most widely distributed wild mammals, feeds on a broad range of food resources, and lives in close contact with humans, it has been proposed as a sentinel species in several studies (Figure 1). A sentinel species is used to detect and monitor the presence and effects of contaminants in the animals introduced or living in their habitat [3,7,8]. It also allows the identification of threats, namely infectious agents (e.g., viruses, bacteria), or other anthropogenic hazards, that represent a risk to the fauna and flora of the ecosystem and potentially to humans [9].

A sentinel species, in a One Health context, can give us the tools to predict environmental changes and disease outbreaks. As a result, early actions could be taken to prevent catastrophic consequences, as we saw in the case of the COVID-19 pandemic. Thus, the aim of this work is to compile the studies that use the red fox (*V. vulpes*) as a sentinel species.

Figure 1. Red fox (*Vulpes vulpes*) as bioindicator sentinel of environmental ecosystem health: zoonotic diseases, environmental contamination, antibiotic resistance and climate changes.

2. Material and Methods

To produce this review, we conducted a literature search through the main web search engines, which included Google Web, Google Scholar, Web of Knowledge, ResearchGate, and PubMed, as well as in the more relevant ecological ecology, chemistry, veterinary, and similar themed journals. To collect articles related to red fox (*V. vulpes*) as environmental sentinel bioindicators, our search terms included combinations of fox, red fox, *Vulpes vulpes*, bioindicator, environmental sentinel, one health, pollution, toxics, antimicrobial resistance, environmental contaminants, heavy metals, disease, poison, morbidity, mortality, persistent organic pollutants, zoonosis, infectious diseases, parasites, organochlorides. As inclusion criteria, only works that describe information regarding *Vulpes vulpes* as environmental sentinels were included.

3. Results Obtained from the Consulted Papers

Overall, we analyzed a total of 112 research works published between the years 1963 to 2021. To facilitate the description of the studies, they were grouped under an integrated "One Health" vision, taking into consideration the main threats to environmental, human, and animal health.

3.1. Red Fox as a Sentinel of Environmental Contamination

Organochlorine pesticides, polychlorinated biphenyls (PCBs), polybrominated diphenyl ethers (PBDEs), and heavy metals are ubiquitous environmental contaminants that originated from human activities, such as agriculture, burning of fossil fuels, industrial activities, and transportation [3,10,11]. They are toxic and have the potential to persist in ecosystems. Due to high lipophilia, they can accumulate in the adipose tissues of vertebrates and biomagnify in food chains [10].

Foxes are significant elements in the food chain [12]. Carnivores, such as foxes, tend to have higher levels of polluting residues than herbivorous animals as a result of bioaccumulation effects between trophic levels. It is, therefore, necessary to trace the presence and the number of chemical substances, such as heavy metals and pesticides, in their tissues. Contaminants studies make it possible to understand the organic changes in the animal, but also the potential dangers for human health [13,14]. Contaminants' exposition, during long times and at low doses, can alter physiological processes (e.g., metabolism, hormonal changes), decrease animal body condition (e.g., small and weak animals), immunotoxic effects, decrease reproductive success (e.g., infertility, abortion, malformations), and can result in genotoxic and mutagenic effects (cancer) [8,15,16].

Table 1 presents the published works associated with environmental contaminants studies in *V. vulpes*. The majority of the studies (out of 35) were conducted in Europe (n = 34), with the largest number in Poland (n = 12) and Italy (n = 7). The research focused on wild foxes, with the exception of two cases where red foxes were raised on farms for fur [17].

With respect to the type of contaminant, 20 studies were performed on heavy metals, 14 on pesticides/PCBs/PBDEs, and one on radioactive compounds.

