Tick-borne encephalitis (TBE) is a viral disease transmitted by Ixodes ticks. It is widespread in the temperate zone of Europe and Asia, with over 200 cases occurring annually in Poland, majority of them in the north-east region of the country. There are 40-50 patients with TBE diagnosis hospitalized in the department of Infectious Diseases and Neuroinfections of the medical University in Białystok annually. No specific treatment directed against TBE virus is available. The natural course of the infection is highly variable, ranging from asymptomatic infections through flu-like disease to severe encephalitis and myelitis, with a significant risk of death or permanent disability. The causes of this variability are not well known, but are likely determined by an individually variable strength and detailed character of the inflammatory and immune response to the infection, at least partially dependent on the genetic background. The response to TBE virus in humans is complex and multi-stage, but also relatively poorly known, and most of the research so far has been conducted on laboratory animals and cell cultures. It is however clear that in some cases the inflammatory and immune mechanisms are ineffective or may become paradoxically harmful, for example by causing an additional damage to the infected tissues of the brain. We attempt to evaluate these processes systematically in a human TBE virus infection.

The planned study will evaluate a large set of parameters characterizing the response of the host to TBE virus infection simultaneously, in a large group of hospitalized patients undergoing lumbar puncture for cerebrospinal fluid collection necessary for the diagnosis. We will study concentrations of the soluble mediators of inflammation and immune response in serum and cerebrospinal fluid, specific antibodies against TBE virus, features of the leukocyte populations infiltrating the cerebrospinal fluid. These data will be compared with virus load in blood and cerebrospinal fluid as well as with the course and manifestation of the disease (involvement of meninges, brain, or spinal cord), severity, occurrence of complications and permanent sequelae. We plan to evaluate 120 patients with different clinical presentations in a 3 year study period, determining which of the studied factors (cytokines and other mediators, leukocyte populations and their surface proteins etc.) are involved in the protection against TBE virus, and which may be dispensable or paradoxically harmful.

In the same group of patients we will evaluate common variants (polymorphisms) in the genes coding proteins participating in the inflammatory and immune response (especially cytokines and their receptors) and the results will be compared between patients with the mild and severe presentation and between patients and healthy persons from the same area (blood donors), to detect genetic variants associated with a higher risk of TBE or of its severe clinical presentation.

The results shall lead to a follow-up research on prophylaxis, diagnostics and treatment of TBE. The study of genetic polymorphisms TBE will eventually make it possible to identify persons with a particularly high risk of TBE, which may be considered an indication for vaccination in endemic areas. Some of the studied parameters may be identified as potential diagnostic markers, for example cytokine concentrations may be used in patients hospitalized with TBE to assess the risk of developing severe complications. The knowledge gained on the pathogenesis of TBE will be a step towards new, better targeted treatment methods, improving the control of the infection and reducing the harmful manifestations of the inflammatory response.