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

Andréia Garcês\textsuperscript{1,2,*} and Isabel Pires\textsuperscript{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 (\textit{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: \textit{Vulpes vulpes}; sentinel; bioindicator; health; contaminant; pollution; zoonosis; antibiotic resistance

1. Introduction

The red fox (\textit{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 (\textit{V. vulpes}) as a sentinel species.
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 di-phenyl 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] |
| 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; Polychlorinated diphenyl ethers—PCBDEs; Dichlorodiphenylhexachloroethane—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; Americium—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* and *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-qaH-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 *Staphylococcus 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 |
|------------------|-----------|
| *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 callipeda | [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] |
| 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) | [81] |
| encephalitis | |
| Avian Influenza Virus (H5N1) | [82] |
| Lymphocytic Choriomeningitis Virus (LCMV) | [83] |
Table 2. Cont.

| Infectious Agent | Reference |
|------------------|-----------|
| Leptospira interrogans, L. canicola, L. icterohaemorrhagica | [83] |
| Streptococcus spp. | [84–86] |
| Salmonella spp. | [87] |
| Coxiella burnetii | [94] |
| 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] |

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, Mesocestoides lineatus, Echinococcus granulosus, E. multilocularis, 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 scabiei 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 Flavivirus, 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, Hepoviridae, Bornavirus, Borna disease virus 1 (BoDV-1), Tick-borne encephalitis virus (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 burgdorferi s.l.*, *Rickettsia conori*, *Escherichia coli*, *Borrelia valaisiana*, *B. burgdorferi s.l.*, *Anaplasma phagocytophilum*, *B. 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].

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.

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 Leishmaniosis.
Author Contributions: Conceptualization, A.G.; methodology, A.G. and I.P.; software, A.G. and I.P.; validation A.G. and I.P.; formal analysis, A.G. and I.P.; investigation, A.G. and I.P.; resources, A.G. and I.P.; data curation, A.G. and I.P.; writing—original draft preparation, A.G. and I.P.; writing—review and editing, A.G. and I.P.; visualization, A.G. and I.P.; supervision, A.G. and I.P.; project administration, A.G.; funding acquisition, I.P. All authors have read and agreed to the published version of the manuscript.

Funding: This work was supported by the project UIDB/CVT/00772/2020 funded by the Fundação para a Ciência e Tecnologia (FCT).

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Hoffmann, M.; Sillero-Zubiri, C. Vulpes vulpes (amended version of 2016 assessment). The IUCN Red List of Threatened Species 2021: e.T23062A193903628. 2021. Available online: https://www.iucnredlist.org/species/23062/193903628 (accessed on 10 August 2021).

2. Brash, M. Foxes. In BSAVA Manual of Wildlife Casualties; British Small Animal Veterinary Association: Gloucester, UK, 2003; pp. 154–166.

3. Corsolini, S.; Burrini, L.; Focardi, S.; Lovari, S. How Can We Use the Red Fox as a Bioindicator of Organochlorines? Arch. Environ. Contam. Toxicol. 2000, 39, 547–556. [CrossRef]

4. Harris, S.; Yalden, D. Mammals of the British Isles: Handbook, 4th ed.; Mammal Society: Southampton, UK, 2008; ISBN 096082659.

5. Kelly, T.R.; Sleeman, J.M.; Box, P.O. Morbidity and Mortality of Red Foxes (Vulpes vulpes) and Gray Foxes (Urocyon cinereoargenteus) Admitted to the Wildlife Center of Virginia, 1993–2001. J. Wildl. Dis. 2003, 39, 467–469. [CrossRef] [PubMed]

6. Turnover, A. Annual Turnover of Fox Populations in Europe*. Zbl. Vet. Med. 1976, 589, 580–589.

7. Kalisińska, E.; Palczewska-Komsa, M. Concentration of heavy metals in hair and skin of silver foxes (Vulpes lagopus) in the environment. Interdiscip. Toxicol. 2011, 477–484. [CrossRef] [PubMed]

8. LeBlanc, G.; Bain, L.J. Chronic toxicity of environmental contaminants: Sentinels and biomarkers. Environ. Heal. Perspect. 1997, 105, 65–80. [CrossRef]

9. National Research Council (US) Committee on Animals as Monitors of Environmental Hazards. Animals as Sentinels of Environmental Health Hazards; National Academies Press (US): Washington, DC, USA, 1991; ISBN 0-309-59489-8.

10. Alleva, E.; Francia, N.; Pandolfi, M.; De Marinis, A.M.; Chiarotti, F.; Santucci, D. Organochlorine and Heavy-Metal Contaminants in the arctic fox (Vulpes lagopus) dietary exposed to persistent organic pollutants (POPs). Environ. Res. 1993, 62, 269–275. [CrossRef]

11. Wang-Andersen, G.; Skaare, J.U.; Prestrud, P.; Steinnes, E. Levels and congener pattern of PCBs in arctic foxes (Vulpes lagopus) and Invasive (Nyctereutes procyonoides Gray) dietary exposed to persistent organic pollutants (POPs). Environ. Res. 2003, 97, 479–765. [CrossRef]

12. Komov, V.T.; Ivanova, E.S.; Gremyachikh, V.A.; Poddubnaya, N.Y. Mercury Content in Organs and Tissues of Indigenous (Vulpes vulpes) and a Gray Fox (Urocyon cinereoargenteus) in the Environment. Environ. Res. 2006, 97, 467–469. [CrossRef] [PubMed]