Research works on pesticides using the fox as a sentinel are more common for the Arctic fox than the red fox [18–22]. Acute toxicity probably appears to be more common in these animals than the non-lethal chronic effects of pesticides [2]. Indeed, accidental or deliberate poisoning by organochlorine pesticides, biocides, and rodenticides is one of the main causes of red fox admission to wildlife rehabilitation centers [23]. Contrary to expectations, since these animals live near farms and agricultural fields, the pesticides levels in red foxes' tissues seem to be low, and probably are not associated with adverse health effects. In a study performed in Germany, the investigation of samples from 1983, 1987, and 1991 showed a reduction in the levels of the highly chlorinated biphenyls 138, 153, and 180 [24]. A similar study conducted in Zurich showed a general reduction in exposure to PCBs, with lower levels of PCBs in samples obtained from 1999 to 2000 [25]. In Poland, the ΣPCBs (sum of PCBs: 28, 52, 101, 118, 138, 153, 180) levels in the liver and lungs were 389.99 ng/g and 110.57 ng/g of lipid weight [26]. In Italy, the investigators found in muscle concentrations of 20.2 µg g µ1 lipid in muscle and 7.2 µg g µ1 lb in adipose tissue [27]. While the levels were found to be low, ongoing studies are important for monitoring pesticides environmental pollution.

Several studies have been carried out to determine heavy metal concentrations (Cd, Cr, Cu, Fe, Mn, Ni, Pb, Zn) in red foxes. Mercury (Hg) is one of the most studied and presents variations according to the geographic location of the animals. Wild foxes living near water sources have naturally higher levels of mercury in their tissues, possibly as a result of feeding higher up the food chain [28]. Studies in Slovakia [14], Russia [14], Poland [29], and Spain [30] have shown toxic levels of mercury in red fox fever, which appear to increase with age. Wild foxes have elevated levels of mercury in their tissues, even in populations living in isolated areas as Alaska [28].

Fluoride ($F-$) pollution has been increasing over the last several decades. In excess, fluoride can cause toxic effects on living organisms, such as dental and bone fluorosis and bone tumors [7]. In Poland, two different studies detected concentrations from 176 to 3668 mg/kg dw in bone [7,31] and 230 and 296 mg/kg dw in mandibular first molars. The interpretation of these values reflects moderate fluoride contamination in the area and makes red foxes a promising sentinel to access industrial pollution [7,31,32].

The study of radioactivity was carried out in the Ukraine, where the Chernobyl nuclear accident occurred. Fox bones did not show a high level of contamination in comparison to the results obtained on the bones of small animals (rodents or insectivorous mammals) previously determined. This suggests that there is no accumulation of bone isotopes at the top of the food chain [33].

Table 1. Review of articles that evaluated environmental contaminates in red fox (*Vulpes vulpes*) regarding the number of animals substance type, year, sample type analyzed, country, the origin of the animals (wild or fur farm).

Substance	Number of Animals	Origin Animal	Sample	Country	Year	Reference
Cr, Cu, Ni, Pb, Zn	20	Wild and Fur farm	Hair and skin	Poland	2011	[17]
Cd, Cr, Cu, Fe, Mn, Ni, Pb, Zn	48	Wild	Small intestines	Czech Republic	2010–2011	[34]
Cd, Pb, Cu, Zn	87	Wild	Kidney and liver	Switzerland	1997–1998	[35]

