WHAT IS PANDAS/PANS?

PANDAS (Pediatric Autoimmune Neuropsychiatric Disorder Associated with group A Streptococci) is a term used to describe a group of patients who experience a sudden and rapid onset of neuropsychiatric symptoms such as OCD-like behavior, anxiety, tics, personality changes, and restrictive eating that are oftentimes disabling. A temporal association with a streptococcal infection is hypothesized, but this remains controversial, as does the diagnosis.

PANS (Pediatric Acute-onset Neuropsychiatric Syndrome) is an analogous term used to describe a similar clinical syndrome compared to PANDAS which may be caused by non-infectious (drugs, metabolic abnormalities) or infectious (mycoplasma, Lyme disease, influenza, etc.).

WHAT ARE THE SYMPTOMS?

• A clinical diagnosis of PANDAS is defined by the following criteria:
  o Abrupt onset of OCD-like behaviors and/or tics
  o Fluctuating severity of symptoms
  o Pre-pubertal onset
  o Association with streptococcal infection
  o Presence of other neuropsychiatric symptoms

• A clinical diagnosis of PANS is defined by the following criteria:
  o Abrupt onset of OCD-like behaviors and/or tics
  o Acute onset of at least 2 concurrent neuropsychiatric symptoms (e.g. anxiety, depression, etc.)
  o Symptoms not better explained by a known neurologic disorder (e.g. Sydenham chorea, Tourette disorder, etc.)
There is no specific diagnostic testing at this time. However, evidence for a group A streptococcal infection may be obtained by:

- A positive throat culture or rapid strep test.
- A rise in antistreptolysin O (ASO) and/or anti-DNase B antibody titers between the onset of symptoms and 4-6 weeks later.

Importantly, a positive titer in either ASO or anti-DNase B may only be diagnostic in the appropriate clinical context. Available commercial antibody testing panels are considered unreliable and lack sufficient evidence to support their use.

- Additional testing may include mycoplasma pneumoniae antibodies, pneumococcal antibody titers, Lyme disease panel, Epstein-Barr virus test, Coxsackie A & B titers, vitamin B12 and D levels, as well as immunoglobulin (IgM, IgA, and IgE titers).

**IS PANDAS AN AUTOIMMUNE DISORDER?**

- The role of autoimmunity in PANDAS/PANS is controversial. Support for a possible autoimmune cause is provided by response to treatment with immune-modifying therapies, such as corticosteroids, intravenous immunoglobulin, and plasma exchange.
- Conflicting evidence against an autoimmune cause include failure of immunologic markers in the blood to correlate with clinical exacerbations in some patients. However, it has been postulated that an unknown immune marker for which there is no current testing may be the culprit of this disease.
- Preliminary data has suggested a possible role for antibodies against striatal cholinergic interneurons has shown promising results, but the research is ongoing and there is no commercially available test for these antibodies at this time.
- The diagnosis of PANDAS/PANS remains largely clinical at this time.

**HOW IS IT TREATED?**

There are no consensus guidelines for treatment at this time. However, various approaches to therapy may include:

- **Antibiotics.** Antibiotic therapy is indicated for the treatment of acute streptococcal infections (amoxicillin, azithromycin, clindamycin, and cephalosporins have been used).
  - Small studies support the use of prophylactic antibiotics in cases that respond to treatment and relapse once treatment is complete.
• **Immune-modulating therapy.** Corticosteroids, intravenous immunoglobulin (IVIG), and plasma exchange have also been used, but there are no large randomized controlled trials at this time, and evidence to support their use in routine clinical practice is lacking.
  
  - Additional immunosuppressive therapies including rituximab, cyclophosphamide, azathioprine, and mycophenolate mofetil have been used in small case series, and they are less commonly used in the treatment of PANDAS/PANS.

• **Tonsillectomy.** This may be beneficial in some patients with recurrent streptococcal infections.

**PROGNOSIS**

The long-term outcome of children who meet criteria for PANDAS/PANS is not yet known. In some cases, patients may respond to treatment within a few weeks. Low-level anxiety and neuropsychiatric symptoms may gradually resolve after several weeks or months. Small case series have reported longer durations of symptoms (up to a few years). Unrecognized and untreated PANDAS may result in an increased risk of progression to lifelong neuropsychiatric and tic disorders that show the more typical waxing and waning pattern and may result from permanent damage to the nerves and/or neuronal networks.

Given the controversial nature of PANDAS/PANS, and the limited number of reported cases, the long-term outcome remains unclear. Additional studies are needed to fully understand the mechanisms of this disease in order to develop more effective ways to treat it. Current diagnostic criteria and therapeutic recommendations are likely to change as ongoing research continues to improve our understanding of this rare condition.

**REFERENCES**


Swedo SE, Leckman JF, Rose NR. From research subgroup to clinical syndrome: Modifying the PANDAS criteria to describe PANS (Pediatric Acute-onset Neuropsychiatric Syndrome). Pediatr Ther 2012; 2.