13. Naccari, C.; Giangrosso, G.; Macaluso, A.; Billone, E.; Cicero, A.; D’Ascenzi, C.; Ferrantelli, V. Red foxes (Vulpes vulpes) bioindicator of lead and copper pollution in Sicily (Italy). Ecotoxicol. Environ. Saf. 2013, 90, 41–45. [CrossRef]

14. Komov, V.T.; Ivanova, E.S.; Gremyachikh, V.A.; Poddubnaya, N.Y. Mercury Content in Organs and Tissues of Indigenous (Vulpes vulpes) and Invasive (Nyctereutes procyonoides Gray) Species of Canids from Areas Near Cherepovets (North-Western Industrial Region, Russia). Bull. Environ. Contam. Toxicol. 2016, 97, 480–485. [CrossRef]

15. Köhler, H.-R.; Triebskorn, R.; Meierbachtol, T.; Harper, J.; Humphrey, N. Wildlife Ecotoxicology of Pesticides: Can We Track Effects to the Population Level and Beyond? Science 2013, 341, 759–765. [CrossRef]

16. Jayaraj, R.; Megha, P.; Sreedev, P. Review Article. Organochlorine pesticides, their toxic effects on living organisms and their fate in the environment. Interdiscip. Toxicol. 2016, 9, 90–100. [CrossRef]

17. Filistowicz, A.; Dobrzarski, Z.; Przysewiec, P.; Nowicki, S.; Filistowicz, A. Concentration of heavy metals in hair and skin of silver and red foxes (Vulpes vulpes). Environ. Monit. Assess. 2011, 182, 477–484. [CrossRef]

18. Rogstad, T.W.; Sonne, C.; Villanger, G.D.; Øystein, A.; Fuglei, E.; Muir, D.C.; Jørgensen, E.; Jenssen, B.M. Concentrations of vitamin A, E, thyroid and testosterone hormones in blood plasma and tissues from emaciated adult male Arctic foxes (Vulpes lagopus) dietary exposed to persistent organic pollutants (POPs). Environ. Res. 2017, 154, 284–290. [CrossRef]

19. Bocharova, N.; Treu, G.; Czirják, G.A.; Krone, O.; Stefanski, V.; Wibbelt, G.; Uhnsteinüdottir, E.R.; Hersteinsson, P.; Schares, G.; Doronina, L.; et al. Correlates between Feeding Ecology and Mercury Levels in Historical and Modern Arctic Foxes (Vulpes lagopus). PLoS ONE 2013, 8, e66879. [CrossRef]

20. Pedersen, K.E.; Styrisheave, B.; Sonne, C.; Dietz, R.; Jenssen, B.M. Accumulation and potential health effects of organohalogenated compounds in the arctic fox (Vulpes lagopus)—A review. Sci. Total. Environ. 2015, 502, 510–516. [CrossRef]
21. Andersen, M.S.; Fuglei, E.; König, M.; Lipasti, I.; Pedersen, Å.O.; Polder, A.; Yoccoz, N.; Routti, H. Levels and temporal trends of persistent organic pollutants (POPs) in arctic foxes (Vulpes lagopus) from Svalbard in relation to dietary habits and food availability. Sci. Total. Environ. 2015, 511, 112–122. [CrossRef] [PubMed]

22. Bolton, J.L.; White, P.A.; Burrows, D.G.; Lundin, J.I.; Yitlaho, G.M. Food resources influence levels of persistent organic pollutants and stable isotopes of carbon and nitrogen in tissues of Arctic foxes (Vulpes lagopus) from the Pribilof Islands, Alaska. Polar Res. 2017, 36, 12. [CrossRef]

23. Mullineaux, E.; Best, D.; Cooper, J.E. BSAVA Manual of Wildlife Casualties; British Small Animal Veterinary Association: Gloucester, UK, 2003; ISBN 0905214633.

24. Georgi, S.; Bachour, G.; Failing, K.; Eskens, U.; Elmadfa, I.; Brunn, H. Polychlorinated biphenyl congeneres in Foxes in Germany from 1983 to 1991. Arch. Environ. Contam. Toxicol. 1994, 26, 1–6. [CrossRef] [PubMed]

25. Dip, R.; Hegglin, D.; Deplazes, P.; Dafflon, O.; Koch, H.; Naegeli, H. Age- and sex-dependent distribution of persistent organochlorine pollutants in urban foxes. Environ. Heal. Perspect. 2003, 111, 1608–1612. [CrossRef] [PubMed]

26. Tomza-Marciniak, A.; Pilarczyk, B.; Bakowska, M.; Tylkowska, A.; Marciniak, A.; Ligocki, M.; Udala, J. Polychlorinated Biphenyl (PCBs) Residues in Suburban Red Foxes (Vulpes vulpes)—Preliminary Study. Pol. J. Environ. Stud. 2012, 21, 193–199.

