



## THE RED FOX: A USEFUL SENTINEL FOR DETECTING TBE FOCI

### Background

In Germany, TBE risk areas are defined on a district level (county) by a minimum incidence of 1 case per 100,000 inhabitants in a gliding five-year period. This definition has the disadvantage that it is based on geographical inaccuracies, that vaccination rates are disregarded, and that notification is carried out by place of living of the patient rather than the place of infection. In addition, most infections in humans are mild or asymptomatic and thus, are not diagnostically detected. It has been shown that sero-epidemiological studies in wild (e.g. roe deer, wild boar) or domestic animals (e.g. dogs, goats, sheep) can contribute to the risk estimation to acquire a TBE virus infection. Here, the seroprevalence of TBE virus specific antibodies in red foxes from Germany was determined to estimate the potential of red foxes as possible sentinels of human TBE risk.

### Results

Between December 2016 and February 2020, a total of 1233 serum samples were collected from foxes shot during traditional hunting. Most of the foxes were adult (98.5%); 59.0% were male foxes, 40.2% were female foxes and in 0.7%, the gender could not be determined. The foxes were shot from districts all over Germany – from officially defined TBE risk areas (n=568/1233, 46.1%) and from TBE non-risk areas (N=665/1233; 53.1%).

In total, 121/1233 samples were positive or borderline by a commercial TBE ELISA, and among these sera, 110 samples could be confirmed by a newly developed micro-neutralization assay. In addition, 150 sera were positive in the micro-NT, which were negative in the ELISA. In total, 973 samples were confirmed negative by micro-NT, of which 11 samples were tested positive by ELISA. Thus, the sensitivity of the commercial ELISA was 42.3% and the specificity reached 98.9%.

By using only sera confirmed by micro-NT, the overall seroprevalence of TBE antibodies in foxes across Germany was 21.1% and did not differ in male and female foxes. In TBE risk areas, the seroprevalence was significantly higher (30.5%) compared to non-risk areas (13.1%) – for this calculation, only districts with at least 10 samples were analysed to get significant results. The geographical distribution of foxes with TBE virus specific antibodies across Germany is shown in a vivid figure. Here, one can clearly see that in regions where no counties have officially been declared as TBE risk areas (e.g., North-Rhine Westphalia), a lot of places have been identified with a relative high percentage of TBE positive fox sera.

### Discussion

A two-step diagnostic system, based on screening by ELISA and confirmation by NT was shown to be a useful means for TBE specific sero-epidemiological investigations of foxes, and possibly, a sentinel investigation of fox sera based only on NT would be sufficient.

The home range of rural foxes is about 2 km<sup>2</sup>, and that of urban foxes is 0.5 km<sup>2</sup>. While the TBE antibody persistence in red foxes is yet not known, it has been shown that experimental TBE virus infection leads to clinical symptoms, viremia, and high antibody titers. In addition, it has been shown that tick species which are common in Germany, like *Ixodes ricinus*, *I. hexagonus* and *Dermacentor reticulatus* and which are proven vectors for TBE virus, can be detected on foxes. The red fox meets the requirement to be a suitable indicator for TBE risk assessment, and the observed seroprevalence of TBE antibodies reflects the different human TBE virus infection rates in Germany. At least 87 TBE-positive fox sera were from officially defined non-risk areas and therefore, analyzing fox sera shows the potential to detect new TBE virus foci.



Investigation of fox sera prevalence could help to locate such TBE foci and can complement the definition of risk areas based on human TBE incidences.

## Literature

Haut et al.

The red fox (*Vulpes vulpes*) as sentinel for tick-borne encephalitis virus in endemic and non-endemic areas

*Microorganisms*. 2020; 8:1817, doi:10.3390/microorganisms 8111817

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