## Growing consensus on link between strep and obsessive-compulsive disorder

■ Cite as: CMAJ 2018 January 22;190:E86-7. doi: 10.1503/cmaj.109-5545

Posted on cmajnews.com on Jan. 2, 2018.

magine your bright, healthy sevenyear-old suddenly developing a grunting tic and a terror of germs. He scrubs his hands until they bleed. Once cheerful, he becomes volatile and talks about hurting himself. His handwriting reverts to a confused scribble, his grades plummet, and he refuses to go to school.

A growing body of evidence suggests that these bewildering changes may be triggered by a streptococcal (strep) infection. Strep bacteria hide from the immune system by mimicking host cells, in some cases provoking antibodies to mistakenly attack the basal ganglia, a part of the brain involved in movement and behaviour. Many parents and doctors are unaware of the possible link, and traditional treatments for obsessive-compulsive disorder (OCD) may fall short of a full solution.

Called PANDAS (pediatric autoimmune disorders associated with streptococcal infections) the rare condition was first described in the 1990s. Researchers at the United States National Institute of Mental Health noticed that some children with OCD had intense symptoms that would appear overnight in the aftermath of a viral or bacterial infection, along with a host of other neuropsychiatric problems, from extreme mood swings to changes in handwriting and attention.

The symptoms could decrease or disappear for months at a time, and just as suddenly return after another infection. "It's either an autoimmune antibody or it's a different type of inflammation that's driving the symptoms in these kids, and when that resolves these symptoms go away," explained Dr. Kyle Williams, direc-



A rare diagnosis is gaining mainstream attention, linking streptococcal infection to obsessive-compulsive symptoms and tics in some children.

tor of pediatric neuropsychiatry and immunology at Massachusetts General Hospital, at a meeting at Sunnybrook Hospital in Toronto. Williams has studied PANDAS for a decade and runs one of the few full-time clinics for children with the condition.

With so much still unknown about PANDAS, it's very difficult to estimate prevalence, he explained. The PANDAS

Network, an American patient group, estimates the condition may affect 1 in 200 US children, or up to a quarter of children diagnosed with OCD and tic disorders, such as Tourette syndrome.

The link between untreated strep infections and OCD symptoms has been noted before, related to Sydenham chorea, a neurological form of rheumatic fever. As far back as 1894, Canadian

physician Dr. William Osler noted odd behaviours among young patients, including compulsively "hiding their clothes away and picking up objects, things we would think of as OCD," Williams said. But unlike in Sydenham chorea, kids with PANDAS "don't have the typical movement disorder that you would expect to see."

Because these children didn't fit the profile of known neurological or medical disorders, a unique diagnosis became important and remains controversial. "There are realistic arguments against this being a unique disorder," Williams explained. About 2% of children develop OCD. Given how often kids get strep infections, "we're bound to see some that just happen to have onset of OCD sometime after."

However, he noted telling differences in PANDAS, such as the stark deteriora-

tion of handwriting. "The change here looks like someone who has had some sort of traumatic brain injury or stroke," but it seems to be temporary and unrelated to tic symptoms. There are also differences in response to treatment to consider, Williams added. "If this is truly an autoimmune disorder, can we affect their symptoms by treating them with anti-inflammatory or anti-autoimmune treatments?"

Clinical trials in the United States are ongoing, but there is growing expert consensus and anecdotal support for combining standard treatment for OCD symptoms with antibiotics, plasma exchange or immunoglobulin to treat the underlying infection and immune response. Families of Canadian patients are also pushing for greater awareness and resources to tackle PANDAS. In sev-

eral news reports in the past year, families described doctors being hesitant to acknowledge the condition or prescribe antibiotics because of concerns about drug resistance.

Complicating the picture, "we don't have a biomarker or an identifying antibody that we can use to separate this population out yet," said Williams. However, "we think we're beginning to identify one." In a recent study, Williams and coauthors found that an antibody taken from children with PANDAS binds to a specific set of neurons in the basal ganglia of mice. Those neurons "have also previously been shown to be abnormal in adults with Tourette syndrome," Williams said. "We're excited that may be an emerging area."

Lauren Vogel, CMAJ