27. Corosolini, S.; Focardi, S.; Kannan, K.; Tanabe, S.; Tatsukawa, R. Isomer-specific analysis of polychlorinated biphenyls and 2,3,7,8-tetrachlorodibenzo-p-dioxin equivalents (TEQs) in red fox and human adipose tissue from central Italy. Arch. Environ. Contam. Toxicol. 1995, 29, 61–68. [CrossRef]

28. Dainowski, B.; Duffy, L.; McIntyre, J.; Jones, P. Hair and bone as predictors of tissular mercury concentration in the western Alaska red fox, Vulpes vulpes. Sci. Total. Environ. 2015, 518–519, 526–533. [CrossRef]

29. Kalisinska, E.; Lisowski, P.; Kosik-Bogacka, D.I. Red Fox Vulpes vulpes (L., 1758) as a Bioindicator of Mercury Contamination in Terrestrial Ecosystems of North-Western Poland. Biol. Trace Element Res. 2012, 145, 172–180. [CrossRef] [PubMed]

30. Corosolini, S.; Focardi, S.; Leonzio, C.; Lovari, S.; Monaci, F.; Romeo, G. Heavy Metals and Chlorinated Hydrocarbon Concentrations in the Red Fox in Relation to Some Biological Parameters. Environ. Monit. Assess. 1999, 54, 87–100. [CrossRef]

31. Palczewska-Komsa, M.; Wilk, A.; Stogiera, A.; Chlubek, D.; Buczkowska-Radlińska, J.; Wiszniewska, B. Animals in Bio-monitoring Studies of Environmental Fluoride Pollution. Fluoride 2016, 49, 279–292.

32. Palczewska-Komsa, M.; Kalisinska, E.; Kosik-Bogacka, D.I.; Lanocha-Arendarczyk, N.; Budis, H.; Baranowska-Bosiacka, I.; Gutowska, I.; Chlubek, D. Fluoride in the Bones of Foxes (Vulpes vulpes Linnaeus, 1758) and Raccoon Dogs (Nyctereutes procyonoides Gray, 1834) from North-Western Poland. Biol. Trace Element Res. 2014, 160, 24–31. [CrossRef] [PubMed]

33. Pietelski, J.W.; Kitowski, I.; Tomankiewicz, E.; Gaca, P.; Blazej, S. Plutonium, americium, 90Sr and 137Cs in bones of red fox (Vulpes vulpes) from Eastern Poland. J. Radioanal. Nucl. Chem. 2007, 275, 571–577. [CrossRef]

34. Sédlaaková, J.; Rezáč, P.; Fišer, V.; Hedbávný, J. Red Fox, Vulpes vulpes L., as a Bioindicator of Environmental Pollution in the Countryside of Czech Republic. Acta Univ. Agrar. Silvic. Mendel. Brun. 2019, 67, 447–452. [CrossRef]

35. Dip, C.S.R.; Steiger, C.; Deplazes, P.; Hegglin, D.; Müller, U.; Dafflon, O.; Koch, H.; Naegeli, H.; Dip, R. Comparison of Heavy Metal Concentrations in Tissues of Red Foxes from Adjacent Urban, Suburban, and Rural Areas. Arch. Environ. Contam. Toxicol. 2001, 40, 551–556. [CrossRef]

36. Cebulski, W.; Andrzej, J. Content of lead, cadmium, and mercury in the liver and kidneys of silver foxes (Vulpes vulpes ) in relation to age and reproduction disorders. Bull Vet Inst Pulawy 2009, 53, 63–69.

37. Heltai, M.; Markov, G. Red Fox (Vulpes vulpes Linnaeus, 1758) as Biological Indicator for Environmental Pollution in Hungary. Bull. Environ. Contam. Toxicol. 2012, 89, 910–914. [CrossRef] [PubMed]

38. Pérez-López, M.; Rodríguez, F.S.; Hernández-Moreno, D.; Rigueira, L.; Fidalgo, L.E.; Beceiro, A.L. Bioaccumulation of cadmium, lead and zinc in liver and kidney of red fox (Vulpes vulpes) from NW Spain: Influence of gender and age. Toxicol. Environ. Chem. 2016, 98, 109–117. [CrossRef]

39. Zieta, J.; Wierzbowska, I.A.; Gdula-Argasinska, J.; Gajda, A.; Laskowski, R. Concentrations of cadmium and lead, but not zinc, are higher in red fox tissues than in rodents—pollution gradient study in the Malopolska province (Poland). Environ. Sci. Pollut. Res. 2019, 26, 4961–4974. [CrossRef]

40. Farkas, A.; Bidló, A.; Bolodár-Varga, B.; Jánoska, F. Accumulation of Metals in Liver Tissues of Sympatric Golden Jackal (Canis aureus) and Red Fox (Vulpes vulpes) in the Southern Part of Romania. Bull. Environ. Contam. Toxicol. 2017, 98, 513–520. [CrossRef] [PubMed]

41. Lanocha-Arendarczyk, N.; Kalisinska, E.; Kosik-Bogacka, D.I.; Budis, H.; Noga-Deren, K. Trace metals and micronutrients in bone tissues of the red fox Vulpes vulpes (L., 1758). Acta Théor. 2012, 57, 233–244. [CrossRef] [PubMed]

42. Borkovcova, M.; Fiser, V.; Bednarova, M.; Havlince, Z.; Adámková, A.; Mleek, J.; Jurikova, T.; Balla, S.; Adámek, M. Effect of Accumulation of Heavy Metals in the Red Fox Intestine on the Prevalence of Its Intestinal Parasites. Animals 2020, 10, 343. [CrossRef] [PubMed]

43. Budis, H.; Kalisinska, E.; Lanocha-Arendarczyk, N.; Kosik-Bogacka, D.I. The Concentration of Manganese, Iron and Strontium in Bone of Red Fox Vulpes vulpes (L. 1758). Biol. Trace Element Res. 2013, 155, 361–369. [CrossRef]

