

On PANDAS, the LeRoy Controversy and False Dichotomies

By Gunilla Gerland

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An epidemic outbreak of tics disorder among young girls in an area in LeRoy, New York has become international news, and a documentary, *The Town That Caught Tourette's*, has aired in several countries (1). In the documentary, as well as in reality, the big question lies in whether the girls' illness was caused by a post-infectious autoimmune disorder, such as PANS or PANDAS, or if it is a psychogenic reaction to emotional trauma, such as in Conversion Disorder. The two conditions are pitted against each other, with the presumption being if one were true then the other must be false. I think it is fair to say that the angle of the film rules in favor of the Conversion Disorder theory.

Let us take a closer look at the dichotomy of the LeRoy cases and PANDAS. First, PANDAS is a disorder closely related to Sydenham's Chorea (SC) and Rheumatic Fever (RF). Dr. Susan Swedo who initially discovered – or should we say rediscovered – the disorder in the early 1990s has used the term “rheumatic fever of the brain” when trying to explain the mechanisms (2). All these disorders PANDAS, SC, and RF occur as a post-streptococcal reaction, where the initial infection may very well have been asymptomatic and therefore unnoticed. The link between SC, RF and strep has been known since the 1950s. The theory is that an autoimmune reaction causes the immune system to attack the brain (or in the case of RF; the joints and the heart.) Research suggests that antibodies against strep throat bacteria mistakenly act upon a brain enzyme, disrupting communications between neurons and causing the symptoms (3). These antibodies somehow cross the blood-brain barrier (BBB), which is breached temporarily. Alternatively, some quality of the antibodies may cause the BBB to allow in the antibodies. Research is ongoing (4).

Now, I will argue that the dichotomy of *either* emotional trauma/conversion disorder *or* post-infectious disorder/PANDAS in the LeRoy cases is a false dichotomy. As you will see, both parts of this presumed dichotomy may very well be true and also the most likely explanation to what has seemed like a mystery to many. However, before I get back to this false dichotomy and to the BBB, we need to pay history a visit.

A History Lesson

I suggested above that Swedo *rediscovered* PANDAS, and the truth is that PANDAS is well described in scientific literature well over 100 years ago (and even earlier than that,) although not under that name. Between the 1880s and the 1930s, there is a substantial number of papers on Sydenham's Chorea describing all the symptoms we now know as PANDAS. The only differences between those descriptions of symptoms and the symptoms we now see in PANDAS patients are that all patients back then seemed to have more obvious choreatic movements than current PANDAS patients do. PANDAS patients now do have choreiform movements, but many are so minor that they may escape the eye unless one knows what to look for. Furthermore, since RF was a common complication, the infectious origin not fully known, and antibiotics not yet that available, the doctors were more concerned with saving the patients lives than with recording psychiatric manifestations. Nevertheless, some records were taken.

While there are several examples in literature, I will for the sake of the length of this text, just quote one record. This example is from the paper titled, *Psychoses Associated with Sydenham's Chorea*, by E. M. Hammes, M.D. , associate Professor of Neurology and Psychiatry, University of

Minnesota Medical School. The paper was published in 1922 in JAMA:

The present illness began early in March, 1921, with an attack of acute articular rheumatism. The patient recovered within one month and remained well till the latter part of April, when she developed a typical Sydenham's chorea of the hémiplégie type, which continued until the first week in July and then completely subsided. In June, 1921, she became unduly irritable and emotional. About one month later, she became depressed, and had frequent crying spells and periods of acute excitement during which she became very noisy and terrified. She developed persecutory ideas, said that she would be tortured, that the milk was poisoned and that the bedclothes were filthy, and she refused to sleep in them. She developed hallucinations, saw bugs and strange people, and complained of smelling gas in her room. (5)

In this same article Hammes writes the following:

In reviewing the literature on the insanities associated with this condition [chorea], one is impressed with the frequency of the statement that mental disturbances in some form are an essential manifestation. (5)

Thus, PANDAS and Sydenham's Chorea may very well be the same disorder, however, with a range of different presentations. In the Western world we now rarely see SC, although PANDAS seems to not be all that uncommon.