Table 1. *Cont.*

Substance	Number of Animals	Origin Animal	Sample	Country	Year	Reference
Pb, Cd, Hg	30	Fur Farm	Kidney	Poland	2008	[36]
Cu, Ni, Zn, Co, Cd, Pb	10	Wild	Kidney	Hungary	2008	[37]
Hg	37	Fur farm	Hair and skin	Poland	2014	[17]
Hg, Pb, Cd, Cr, As	18	Wild	Liver, kidneys, and muscles	Slovak Republic	1998–1999	[12]
Cd, Pb, Zn	250	Wild	Kidney	Spain	2003–2011	[38]
Cd, Pb, Zn.	36	Wild	Kidney, liver and muscle	Poland	2002–2003	[39]
Hg	6	Wild	Liver and kidney	Russia	2007–2011	[14]
Al, Ca, Cr, Cu, Fe, Mg, Mn, Ni, Pb	56	Wild	Liver	Romania	May–September 2014	[40]
Hg	200	Wild	Liver, muscle, kidney, hair, bone	Alaska	2010–2011	[28]
Zn, Cu, Pb, Cd, Hg	30	Wild	Cartilage, compact bone, and spongy bone	Poland	2008–2009	[41]
Pb, Cu	42	Wild	Muscle and skin	Italy	2010	[13]
Cd, Pb, Cr, Cu, Zn, Mn, Ni	27	Wild	Intestine	Czech Republic	2009 to 2010	[42]
Hg	27	Wild	Liver, muscle, and kidney	Poland	2004–2006	[29]
Mn, Fe, Sr	38	Wild	Bone	Poland	2008–2009	[43]
Hg, Cd, Pb	46	Wild	Liver	Italy	1992	[30]
As, Cd, Cu, Pb, Hg	28	Wild	Liver, kidney and muscle	Croatia	2008–2009	[44]
Pb, Cd, Cr, Hg	Unknown	Wild	Heart, liver, diaphragm, kidney, muscle, and adipose tissue	Italy	1994–1995	[10]
PCB, DDE	Unknown	Wild	Heart, liver, diaphragm, kidney, muscle, and adipose tissue	Italy	1994–1995	[10]
PCB, Dieldrin, DDT, Endosulfan, HCB, Heptachlor	192	Wild	Perirenal adipose tissue, Kidney	Switzerland	1999–2000	[25]
PCB	80	Wild	Muscle	Germany	1983–1991.	[24]
PCBs, DDT	23	Wild	Adipose tissue	Italy	1991–1992	[3]
HCB, DDT, PBC	57	Wild	Muscle and adipose tissue	Italy	1992–1993	[3]
PBDEs	33	Wild	Adipose tissue, liver, and muscle	Belgium	2003–2004	[45]
HCB, DDT, PCB	36	Wild	Adipose tissues and muscle	Italy	1992	[30]
PCB	20	Wild	Liver, lungs	Poland	2008–2009	[26]
Aldrin, cis-chlordane, trans-chlordane, DDE, DDD, DDT, dieldrin, endosulfan, endrin, HCB, heptachlor, heptachlor-exo-epoxide, iso-drin, methoxychlor, mirex, PBC	18	Wild	Plasma, liver, and adipose tissue	Spain	2004–2006	[46]
Fluoride	32	Wild	Bone	Poland	2014	[32]

Table 1. *Cont.*

Substance	Number of Animals	Origin Animal	Sample	Country	Year	Reference
Fluoride	34	Wild	Teeth	Poland	Unknown	[31]
Fluoride	182	Wild	Mandible	Great Britain	Unknown	[31]
Fluoride	35	Wild	Teeth	Poland	2004/2005 and 2005/2006	[7]
90Sr, 238,239+240Pu, 241Am and 137Cs	183	Wild	Jaw bones	Poland	2008	[33]

Dichlorodiphenyltrichloroethane—DDT; Hexachlorobenzene—HCB, Polychlorinated biphenyls—PCB; Polybrominated diphenyl ethers—PBDEs; Dichlorodiphenyldichloroethylene—DDE; Dichlorodiphenyldichloroethane—DDD, Chromium—Cr; Copper—Cu, Nickel- Ni, Lead—Pb; zinc—Zn; Cadmium—Cd; Manganese—Mn; Mercury—Hg; Aluminum—Al; Calcium—Ca; Iron—Fe; Magnesium—Mg, Arsenic—As, Strontium—Sr; Americcium—Am; Caesium—Cs; Plutonium—Pu; Cobalt—Co.

3.2. Red Foxes as a Sentinel of Antimicrobial Resistance (AMR)

Antimicrobial resistance (AMR) is a major public health problem of modern times and has increased worldwide, not only in humans but also in animals, due to a continued spread of antimicrobial-resistant bacteria in the environment through different pathways [47,48]. The production of extended-spectrum b-lactamases (ESBLs) by Enterobacteriaceae, in particular by *Escherichia coli*, vancomycin-resistant Enterococci (VRE), Methicillin-resistant *Staphylococcus pseudointermedius* (MRSP), and Methicillin-resistant *Staphylococcus aureus* (MRSA) have been some of the main public health concerns in the last years [49,50].

Some red fox populations are urban and may therefore acquire antimicrobial-resistant bacteria directly from man and other animals or indirectly through reservoirs, such as food waste, garbage, sewage, and wastewater [47]. Consequently, the red fox can be a hopeful sentinel for monitoring the occurrence of AMR, providing a better understanding of resistance dynamics and factors [49,50].