44. Biliandžić, N.; Đezdeč, D.; Sedak, M.; Đokić, M.; Solomun, B.; Varenina, I.; Knežević, Z.; Slavica, A. Concentrations of Trace Elements in Tissues of Red Fox (Vulpes vulpes) and Stone Marten (Martes foina) from Suburban and Rural Areas in Croatia. Bull. Environ. Contam. Toxicol. 2010, 85, 486–491. [CrossRef]
45. Voorspoels, S.; Covaci, A.; Lepom, P.; Escutenaire, S.; Schepens, P. Remarkable Findings Concerning PBDEs in the Terres-trial Top-Predator Red Fox (Vulpes vulpes). Environ. Sci. Technol. 2006, 40, 2937–2943. [CrossRef]

46. Mateo, R.; Millán, J.; Rodríguez-Estival, J.; Camarero, P.R.; Palomares, F.; Ortiz-Santaliestra, M.E. Levels of organochlorine pesticides and polychlorinated biphenyls in the critically endangered Iberian lynx and other sympatric carnivores in Spain. Chemosphere 2012, 86, 691–700. [CrossRef]

47. Plaza-Rodríguez, C.; Alt, K.; Grobbel, M.; Hammerl, J.A.; Irrgang, A.; Szabo, I.; Stingle, K.; Schuh, E.; Wiehle, L.; Pfefferkorn, B.; et al. Wildlife as Sentinels of Antimicrobial Resistance in Germany? Front. Vet. Sci. 2021, 7, 627821. [CrossRef]

48. Caprioli, A.; Busani, L.; Martel, J.L.; Helmuth, R. Monitoring of antibiotic resistance in bacteria of animal origin: Epidemiological and microbiological methodologies. Int. J. Antimicrob. Agents 2000, 14, 295–301. [CrossRef] [PubMed]

49. Radhouani, H.; Igrejas, G.; Gonçalves, A.; Estepe, V.; Sargo, R.; Torres, C.; Poeta, P. Molecular characterization of extended-spectrum-beta-lactamase-producing Escherichia coli isolates from red foxes in Portugal. Arch. Microbiol. 2013, 195, 141–144. [CrossRef] [PubMed]

50. Lineages, C.; Resistance, A. Clonal Lineages, Antibiotic Resistance and Virulence Factors in Vancomycin-Resistant Enterococci Isolated from Fecal Samples of Red Foxes (Vulpes vulpes). J. Wildl. Dis. 2011, 47, 769–773.

51. Mo, S.S.; Urdahl, A.M.; Madslien, K.; Sunde, M.; Nesse, L.L.; Slettemæs, J.S.; Norstrøm, M. What does the fox say? Monitoring antimicrobial resistance in the environment using wild red foxes as an indicator. PLoS ONE 2018, 13, e0198019. [CrossRef] [PubMed]

52. Radhouani, H.; Igrejas, G.; Gonçalves, A.; Pacheco, R.; Monteiro, R.; Sargo, R.; Brito, F.; Torres, C.; Poeta, P. Antimicrobial resistance and virulence genes in Escherichia coli and enterococci from red foxes (Vulpes vulpes). Anaerobe 2013, 23, 82–86. [CrossRef] [PubMed]

53. Carson, M.; Meredith, A.; Shaw, D.J.; Giotis, E.S.; Lloyd, D.H.; Loeffler, A. Foxes As a Potential Wildlife Reservoir for mecA-Positive Staphylococci. Vector-Borne Zoonotic Dis. 2012, 12, 583–587. [CrossRef]

54. Chiari, M.; Ferrari, N.; Giardiello, D.; Lanfranchi, P.; Zanoni, M.; Lavazza, A.; Alborali, L.G. Isolation and identification of Salmonella spp. from red foxes (Vulpes vulpes) and badgers (Meles meles) in northern Italy. Acta Veter-Scand. 2014, 56, 1–4. [CrossRef] [PubMed]

55. Lopes, A.P.; Vila-Viçosa, M.J.; Coutinho, T.; Cardoso, L.; Gottstein, B.; Müller, N.; Cortes, H.C. Trichinella britovi in a red fox (Vulpes vulpes) from Portugal. Vet. Parasitol. 2015, 189, 260–263. [CrossRef] [PubMed]

56. Nicholas, B.; Ravel, A.; Leighton, P.; Stephen, C.; Iqbal, A.; Ndao, M.; Konecsni, K.; Fernando, C.; Jenkins, E. Foxes (Vulpes vulpes) as sentinels for parasitic zoonoses, Toxoplasma gondii and Trichinella nativa, in the northeastern Canadian Arctic. Int. J. Parasitol. Parasites Wildl. 2018, 7, 391–397. [CrossRef] [PubMed]

57. Carrera, J.P.; Almeida, D.; Merigo, E.; Checa, R.; Lópe, A.M.; Fidalgo, L.E.; Gálvez, R.; Marino, V.; Fuentes, I.; Miró, G.; et al. The red fox (Vulpes vulpes) as a potential natural reservoir of human cryptosporidiosis by Cryptosporidium hominis in Northwest Spain. Transbound. Emerg. Dis. 2020, 67, 2172–2182. [CrossRef]

58. Papini, R.A.; Verin, R. Giardia and Cryptosporidium in Red Foxes (Vulpes Vulpes): Screening for Coproantigens in a Population of Central Italy and Mini-Review of the Literature. Muced. Vet. Rev. 2019, 42, 101–106. [CrossRef]

59. Ebani, V.V.; Rocchigiani, G.; Nardoni, S.; Bertelloni, F.; Vasta, V.; Papini, R.A.; Verin, R.; Poli, A.; Mancianti, F. Molecular detection of tick-borne pathogens in wild red foxes (Vulpes vulpes) from Central Italy. Acta Trop. 2017, 172, 197–200. [CrossRef] [PubMed]