The Equation of PANDAS

How do we explain the change in presentation? Today, OCD and/or tics, along with other psychiatric symptoms and minor choreiform movements are more prevalent, whereas, in the past, the presentation was primarily choreatic with the psychiatric symptoms in the aftermath. Well, we know that the Strep bacteria exist in various strains. Being a true survivor, strep has mutated many times and continues to do so. There is a possibility that the Western world has so effectively treated Sydenham's Chorea with antibiotics that we caused these strains of strep to die out, while it at the same time promoting mutations of strep which does not present with such physical obviousness. This new strain of strep would therefore not be treated as rapidly, or even at all, with antibiotics.

There are 'milder', less harmful strains of strep and other, more aggressive strains. The suggested equation for PANDAS is that you need a susceptible individual an aggressive strain of strep and "bad timing" (i.e. occurring at an age when the individual has not yet developed a mature immune response to strep).

Thus, the following equation is given for PANDAS:

Susceptible Individual + 'Mean Strep' + Bad Timing = PANDAS (or SC)

The bad timing part could be closely linked to susceptibility, since a person who is not necessarily genetically predisposed to develop an autoimmune reaction to strep may be susceptible due to other factors. Such factors could be that the immune system is weakened by repeated strep infections, for example (again, which may or may not have been asymptomatic,) or that the blood brain barrier is temporarily in a weakened state, thus letting in the antibodies. (How do we know the antibodies are in the brain? Well, because they are present in the cerebrospinal fluid.)

We are now getting close to the really interesting part of this text: that is to why, on the PANDAS scene, the dichotomy of an emotional trauma or a post-infectious process is a false dichotomy. You see, emotional trauma – in scientific literature referred to as 'acute stress' – *increases permeability of the blood-brain-barrier!* (6).

A Glance at Epidemiology and Back to LeRoy

But before connecting the dots, I need to tell you a little something about epidemiology. Looking at SC and RF, which, as you recall, are closely linked to PANDAS, we can see that these normally occur as single cases. Even if strep is contagious, the susceptibility and bad timing part of the equation mean that we see individual cases. Nevertheless, epidemics of both SC and RF have occurred throughout history. How can this be explained? Probably this means that at least one thing in the equation is different. The most probable one is that at these times there is a more aggressive strain of strep, one that overrides the normal susceptibility factor in many individuals.

So, if we have an outbreak of what certainly, when it comes to symptomatology, looks like PANDAS in a high school, how can some of the patients seem to be triggered by an emotional trauma (acute stress), while others are not? First, just let me point out that in the documentary it was mentioned that while all the students had tics, several also had other symptoms such as fatigue and facial nerve paresis, or Bell's palsy, which is thought to be caused by an inflammatory condition. Lori, one of the girls in the film, describes the L'hermitte's sign, an electric current-like sensation down the back. L'hermitte's is a known neurological sign which is thought to indicate dysfunction of the dorsal columns of the cervical spinal cord. It is most often associated with Multiple Sclerosis, but also with other conditions such as B12-deficiency. Symptoms such as stuttering and feelings of not being 'one's self' are also mentioned in the film. Both are quite common in PANDAS patients.

Any other symptoms the LeRoy girls have experienced is shrouded in darkness as the film does not explore this topic further. But altogether, the picture points towards a physiological condition. How the Dent neurologists can overlook this is a mystery to me. In the film, Dr Jennifer McVige, a neurologist at the Dent institute who advocates the conversion disorder theory, states that the placebo effect explains why antibiotics seem to work for the group of LeRoy girls who were treated for PANDAS. It is highly surprising that a person of such education would not consider that the same explanation could be true as to why treatment for conversion disorder seems to work for her patients.

The truth is that if we suppose that all LeRoy cases are due to a post-infectious encephalitis-like process, which actually seems – given the knowledge of the PANDAS nature of symptoms, the kinship with and epidemiology of SC and RF – to be the most probable explanation, then most of the girls would get better in time even without treatment. PANDAS is known to have a saw-toothed course. However, my hypothesis is that the LeRoy students treated for conversion disorder will have exacerbations with new infections to a higher degree than the students treated with prophylactic antibiotics.