The studies of AMR conducted in foxes are still scarce. *Escherichia coli* displaying carbapenem or colistin resistance was isolated in 387 out of 528 samples of wild red foxes evaluated in Denmark. In addition, the total occurrence of AMR was significantly higher in areas where the population density was higher [51].

In a Portuguese study, cefotaxime-resistant *E. coli* was isolated from 2 of the 52 fecal samples (4%), being both ESBL producers. The b-lactamase genes found in the two isolates were *blaSHV-12+blaTEM-1b*. The *tet (A)* and *sul2* genes were also detected in these isolates, together with the non-classical class 1 integrin (*intI1-dfrA12-orfF-aadA2-cmlA1- aadA1-qacH-IS440-sul3*) with the *PcH1* promoter [49]. In other study, 14 VRE were detected in 7 of 52 fecal samples (13.5%) [50,52].

In an investigation carried out in the United Kingdom, including 38 foxes (*Vulpes vulpes*) samples from rural and semirural areas, 35 presented isolates of coagulase-negative *Staphilococcus sciuri* group (35%), *S. equorum* (27%), and *S. capitis* (22%). All were phenotypically resistant to methicillin, and *mecA* was detected in 33 (89%) of the isolates and 10 (27%) showed broad b-lactam antibiotic resistance [53]. Resistance/intermediate resistance to at least one class of antibiotics and the highest resistance values were observed in the tetracycline class, with 33 strains being Multiple drug resistance (MDR). In another study, *Salmonella* spp. isolated from red foxes showed resistance/intermediate resistance to at least one class of antibiotics with the highest resistance values observed in the tetracycline class, with 33 strains being MDR [54].

3.3. Red Foxes as a Sentinel of Zoonotic Diseases

Animals could act as sentinels for the current health status in the ecosystem where they live. This status is an important parameter when evaluating pathogen spread and disease surveillance. The red fox is the main carrier and vector of the most important endemic zoonosis, including virus, bacteria, and parasites. In numerous regions, there has been an increase in red fox populations in recent years, particularly in urban areas. As a result, foxes live today in close contact with humans and their pets/livestock, and zoonotic agents they carry plays a major role in public health [54] Furthermore, the fact that these animals are scavengers, consuming the corpses in decomposition and look for food in wastes, leads them to spread certain diseases in the environment and to other vertebrates [2,55]. The importance of these animals as a reservoir of zoonotic diseases should be taken into account, particularly in frontier areas [55,56].

There is extensive literature describing the occurrence of diseases or the first detection of an etiologic agent in foxes in different countries. Although this list has continuously been updated, Table 2 describes the zoonotic agents reported in *V. vulpes*, according to the search terms used in this work (see material and methods).

Table 2. Zoonotic agents reported in red foxes (*Vulpes vulpes*).

	Infectious Agent	Reference
Parasites	*Cryptosporidium parvum, C. hominis*	[57,58]
	Babesia spp.	[59]
	Hepatozoon canis	[59]
	Giardia spp.	[58]
	Capillaria hepatica, C. aerophilia	[60]
	Leishmania infantum	[61,62]
	Trichinella spiralis, Trichinella britovi	[55,63]
	Toxocara canis, T. leonina, T. gondii	[60,63]
	Uncinaria stenocephala	[63]
	Thelazia callipaeda	[64]
	Mesocestoides lineatus	[34]
	Echinococcus granulosus, E. multilocularis	[55,60,63]
	Dipylidium caninum	[65,66]
	Alaria alata	[60]
	Linguatula serrata	[60,67]
	Ixodes spp.	[2]
	Sarcoptes scabiei	[68–70]
	Demodex folliculorum	[69]
	Rhipicephalus sanguineus sensu lato (s.l.).	[71]
	Notoedres spp.	[72,73]
Virus	*Lyssavirus*	[74,75]
	Puumala Hantavirus	[76]
	Picornaviridae	[77]
	Picobirnaviruses	[77]
	Astrovirus	[77]
	Hepeviridae	[77]
	Borna disease virus 1 (BoDV-1)	[78]
	Tick-borne encephalitis (TBE)	[79]
	Crimean-Congo hemorrhagic fever virus (CCHFV)	[80]
	LaCrosse virus (LACV) encephalitis	[81]
	Avian Influenza Virus (H5N1)	[82]
	Lymphocytic Choriomeningitis Virus (LCMV)	[83]