60. Gicik, Y.; Kara, M.; Sari, B.; Kiliç, K.; Arslan, M.O. Intestinal Parasites of Red Foxes (Vulpes vulpes) from Central Turkey. Mediterr. Wildl. Dis. 2009, 14, 1574–1578. [CrossRef]

61. Dipinetto, L.; Manna, L.; Baiano, A.; Gala, M.; Fioretti, A.; Gravino, A.E.; Menna, L.F. Presence of Leishmania infantum in Red Foxes (Vulpes vulpes) in Southern Italy. J. Wildl. Dis. 2007, 43, 518–520. [CrossRef] [PubMed]

62. Karayiannis, S.; Ntais, P.; Messaritakis, I.; Tsrigotakis, N.; Dokianakis, E.; Antoniou, M. Detection of Leishmania infantum red foxes (Vulpes vulpes) in Central Greece. Parasitology 2015, 142, 1574–1578. [CrossRef]

63. Smith, G.C. Prevalence of zoonotic important parasites in the red fox (Vulpes vulpes) in Great Britain. Vet Parasitol. 2003, 118, 133–142. [CrossRef] [PubMed]

64. Sargo, R.; Loureiro, F.; Catario, A.L.; Valente, J.; Silva, F.; Cardoso, L.; Otranto, D.; Maia, C. First report of thelazia callipaeda red foxes (Vulpes vulpes) from Portugal. J. Zoo Wildl. Med. 2014, 45, 458–460. [CrossRef] [PubMed]

65. Martínez-Carrasco, C.; Ruiz De Ybáñez, M.R.; Sagarinagana, J.L.; Garío, M.M.; Moreno, F.; Acosta, I.; Hernández, S.; Alonso, F.D. Parasites of the Red Fox (Vulpes vulpes Linnaeus, 1758) in Murcia, Southeast Spain. Med. Vet. 2007, 158, 331–335.

66. Dybing, N.A.; Fleming, P.A.; Adams, P.J. Environmental conditions predict helminth prevalence in red foxes in Western Australia. Int. J. Parasitol. Parasites Wildl. 2013, 2, 165–172. [CrossRef]

67. Shamsi, S.; Mcspadden, K.; Baker, S.; Jenkins, D.J. Occurrence of tongue worm, Linguatula cf. serrata (Pentastomida: Linguatulidae) in wild canids and livestock in south-eastern Australia. Int. J. Parasitol. Parasites Wildl. 2017, 6, 271–277. [CrossRef] [PubMed]

68. Scott, D.M.; Baker, R.; Tomlinson, A.; Berg, M.J.; Charman, N.; Tolhurst, B.A. Spatial distribution of sarcocystic mange (Sarcoptes scabiei) in urban foxes (Vulpes vulpes) in Great Britain as determined by citizen science. Urban Ecosyst. 2020, 23, 1127–1140. [CrossRef]

69. Soulsbury, C.D.; Iossa, G.; Baker, P.J.; Cole, N.C.; Funk, S.M.; Harris, S. The impact of sarcocystic mange Sarcoptes scabiei on the British fox Vulpes vulpes population. Mammal Rev. 2007, 37, 278–296. [CrossRef]

70. Dietary control of exertional rhabdomyolysis in horses. J. Equine Veter-Sci. 1998, 18, 450. [CrossRef]
71. Bezerra-Santos, M.A.; Nguyen, V.-L.; Jatta, R.; Manoj, R.R.S.; Latrofa, M.S.; Hodžić, A.; Dantas-Torres, F.; Mendoza-Roldan, J.A.; Otranto, D. Genetic variability of *Ehrlichia canis* TRP36 in ticks, dogs, and red foxes from Eurasia. *Vet-Bact-Microbiol*. 2021, 255, 109037. [CrossRef]

72. Niedringshaus, K.D.; Brown, J.D.; Sweeney, K.M.; Yabsley, M.J. A review of sarcoptic mange in North American wildlife. *Int. J. Parasitol.-Parasites Wildl.* 2019, 9, 285–297. [CrossRef] [PubMed]

73. Foley, J.; Serrieys, L.E.K.; Stephenson, N.; Riley, S.; Foley, C.; Jennings, M.; Wengert, G.; Vickers, W.; Boydston, E.; Lyren, L.; et al. A synthetic review of notoedres species mites and mange. *Parasitology* 2016, 143, 1847–1861. [CrossRef]

74. Vos, A.; Müller, T.; Neubert, L.; Zurbriggen, A.; Botteron, C.; Pühle, D.; Schoon, H.; Haas, L.; Jackson, A.C. Rabies in Red Foxes (*Vulpes vulpes*) Experimentally Infected with European Bat Lyssavirus Type 1. *J. Vet-Med. Ser. B* 2004, 51, 327–332. [CrossRef]

75. Chautan, M.; Pontier, D.; Artois, M. Role of rabies in recent demographic changes in Red Fox (*Vulpes vulpes*) populations in Europe. *Mammalia* 2000, 64, 391–410. [CrossRef]

76. Escutenaire, S.; Pastoret, P.-P.; Sjolander, K.B.; Lundkvist, Å.; Waldenström, J.; Hansson, L.; Arneborn, M.; Olsen, B. Red fox and *Hemivirinae* subfamily (Bunyaviridae) populations in North America and Europe. *J. Wildl. Med.* 2004, 35, 980–986. [CrossRef]

