The immune system in Gilles de la Tourette syndrome

PART I

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Presentation outline

1. Tourette syndrome and infections: PANDAS as the prototype of “post-infectious tourettism”
   Epidemiology and diagnostic criteria

2. The organisation of immune response in Tourette syndrome

3. Autoimmunity in Tourette and post-streptococcal tourettism

Why is immunity explored in CTS?

- Common cold
- Dysphagia

- Tonsillitis

- Group A Streptococcus and PANDAS

- Compulsive and frequent urination
- Deterioration handwriting and school performance
- Diminished and regression of fine motor skills

- Lecouteux et al. / Child Adolescent Psychiatry 2010; Murphy et al. / Pediatrics 2012
STREPTOCOCCAL INFECTIONS & OCD/TIC DISORDERS:
epidemiological evidence

- Cross-sectional studies document an association between TS/OCD and raised anti-streptococcal antibody titres
  (Wallis et al., 2008; Cardona & Onofri, 2010; Merced-Arreola et al., 2001; Chau et al., 2012; Lépine et al., 2010; Martino et al., 2009; Rizzuto et al., 2004; Dehnbostel et al., 2009)

- Retrospective studies suggested higher risk of GAS infections in TS/OCD patients in the months prior to onset, but discrepancy exists
  (Wallis et al., 2010; Leclerc et al., 2008; Schrag et al., 2005)

- Prospective studies were inconclusive in showing a clear association
  (Lee et al., 2008; Prina et al., 2007; Acheson & MacMillan, 2004; Murphy et al., 2004; Martino et al., 2005; Badger et al., 2001)

- Multi-centre prospective studies comparing PANDAS to non-PANDAS GAS/Inx failed to show a higher number of GAS-linked exacerbations
  (Shulman et al., 2000; Leclerc et al., 2008; Leclerc et al., 2008; Shulman et al., 2000; Leclerc et al., 2008; Leclerc et al., 2008; Leclerc et al., 2008)

Are PANDAS criteria reliable???
Flow cytometry

- Activated B-lymphocytes are increased in number in GTS
- 65-75% higher number of CD69+ B-cells (Moller et al., J Neurol 2008)
- Fas is over-expressed on the surface of B-cells (Kehn et al., Eur J Psychiatry 2004)
- Increased apoptosis of T-lymphocytes (secondary to functional exhaustion)
- 65% higher number of CD69+ T-cells (Moller et al., J Neurol 2008)

T regulatory lymphocytes (CD4+CD25+)

- Reduced number of Treg in children with GTS/OCD, particularly during symptom exacerbation (Moller et al., J Neurol 2008)
- No influence of exposure to GABA or anti-dopaminergic drugs
- Dopamine receptor D2 expressed on the surface of Treg has an inhibitory effect (Kehn et al., Neurol 2004)
- DRD5 mRNA levels may be higher in peripheral lymphocytes from GTS patients, and positively correlate to the severity of compulsions (Ferrini et al., J Neurol 2006)