Table 2. *Cont.*

	Infectious Agent	Reference
Bacteria	*Leptospira interrogans, L. canicola, L. icterohaemorrhagica*	[83]
	Streptococcus spp.	[84–86]
	Salmonella spp.	[87]
	Coxiella burnetii	[54]
	Mycobacterium avium subsp. paratuberculosis, M. bovis, M. caprae	[88–91]
	Anaplasma phagocytophilum	[88,89,91,92]
	Borrelia valaisiana, B. burgdorferi s.l.	[93]
	Rickettsia conori	[94,95]
	Escherichia coli	[96]
	Brucella suis biovar 2, B. microti, B. vulpis	[97–100]
	Yersinia pseudotuberculosis, Y. pestis	[101–103]
	Listeria monocytogenes	[104]
	Ehrlichia canis	[71]
Fungi	*Microsporum* spp.	[105]
	Trichophyton spp.	[106]
	Pneumocystis carinii	[107]
	Blastomyces dermatitidis	[108]

Regarding parasitic diseases, the following parasites which may also affect humans have been described in foxes, namely *Cryptosporidium parvum*, *C. hominis*, *Babesia* spp., Hepatozoon canis, Giardia spp., Capillaria hepatica, *C. aerophilia*, *Leishmania infantum*, *Trichinella spiralis*, *Toxocara canis*, *T. leonina*, *T. gondii*, *Uncinaria stenocephala*, *Thelazia callipaeda*, *Mesocestoides lineatus*, *Echinococcus granulosus*, *E. multilocularis*, *Dipylidium caninum*, *Alaria alata*, *Linguatula serrata*, *Ixodes* spp., *Sarcoptes scabiei*, *Demodex folliculorum*, *Rhipicephalus sanguineus* s.l., *Notoedres* spp. Therefore, red foxes can be an important reservoir of many endoparasites and ectoparasites, as shown in the following studies. Epidemiological studies conducted in Slovakia on trichinellosis revealed a prevalence of *T. britovi* ranging from 2.3% to 16.3% [109]. In Switzerland, studies of foxes estimated by camera trapping have shown a prevalence of *Sarcoptes scabiae* mange between 0.1% and 12% over the 2005-2018 period [110]. Therefore, contamination of the soil with parasitic eggs in recreational areas where these animals can access should be considered [63,65,110].

The importance of identifying parasitic foxes in a One Health context is also linked to their role in the spread of vector-borne diseases. The fox is parasitized by many ticks of various species, some of which carry several zoonotic vector agents [94]. An example is *Ixodes ricinus,* one of the carriers of tick-borne encephalitis virus (TBE) [79]. This virus, belonging to the genus Flavirus, causes Tick-borne encephalitis, an important zoonosis that courses with meningitis or meningoencephalitis and can leave serious neurological sequelae in human patients [79]. *Ixodes ricinus* may also be a carrier for *Borrelia burgdorferi s.l.* (the agent of Lyme diseases). *B. burgdorferi s.l.* was detected in foxes from all over Europe. On a survey in Serbia, *B. burgdorferi s.l.*, *Borrelia lusitaniae,* and *Borrelia garinii* were detected in 6 (4.7%), 1 (0.8%), 2 (1.6%), and 1 (0.8%) of animals, respectively [111]. *Ixodes* spp. are also vectors of other zoonotic pathogens, such as *A. phagocytophilum.* Surveys carried out in Europe found prevalence rates of 16.6% in Italy [112].

Among viruses, the following agents have been described in red foxes: *Lyssavirus*, *Puumala Hantavirus*, *Picornaviridae*, *Picobirnaviruses*, *Astrovirus*, *Hepeviridae*, *Borna disease virus 1 (BoDV-1)*, *Tick-borne encephalitis (TBE)*, *Crimean-Congo hemorrhagic fever virus (CCHFV)*, *LaCrosse encephalitis virus (LACV)*, *Lymphocytic Choriomeningitis Virus (LCMV)*, *Avian Influenza Virus (H5N1)*, and *Influenza A virus*.

