FAQs on Human Borna Disease Virus Infection
for medical practitioners (family physicians, psychiatrists, pediatricians) and patients
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What are Bornaviruses?
- They are small, coated RNA viruses that infect preferentially brain-, but also blood cells, and are genetically related to measles and rabies viruses.
- They have been found in many countries, globally, and comprise a separate family of viruses (Bornaviridae).
- BDV (Borna disease virus) is persistently present in humans and many other mammals, and the recently discovered ABV (avian Bornavirus) infects exotic birds.
- They have zoonotic potential, i.e., transmission to humans from infected pets or other domestic animals, such as horses, cats or dogs, is possible but not usual.

What is different about Bornaviruses?
- In evolutionary terms they are among the oldest viruses, reproducing in the host cell nucleus (the only negative-strand RNA viruses to do so), and have been finding their way into our and our ancestors' genetic material for at least 40 million years.
- They remain in the infected organism throughout their lifespan (no cell destruction).
- They primarily attack the older portion of the brain (the limbic system) and contribute to behavioral and mood alteration (it can be assumed that viral proteins disturb the neurotransmitter equilibrium).

How dangerous are Bornaviruses to human health?
- They are found in about one third (30%) of the adult population (as documented in Germany and Australia). In children the prevalence is about twice as high.
- Most of those infected (>80%) show no symptoms.
- Every sixth person infected (16-17%) has an increased risk of developing some form of mental illness during the course of his or her life. As a proportion of the overall population, one in twenty (5 out of every 100 persons, or 5%) is at increased risk of becoming ill.

What medical conditions are associated with a significantly higher rate of active Bornavirus infection than in the general population?
- Acute depressive episodes (uni- and bipolar), in 80-90% of patients.
- Chronic obsessive-compulsive disorders (OCD), in at least 50-60% of patients.
- Chronic fatigue syndrome (CFS/ME), in at least 40% of patients.

What symptoms are common to the majority of these patients?
- Cognitive deficits, bradylogia (abnormally slow speech).
- Reduced intellectual capability.
- Attention and concentration deficits (especially among children and young adults).
- Memory loss (not age-related).
- Learning disabilities (especially among children and young adults).
How can a Bornavirus infection be diagnosed?
- From a small blood sample (5 -10 ml citrated blood or serum, children 1 ml) using special assays (ELISA formats). May be transported without refrigeration.
- A screening test measures Bornavirus-specific circulating immune complexes (CICs) consisting of viral proteins and the patient’s antibodies, detectable only once the virus has replicated.
- In the case of an acute illness, it is necessary also to test for the viral proteins (antigens) that together with the CICs signal an acute episode of viral activation.
- The presence of antibodies is not an indication of viral activity. A negative antibody test does not rule out the possibility of infection.

Where can blood be tested for Borna virus infection?
- Accredited medical laboratory: DIAMEDIS, Virus Diagnostics, Dunlopstr. 50, D-33689 Bielefeld-Sennestadt. http://www.diamedis.com Tel. +49 5205-7299-0
- Consulting service: Prof. Hanns Ludwig, cell +49 171 754 2997; hanns.ludwig@web.de

Is there a therapeutic option for patients diagnosed with a BDV infection?
- Yes, a drug that has been approved for the past 40 years for treatment of the influenza A virus (active ingredient: amantadine sulphate) has been shown both in vitro and in clinical studies to be highly effective against natural Bornaviruses (till now, off-label use).
- Amantadine sulphate (AS) is a virostatic agent. It inhibits virus replication and thereby the formation of harmful viral proteins.
- The majority (70 to 80%) of infected acute depressive patients derive a long-term benefit in the form of reduced symptoms (study results) in parallel with the disappearance of viral markers in the blood.
- AS can be prescribed as an add-on medication to antidepressants (no undesirable interactions).
- Dose level: 2-4 mg AS orally per day per kg of body weight. A patient weighing 75 kg would thus take 150 to 300 mg of AS daily. Initial dose of 1 mg AS per kg of body weight for the first three or four days.
- Dosing interval: 1-1-0 or 1-0-0.
- Treatment duration: normally 3 months; clinical improvement to be expected in the first month (laboratory testing of the blood markers advised).
- Tolerance: very well tolerated within the dosage range indicated. During the first week some restlessness and sleep disturbances are possible (in which case the dosing interval should be 1-0-0).

Which patients can expect to benefit from antiviral therapy?
- In principle all patients who have been diagnosed with BDV infection and mental disturbances (but not dementia):
  o In uni-/bipolar patients who have developed a tolerance for antidepressants
  o In patients with obsessive-compulsive or anxiety disorders, such as ADHD
  o In patients with chronic fatigue syndrome (CFS/ME)
  o In patients with chronic-stress-induced cognitive deficits

How often should therapeutic drug monitoring be carried out?
- Optional after 6 weeks of therapy, in order to adjust the dosage if necessary.
- Obligatory after 12 weeks of standard therapy or before discontinuing medication.
What risk factors predispose to an activation of Bornavirus infection?
- **Significant risk:** chronic stress, which weakens the immune system over time and allows dormant Bornaviruses to become active:
  - Chronic stress can be brought about by a systematically over- or underdemanding work life, psychosocial stressors (unresolved conflicts, loss of close friends or relatives) and poor coping strategies.
- **A weakened immune system,** whether medically induced (by corticosteroid therapy, for example) or as a result of illness, likewise increases the risk of virus activation:
  - At particular risk are adult oncology patients and children with leukemia, and patients with auto-immune diseases.

What preventive strategies could be put in place to combat Bornaviruses?
- **Infection not easily prevented because**
  - Transmission occurs early and unnoticed (generally vertical, intrauterine or perinatal; sometimes horizontally through nasal secretions and probably saliva)
  - The prevalence of symptom-free carriers is relatively high (30% among adults, 60% in children on average).
- **Disease quite preventable because**
  - Increased risk is testable from blood samples (high CIC values are an indicator)
  - Prophylactic antiviral therapy is a short-term (4 weeks) option for patients in long-term care, and also for stressed healthy persons with high CIC values (and who do not respond to stress reduction).