It is probably clear to the reader already that I think *there is no LeRoy controversy* other than in the minds of some people. If a very aggressive strain of strep, perhaps even a strep prone causing post-infectious autoimmunity, affects an area and spreads within a school, susceptible individuals will develop the disease. I have mentioned the susceptible individuals may be persons prone to autoimmunity in general or specifically to autoimmune reactions to strep. It is known that SC and RF runs in families. Therefore some sort of genetic predisposition is highly probable. However, the girls who did not have this predisposition may have developed the same autoimmune reaction after this acute strep infection pervaded their school when combined with a state of acute stress (emotional trauma) which made their blood-brain barrier more permeable.

'Fright' or Emotional Trauma

The connection to emotional trauma is not new. In fact, in his book, *On Chorea and Choreiform Affections* (1894), William Osler states that 15.5% of the cases of Sydenham's Chorea he reviewed were caused by 'fright':

In 86 cases, 15,5 per cent, fright was given as the exciting cause. In the majority of these no very close connection existed between the fright and the onset of the chorea, as usually an interval of two or more days had elapsed but in a few cases, the attack came on at once. (7)

When I researched a parental forum on the internet, I also found some cases of PANDAS associated with ‘fright’, or emotional trauma as we would rather put it nowadays. Examples of these traumas were: being seriously attacked by a dog, watching a house with people in it burn down, being nearly drowned.

I think the most probable explanation of the role of emotional trauma in these cases lies in the effect acute stress has on the immune system and in particular on the BBB. We also know that the two immune systems, the innate and the adaptive, do not work well at the same time. When one is operating the other ‘stands back’. In a state of prolonged acute stress (normally acute stress would activate the innate immune system to set off a flee or fight reaction, or heal a bleeding wound), the adaptive immune system (which handles infections) cannot do its job well (8).

Thus, in conclusion, yes, an emotional trauma might result in some PANDAS cases, but this makes the person susceptible to the post-infectious auto-immune process, not what causes the symptoms on a psychological level. Nevertheless, learning to cope with the traumatic event will probably help those individuals by making their immune system and BBB more functional again. On the other hand, a treatment for conversion disorder would not help the affected individuals who caught PANDAS because of genetic susceptibility. Furthermore, the individuals with the acute stress involvement at onset will probably gain more from having their illness treated both at the stress level and at the autoimmune, infectious level.

This connection between ‘fright’ and the BBB becoming increasingly permeable by acute stress may also explain the idea, now considered a myth, that stuttering was caused by being scared as a child, as stuttering is linked to PANDAS.

Age and Sex

But we do still have some loose ends to tie up in LeRoy, don’t we? Why teenagers, and why girls? It is well known that Rheumatic Fever affects more girls than boys, and one study of Sydenham’s Chorea shows that after 9 years of age there is a female predominance (9). The authors write: “There was an increased incidence of Sydenham’s chorea after 9 years of age in girls possibly suggesting the influence of female sex hormones.”

Thus, it may very well be that various complications of strep infections have different effects according to age and sex. Therefore, this particular variant, the ‘LeRoy strep,’ affects girls more than boys. A certain age group sharing classes, the cafeteria, corridors and locker rooms in a school would be affected more by a contagious disease. Unfortunately, teenage girls will probably be diagnosed as with conversion disorder. A multitude of conditions throughout history, such as autism, epilepsy and ulcers have been believed to be psychogenic in origin until proven wrong. I think a fair conclusion is that man is prone to dismiss conditions as psychogenic as long as the biological cause remains unknown.

And yes, PANDAS is a puzzling condition with many faces. However, it is my firm belief that understanding PANDAS, or encephalitis-like post-infectious conditions with psychiatric presentations, is the key to the understanding and treatment of many psychiatric conditions. To have such a key in front of you and to not examine it further, just because you do not yet know which

lock it fits, is almost a crime in my eyes.

Gunilla Gerland, 2013

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