Rabies (caused by the *Lyssavirus* virus) is one of the world's deadliest and oldest zoonoses, killing 59,000 people annually, mainly in developing countries. While many Western European countries are now free of the virus, the disease remains endemic in Eastern Europe. The red fox is the main wildlife carrier of rabies in Europe [113]. There are virus variants known to circulate within determined species groups (e.g., fox rabies circulates only in the fox population and the dog rabies on dogs, etc.), and those variants tend not to be sustained outside of that group [74,114]. There is, however, sometimes spill-over between closely related hosts, for example, dogs and foxes [61]. Eradication in some countries has been achieved through the elimination of infected foxes and vaccination (baits containing vaccine capsules). In addition, the control and elimination of rabies in domestic dogs have a huge role in stopping the spread of rabies in fox populations [113]. Therefore, it remains to be seen whether outbreaks arise if the number of immune animals drops. This is particularly important in areas where neighboring countries are free of the disease. Greece, for instance, has been declared rabies-free since 1987, but in 2012 a red fox was found in a Greek village (Palaiokastro). This animal was native to one of the neighboring countries, probably Albanian that still has rabies in wild and domestic animals [74,75,114].

In respect to zoonotic bacteria, the following agents have been found in *V. vulpes*: *Leptospira interrogans*, *L. canicola*, *L. icterohaemorrhagica*, *Streptococcus* spp., *Salmonella* spp., *Coxiella burnetii*, *Mycobacterium avium* subsp. *paratuberculosis*, *M. bovis*, *M. caprae*, *Anaplasma phagocytophilum*, *Borrelia valaisiana*, *B. burgdorferi s.l.*, *Rickettsia conori*, *Escherichia coli*, *Brucella suis biovar 2*, *B. microti*, *B. vulpis*, *Yersinia pseudotuberculosis*, *Y. pestis*, *Ehrlichia canis* and *Listeria monocytogenes*.

Salmonella spp., for example, was detected within *V. vulpes*. in northwestern Italy, between 2002 and 2010, in 29 (5.70%) among 509 red foxes. Thirty-one strains belonging to several serotypes were isolated, and *S. typhimurium* was the most common serotype found [54].

Brucella spp. and *Mycobacterium* spp. were also isolated in red foxes' samples. Although the impact on their health is considered low, foxes should be regarded as a potential reservoir of these agents, and their interaction with livestock animals may justify the failure of eradication schemes [111,112]. *Brucella suis biovar 2, B. microti*, and *B. vulpis* have been isolated from wild red foxes in Austria, Poland, Bulgaria, and Russia [97,98,100,103]. *Mycobacterium bovis* has been reported in foxes from France, Portugal, and Spain [88,91,92]; *M. caprae* in Austria [89], and *M. avium* in foxes from Portugal [90].

C. burnetii, the zoonotic agent of Q Fever, has a 41.2% seroprevalence in the population of UK foxes [115]. In Spain, 2/12 foxes tested positive *C. burnetii* in PCR tests [116]. Surveys carried out in Europe found prevalence rates ranging from 0% to 8.2% for *A. phagocytophilum* and from 0% to 52% for *E. canis* [93,112,117,118].

Fox fungi may also be etiological agents in human diseases. One of the examples is *Blastomyces dermatitidis.* Blastomycosis is a life-threatening disease that affects people, canids, and other mammals. The behavior of foxes makes them potential sentinels of blastomycosis. Their close contact with the ground during digging and denning can increase exposure to fungal conidias and their inhalation. Furthermore, red fox dens are often dug in sandy and acidic soils, a condition that, with humidity, can promote fungal growth. Red foxes could be important sentinels for identifying geographical areas with the presence of the fungus in the soil [119].

Figure 2 illustrates some examples of zoonosis observed in red foxes during necropsy at the University of Trás-os-Montes e Alto Douro (Vila Real, Portugal).

3.4. Red Fox as Sentinel of Climatic Changes

Other anthropogenic impacts are more challenging to quantify in the short- and medium-term, such as the impact of climate change. Studies on sentinel animal populations may provide important data that highlight the effects of climate change on habitats, food webs, and population decline or growth that could affect biodiversity and species survival.

