# Childhood Post-infectious Autoimmune Encephalopathy: Telehealth Opportunities

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### Agenda

## Condition

- History of
  PANS/PANDAS/CPAE
- Pathophysiology
- Diagnosis
- Treatment
- Role of IVIG



**PANDAS:** Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcus

**PANS:** Pediatric Acute-Onset Neuropsychiatric Syndrome

**CPAE:** Childhood Postinfectious Autoimmune Encephalopathy



### NIMH - Sue Swedo, MD

- Based on experience at NIMH after an outbreak of Rheumatic Fever/Sydenham's Chorea in the late 1980's
- Abrupt onset OCD after streptococcal infections (PANDAS) in prepubertal children
- Later expanded to OCD after other infections (PANS)
- National university-based network:
  - Harvard
  - Stanford
  - University of Wisconsin
  - University of Arkansas
  - ✤ Dartmouth
  - Columbia
  - ✤ UCLA



- Biological explanation
- Overtreatment

## Response to Controversy

- Mouse models
  - Injury to BBB mediated by IL-17
  - Serum from patients causes OCD in mice
- Clinical research (BG imaging)
- Clinical outcomes research
  - Response to antiinflammatories
    - IVIG

# Pathophysiology

### Pathophysiology

Rheumatic feverSydenham's Chorea





Sweeten, Nature Medicine 9(7):823-5



Prospective community cohort study: 693 school-aged children followed for 8 months, strep cultures, movement, behavior assessments

- 3 months post-streptococcal infection:
  - 3x as likely to have movement problems
  - $\circ~$  2x as likely to have behavior problems
  - $\circ~$  Children with more strep infections had greater symptoms

Murphy TK, Snider LA, Mutch PJ, et al. Relationship of Movements and Behaviors to Group A Streptococcus Infections in Elementary School Children. Biol Psychiatry. 2007;61(3):279-284. doi:https://doi.org/10.1016/j.biopsych.2006.08.031 Denmark: January 1, 1996 to December 31, 2013, all children who received a throat culture (1, 067, 743 children, over 600,000 had throat culture)

- Presumed strep if given antibiotics in 2 weeks
- Presumed not strep if no antibiotics
- OCD increased 51% in presumed strep, 28% in not strep group
- Tics increased 35% in presumed strep, 25% in not strep group

Orlovska S, Vestergaard CH, Bech BH, Nordentoft M, Vestergaard M, Benros ME. Association of Streptococcal Throat Infection With Mental Disorders: Testing Key Aspects of the PANDAS Hypothesis in a Nationwide Study. JAMA Psychiatry. 2017;74(7):740-746. doi:10.1001/jamapsychiatry.2017.0995

### Diagnosis

- Dramatic onset of OCD/severely restricted food intake
- Presence of *at least two* of the following:
  - Anxiety
  - $\circ$  Emotional lability and/or depression
  - $\circ\,$  Irritability, aggression, oppositional behavior
  - $\circ$  Behavioral/Developmental regression
  - Deterioration in school performance (ADHD, memory, cognition)
  - Sensory or motor abnormalities (tics, chorea)
  - Somatic signs and symptoms (sleep, enuresis, urinary frequency)

Chang, et al Clinical Evaluation of Youth with Pediatric Acute Onset Neuropsychiatric Syndrome (PANS): Recommendations from the 2013 PANS Consensus Conference. Journal of Child and Adolescent Psychopharmacology. 25(1):3-13, 2015.

### Somatic

- Tics
- Urinary frequency/enuresis
- Handwriting changes



### Handwriting

PROJECTS ARE MAINLY DONE IN CLASS; PRESENT WEEK OF MAY 18-22
This completed worksheet is due Wed, April B at the beginning of class. HANDED OUT April 1.2015 You may gather information using ColtureGrams, the classroom textbook, by looking at maps, library book, the leternet, of any other printed resources. LIST ALL RESOURCES YOU USED ON ONE PAOEADD TO IT AS YOU USE MORE RESOURCES THROUGHOUT THE PROJECT. Even people you talk with/interview who are from the country or extremely knowledgeable about it can be considered a resource. The mene completely you fill out this sheet, the more information you will have to pull from when you do various aspects of your project in class. You may use words and/or illustrations. ******ATTACH EXTRA PAPER IF YOU NEED IT. WE WILL BEGIN WORKING ON THIS PROJECT IN CLASS APRIL 8.*****
Country name Boli VIO_ Population 10,631,486
Ather native languages. Hola - Hello, Advos- Goodbye, Por
favor-please, Gracias-Thank you, or-yes, no-no.
Main Religion(s) and % Bornan Catholic 93 %, Protestant 5 %
Name/describe geographical features of the country (landforms, water bodies, forests, volcanoes, deserts, etc.)
One of the main water boddies is the second
largest lance. The name is lake Tilicaca. Bach
In 1544 many perces of silver was found at the
base of rich mountain hill.
Government: Leaders, type of government system (with explanation), government conflicts, etc.
Capital-La Paz, Head of State-Pres, Evomprales
Head of Governent - Evo morales, Members of the
Gongreso Nocional are cleared to represent their homoisticts.
The voting age is 18.
Daily Life - include at least 10 ideas of food, clothing, shelter, schools, sports & activities, holidays, animals, plants, etc. and <u>know</u> how they are different from or similar to the U.S. (Don't have to write down similarities/differences.)
The Bolivian diet centers on the polator There
are more types of potatoes in the Andes then
enjumere splee in the world. The Bolivian people
usually have soup, with maniforferent kinds of vegetables,
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Handwriting Changes