77. Campbell, S.J.; Ashley, W.; Gil-Fernández, M.; Newsome, T.M.; Di Giallonardo, F.; Ortiz-Baez, A.S.; Mahar, J.; Towerton, A.L.; Liu, G.; Zhao, S.; Tan, W.; Hornok, S.; Yuan, W.; Mi, L.; Wang, S.; Liu, Z.; Zhang, Y.; Hazihan, W.; et al. Rickettsiae in red fox (*Vulpes vulpes*). *Ann. Agric. Environ. Med.* 2019, 26, 356–360. [CrossRef]

78. Negredo, A.; Habela, M. Prevalence of *Mycobacterium avium*-subspecies paratuberculosis in road-killed wild carnivores in Portugal. *J. Vet-Microbiol.* 2021, 60, 1177–1184. [CrossRef] [PubMed]

79. Márian, D.; Akári, K.; Farkas, Z.; Varga, J.; Horváth, K.; Serendi, P. Anaplasma Phagocytophilum Infection of Red Foxes (Vulpes vulpes) subpopulation in Hungary. *Parasit-Parasites Wildl.* 2020, 6, eaa065. [CrossRef]

80. Negredo, A.; Habela, M.A.; De Arelanno, E.R.; Diez-Fuertes, F.; Al, A.N.E.; López, P.; Sarriá, I.; Labiod, N.; Calero-Bernal, R.; Arenas, M.; et al. Survey of Crimean-Congo Hemorrhagic Fever Enzootic Focus, Spain, 2011–2015. *Emerg. Infect. Dis.* 2019, 25, 1177–1184. [CrossRef] [PubMed]

81. Tatum, L.M.; Frazier, K.S.; Weege, J.F.; Baldwin, C.A.; Hullinger, G.A.; Bossart, G.D.; Altman, N.H. Canine LaCrosse Viral Meningoencephalomyelitis with Possible Public Health Implications. *J. Vet-Diagn. Investig.* 1999, II, 184–188. [CrossRef] [PubMed]

82. Reperant, L.A.; Van Amerongen, G.; Van De Bildt, M.W.; Rimmelzwaan, G.F.; Dobson, A.P.; Osterhaus, A.D.; Kuiken, T. Highly Pathogenic Avian Influenza Virus (H5N1) Infection in Red Foxes Fed Infected Bird Carlusses. *Emerg. Infect. Dis.* 2008, 14, 1835–1841. [CrossRef] [PubMed]

83. Lledó, L.; Serrano, J.L.; Giménez-Pardo, C.; Gegündez, I. Wild Red Foxes (*Vulpes vulpes*) as Sentinels of Rodent-Borne Hantavirus and Lymphocytic Choriomeningitis Virus in the Province of Soria, Northern Spain. *J. Wildl. Dis.* 2020, 56, 658–661. [CrossRef] [PubMed]

84. Slavica, A.; Deždek, D.; Konjević, D.; Cvetnić, Ž.; Sindirc, M.; Stanin, D.; Habus, J.; Turk, N. Prevalence of leptospiral antibodies in the red fox (*Vulpes vulpes*) population of Croatia. *Veterinární Med.* 2011, 56, 209–213. [CrossRef]

85. Negredo, A.; Habela, M.A.; De Arelanno, E.R.; Diez-Fuertes, F.; Al, A.N.E.; López, P.; Sarriá, I.; Labiod, N.; Calero-Bernal, R.; Arenas, M.; et al. Survey of Crimean-Congo Hemorrhagic Fever Enzootic Focus, Spain, 2011–2015. *Emerg. Infect. Dis.* 2019, 25, 1177–1184. [CrossRef] [PubMed]

86. Barrat, J.; Blancou, J.; Demantke, C.; Gerard, Y. β Hemolytic streptococcal infection in red foxes (*Vulpes vulpes*) in France: The natural disease and experimental studies. *J. Wildl. Dis.* 1985, 21, 141–143. [CrossRef] [PubMed]

87. Steinparzer, R.; Stanclova, G.; Bagó, Z.; Revilla-Fernández, S.; Leth, C.; Hofer, E.; Pohl, B.; Schmoll, F. Generalized Tuberculosis due to Mycobacterium avium subsp. paratuberculosis in red foxes (*Vulpes vulpes*) in the Czech Republic. *Vet. J.* 2000, 160, 141–145. [CrossRef]

88. Steiner, N.; Hénaud, S.; Babbage, J.; Richomme, C.; Réveillaud, Édouard; Gares, H.; Moyen, J.-L.; Boschiroli, M.L. Mycobacterium bovis Infection of Red Fox, France. *Emerg. Infect. Dis.* 2018, 24, 1150–1153. [CrossRef]

89. Steinparzer, R.; Stanclova, G.; Bagó, Z.; Revilla-Fernández, S.; Leth, C.; Hofer, E.; Pohl, B.; Schmoll, F. Generalized Tuberculosis due to Mycobacterium avium subsp. paratuberculosis in red foxes (*Vulpes vulpes*) in Austria. *J. Wildl. Dis.* 2020, 56, 956–958. [CrossRef]

90. Matos, A.C.; Figueira, L.; Martins, M.H.; Loureiro, F.; Pinto, M.L.; Matos, M.; Coelho, A.C. Survey of *mycobacterium avium* subspecies paratuberculosis in road-killed wild carnivores in Portugal. *J. Zoo Wildl. Med.* 2014, 45, 775–781. [CrossRef]