By interacting with various players in the ecosystem, changes in the red fox population may affect the structure and functioning of the ecosystem and play an important role in the food chain because of its predation activities. Being so, the red fox could serve as a sentinel in particular cases [3,9,120]. One of the impacts of climate change on the Arctic is related to the geographic distribution of Red fox populations with respect to the Arctic fox. Red foxes moved north due to global warming that transforms tundra into bushes. The red fox is a dominant competitor with Arctic foxes and could compromise their survival [121].

Red foxes are susceptible to certain diseases whose prevalence and duration are responsive to climate change. Studies carried out in these animals, in a dynamic perspective, could predict the evolution of these diseases in other animals and humans [122].

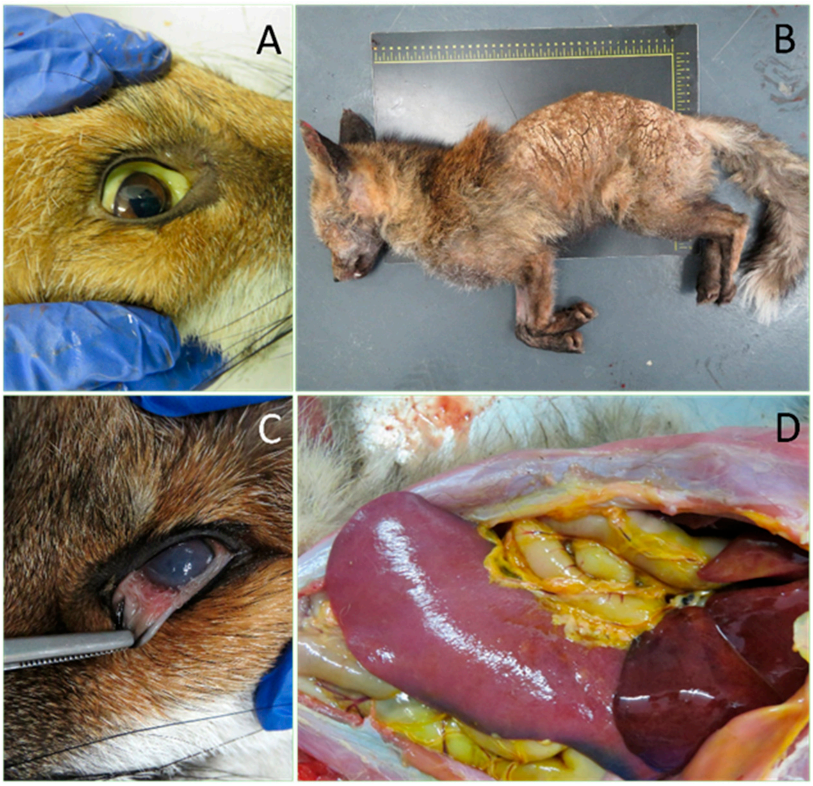

Figure 2. Zoonotic diseases in red foxes: (**A**) Icteric mucosa due to Leptospirosis; (**B**) Cutaneous lesions in sarcoptic scabies (**C**) Presence of eyeworms *Thelazia* spp.; (**D**) Enlarged spleen due to Leishmanio-sis.

4. Conclusions

This review indicates that the red foxes (*V. vulpes*) are undoubtedly important biological indicators of environmental health. In this review, we presented some of the most important agents reported in this species, but many more are present, and some have not been reported at the moment. As foxes are very adaptable, they have become one of the most urban species and therefore excellent models for understanding the health status of ecosystems to which humans belong. Their role as a zoonosis sentinel is even more important today with the emergence of new pandemics that, in most cases, have originated in wildlife. Nevertheless, there are still significant knowledge gaps, as these animals are often forgotten and neglected in wildlife epidemiological surveillance and disease control. In the future, it will be important to develop One Health projects that include the red fox as a sentinel for environmental pollution, zoonosis, climate change, and other anthropogenic threats. Under the One Health system, we can identify threat factors, understand their impact, establish measures to prevent or minimize their consequences and predict the appearance or re-emergence of diseases in the different ecosystems. Listening to what the fox says may be one more way to preserve life on earth

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