91. Matos, A.; Figueira, L.; Martins, M.H.; Matos, M.; Morais, M.; Dias, A.P.; Pinto, M.; Coelho, A. Disseminated *Mycobacterium bovis* Infection in Red Foxes (*Vulpes vulpes*) as a Potential Indicator of Public Health Implications. *Vector-Borne Zoonotic Dis.* 2020, 20, 531–533. [CrossRef]
96. Ortúñov, A.; Sanfeliú, I.; Nogueras, M.-M.; Pons, I.; López-Claessens, S.; Castellà, J.; Antón, E.; Segura, F. Detection of Rickettsia massiliae/BaR29 and Rickettsia conorii in red foxes (Vulpes vulpes) and their Rhipicephalus sanguineus complex ticks. *Ticks Tick-borne Dis.* 2018, 9, 629–631. [CrossRef]

97. Szyfres, B.; González Tomé, J.; Tomé, J.G. Natural Brucella Infection in Argentine Wild Foxes*. *Bull. Org. mond. Sante* 1966, 1, 919–923.

98. Morgan, W.J.B. The Examination of Brucella Cultures for Lysis by Phage. *J. Gen. Microbiol.* 1963, 30, 437–443. [CrossRef]

99. Zhou, Y.; Meng, Y.; Ren, Y.; Liu, Z.; Li, Z. A Retrospective Survey of the Abortion Outbreak Event Caused by Brucellosis at a Blue Fox Breeding Farm in Heilongjiang Province, China. *Front. Vetér-Sci.* 2021, 8, 409. [CrossRef]

100. Malmasi, A.; Khosravi, A.R.; Selk Ghaffari, M.; Shojaee Tabrizi, A. A potential novel Brucella species isolated from mandibular lymph nodes of red foxes in Austria. *Veter-Microbiol.* 2012, 155, 93–99.

101. Nikolova, S.; Tzvetkov, Y.; Najdenski, H.; Vesselinova, A. Isolation of Pathogenic *Yersinia* from Wild Animals in Bulgaria. *J. Vêter-Med. Ser.* 8 2001, 48, 203–209. [CrossRef] [PubMed]

102. Östrevand, S.; Tjörnstrand, J.; Antin, S.; Antin, S.; Segura, F. Detection of *Rickettsia* spp. in Red Foxes (Vulpes vulpes, 1758) and Raccoon dogs (Nyctereutes procyonoides, with special emphasis on infectious and zoonotic agents in Northern Germany. PLoS ONE 2017, 12, e0175469. [CrossRef]

103. Lemp, C.; Jungwirth, N.; Grilo, M.L.; Reckendorf, A.; Ulrich, A.; van Neer, A.; Bodewes, R.; Pfankuche, V.M.; Bauer, C.; Hofer, E.; Revilla-Fernández, S.; Al Dahouk, S.; Siegel, J.; Scholz, H.C. A potential novel Brucella species isolated from mandibular lymph nodes of red foxes in Austria. *Vetér-Microbiol.* 2012, 155, 93–99.

104. Nicolová, S.; Tzvetkov, Y.; Najdenski, H.; Vesselinova, A. Isolation of Pathogenic *Yersinia* from Wild Animals in Bulgaria. *J. Vêter-Med. Ser.* 8 2001, 48, 203–209. [CrossRef] [PubMed]

105. Ortuño, A.; Sanfeliú, I.; Nogueras, M.-M.; Pons, I.; López-Claessens, S.; Castellà, J.; Antón, E.; Segura, F. Detection of Rickettsia massiliae/BaR29 and Rickettsia conorii in red foxes (Vulpes vulpes) and their Rhipicephalus sanguineus complex ticks. *Ticks Tick-borne Dis.* 2018, 9, 629–631. [CrossRef]

106. Ortuño, A.; Sanfeliú, I.; Nogueras, M.-M.; Pons, I.; López-Claessens, S.; Castellà, J.; Antón, E.; Segura, F. Detection of Rickettsia massiliae/BaR29 and Rickettsia conorii in red foxes (Vulpes vulpes) and their Rhipicephalus sanguineus complex ticks. *Ticks Tick-borne Dis.* 2018, 9, 629–631. [CrossRef]

107. Knudtson, W.U.; Gates, C.E.; Ruth, G.K.; Whatmore, A.; Blom, J.; Vergnaud, G.; et al. *Brucella* sp. nov. isolated from mandibular lymph nodes of red foxes (Vulpes vulpes). *Int. J. Syst. Evol. Microbiol.* 2016, 66, 2090–2098. [CrossRef]

108. Riebold, D.; Lubig, J.; Wolf, P.; Wolf, C.; Russow, K.; Loebermann, M.; Bodewes, R.; Pfankuche, V.M.; Bauer, C.; Osterhaus, A.D.M.E.; et al. Pathological findings in the red fox (Vulpes vulpes), stone marten (Martes foina) and raccoon dog (Nyctereutes procyonoides), with special emphasis on infectious and zoonotic agents in Northern Germany. PLoS ONE 2017, 12, e0175469. [CrossRef]

109. Lemp, C.; Jungwirth, N.; Grilo, M.L.; Reckendorf, A.; Ulrich, A.; van Neer, A.; Bodewes, R.; Pfankuche, V.M.; Bauer, C.; Hofer, E.; Revilla-Fernández, S.; Al Dahouk, S.; Siegel, J.; Scholz, H.C. A potential novel Brucella species isolated from mandibular lymph nodes of red foxes in Austria. *Vetér-Microbiol.* 2012, 155, 93–99.

110. Sikara, R.; Juwaid, S.; Ćirović, D.; Penezić, A.; Mihaljica, D.; Veinović, G.; Radojičić, S.; Hodžić, A.; Duscher, G.G.; Tomanović, S. Isolation of Pathogenic *Yersinia* from Wild Animals in Bulgaria. *J. Vêter-Med. Ser.* 8 2001, 48, 203–209. [CrossRef] [PubMed]

111. Emilia, V.V.; Verin, R.; Fratini, F.; Poli, A.; Cerri, D. Molecular Survey of *Anaplasma phagocytophilum* and *Ehrlichia canis* in Red Foxes (Vulpes vulpes) from Central Italy. *J. Wildl. Dis.* 2011, 47, 699–703. [CrossRef]

112. Emilia, V.V.; Verin, R.; Fratini, F.; Poli, A.; Cerri, D. Molecular Survey of *Anaplasma phagocytophilum* and *Ehrlichia canis* in Red Foxes (Vulpes vulpes) from Central Italy. *J. Wildl. Dis.* 2011, 47, 699–703. [CrossRef]

113. Emilia, V.V.; Verin, R.; Fratini, F.; Poli, A.; Cerri, D. Molecular Survey of *Anaplasma phagocytophilum* and *Ehrlichia canis* in Red Foxes (Vulpes vulpes) from Central Italy. *J. Wildl. Dis.* 2011, 47, 699–703. [CrossRef]

114. Emilia, V.V.; Verin, R.; Fratini, F.; Poli, A.; Cerri, D. Molecular Survey of *Anaplasma phagocytophilum* and *Ehrlichia canis* in Red Foxes (Vulpes vulpes) from Central Italy. *J. Wildl. Dis.* 2011, 47, 699–703. [CrossRef]

115. Emilia, V.V.; Verin, R.; Fratini, F.; Poli, A.; Cerri, D. Molecular Survey of *Anaplasma phagocytophilum* and *Ehrlichia canis* in Red Foxes (Vulpes vulpes) from Central Italy. *J. Wildl. Dis.* 2011, 47, 699–703. [CrossRef]

116. Emilia, V.V.; Verin, R.; Fratini, F.; Poli, A.; Cerri, D. Molecular Survey of *Anaplasma phagocytophilum* and *Ehrlichia canis* in Red Foxes (Vulpes vulpes) from Central Italy. *J. Wildl. Dis.* 2011, 47, 699–703. [CrossRef]

117. Emilia, V.V.; Verin, R.; Fratini, F.; Poli, A.; Cerri, D. Molecular Survey of *Anaplasma phagocytophilum* and *Ehrlichia canis* in Red Foxes (Vulpes vulpes) from Central Italy. *J. Wildl. Dis.* 2011, 47, 699–703. [CrossRef]

118. Emilia, V.V.; Verin, R.; Fratini, F.; Poli, A.; Cerri, D. Molecular Survey of *Anaplasma phagocytophilum* and *Ehrlichia canis* in Red Foxes (Vulpes vulpes) from Central Italy. *J. Wildl. Dis.* 2011, 47, 699–703. [CrossRef]

119. Emilia, V.V.; Verin, R.; Fratini, F.; Poli, A.; Cerri, D. Molecular Survey of *Anaplasma phagocytophilum* and *Ehrlichia canis* in Red Foxes (Vulpes vulpes) from Central Italy. *J. Wildl. Dis.* 2011, 47, 699–703. [CrossRef]

120. Emilia, V.V.; Verin, R.; Fratini, F.; Poli, A.; Cerri, D. Molecular Survey of *Anaplasma phagocytophilum* and *Ehrlichia canis* in Red Foxes (Vulpes vulpes) from Central Italy. *J. Wildl. Dis.* 2011, 47, 699–703. [CrossRef]

121. Emilia, V.V.; Verin, R.; Fratini, F.; Poli, A.; Cerri, D. Molecular Survey of *Anaplasma phagocytophilum* and *Ehrlichia canis* in Red Foxes (Vulpes vulpes) from Central Italy. *J. Wildl. Dis.* 2011, 47, 699–703. [CrossRef]

122. Emilia, V.V.; Verin, R.; Fratini, F.; Poli, A.; Cerri, D. Molecular Survey of *Anaplasma phagocytophilum* and *Ehrlichia canis* in Red Foxes (Vulpes vulpes) from Central Italy. *J. Wildl. Dis.* 2011, 47, 699–703. [CrossRef]
120. Moreno, J.M.; Aguiló, E.; Alonso, S.; Cobelas, M.Á.; Anadón, R.; Ballester, F.; Benito, G.; Catalán, J.; de Castro, M.; Cendrero, A.; et al. A Preliminary General Assessment of the Impacts in Spain Due to the Effects of Climate Change. Ambiente. Ministry of Environment 2005. Available online: https://www.miteco.gob.es/es/cambio-climatico/temas/impactos-vulnerabilidad-y-adaptacion/Full%20report_tcm30-178514.pdf (accessed on 15 August 2021).

121. Fuglei, E.; Ims, R.A. Global Warming and effects on the Arctic Fox. Sci. Prog. 2008, 91, 175–191. [CrossRef] [PubMed]

122. Kim, B.I.; Blanton, J.D.; Gilbert, A.; Castrodale, L.; Hueffer, K.; Slate, D.; Rupprecht, C.E. A conceptual model for the impact of climate change on fox rabies in Alaska, 1980-2010. Zoonoses Public Heal. 2013, 61, 72–80. [CrossRef] [PubMed]