Country name Boli VIO. Population 10,631, 486 Main Language(s) Spanish, Aymara, Quechua, and thirty-four Other native languages. Hola - Hello, Alios- Goodbye, R Hola - Hello, Adio's - Goodbye, Por tavor-please, Gracias-Thank you, of-yes, no-no. Main Religion(s) and % Poman Catholic 93 %, Protestant 5 %. ne/describe geographical features of the country (landforms, water bodies, forests, volcanoes, deserts, etc.) One of the main water boddies is the second brarst lane. The name is lake Iticaca. Bach The In 1544 many peices of silver was found at i tame DUt base of rich mountain hill, Government: Leaders, type of government system (with explanation), government conflicts, etc. ine Capital-la Paz, Head of State-Pres, Evomprales PLM PLM Head of Governement - Evo morales, Members of -WHI trongress Nocional are cleared to represent their home 10mber The voting age is 18. Daily Life - include at least 10 ideas of food, clothing, shelter, schools, sports & activities, holidays, animals, pla etc. and know how they are different from or similar to the U.S. (Don't have to write down similarities/different Conclusion The Bolivian diet centers on the polator These Carn are more types of potatoes in the Andes then enjumere celes in the world. The Bolivian people the USUALLY Marc SOUP, with manijorfferent kinds of vegetables, the 10+

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### Cognitive/Behavior

- Separation anxiety
- ADHD
- Developmental regression
- Academic regression



#### Banner Children's.

## Treatment



### Theory: Reduce inflammation

- Tiered treatment:
  - Antibiotics
  - Nonsteroidal medications (ibuprofen, naproxen)
  - Less common, Prednisone
  - Much less common, Intravenous immune globulin

### Immunology, Immunomodulation, and IVIG







What we ask our immune system to do every day







100,000 different possible house keys

1,000,000 different possible car keys



Sometimes one key fits two locks







# Why is this so hard?

- The bacteria that are triggering the autoimmune reaction are everywhere
- Other types of infections can trigger the same immune cross reaction issues
- The antibodies can last months, but the cells that produce them can live for decades
- Late recognition and delayed treatment can lead to damage and persistent defects

## Telehealth





- 10 year old boy
- Strep pharyngitis
- 10 days later, he had overnight refusal to eat anything that his sister breathed on
- Seen in clinic 4 months after onset
- Treated with naproxen and symptoms resolved in one week
- Naproxen with flares for 2 years with viral illness





# Story: 7-year-old girl with 3 siblings

### Influenza

- 1 week later:
- OCD
- Restricted eating
- Tics (eye blinking, throat clearing)
- Anxiety
- Bedwetting



## Symptoms

- Weight loss
- Weather obsession/compulsions
- School refusal
- Handwriting decline
- Slept on parents' floor
- To bathroom with mother



## Treatment

- Naproxen
- Azithromycin
- Prednisone



## Resolution

### • Resolved symptoms

Refused to return to previous routine



## Accommodations

- Served all meals in her room watching videos
- No school
- No chores
- Routine expectations for other children

Case 3: Severe PANS

- •7 year old boy
- •Previously healthy, normal frequency/severity of infections
- •Family history of autoimmune diseases
- •6 year old sibling, overall healthy also
- Several strep infections this year

# Symptoms at onset

- Strep pharyngitis
- Sudden onset of all symptoms, over a 48 hour period
- Fear of flies because of germs and uncleanliness
- Fear of food contamination
  - Food restriction and refusal
  - Weight loss
- Separation anxiety, mood swings
- Developmental regression, loss of math skills, baby talk
- Increased urinary frequency
- Thoughts of self harm



# Symptoms continued

### • OCD

- Thinks about death, afraid of harming others
- Disgusted with body waste, toilet routines
- Hand washing rituals
- Licks hands because they always feel sticky
- Compulsive counting, ordering, and sorting
- Eating toilet paper
- CY-BOCS 35



## **Prior treatments**

- Seen by outside physician, collaboration with Tucson via telehealth
  - Azithromycin
  - Ibuprofen
  - Melatonin
- Initially improved
  - Less OCD
  - Improved appetite
  - Reduced thoughts of self harm



## Exacerbation and enrollment in clinical trial

- Contracted COVID, immediately back to severe symptoms including food refusal, thoughts of self harm, and severe OCD
- Because of severity of illness and the sudden onset of OCD was We elected to begin IVIG treatment
- 2g/kg IVIG over 2 days q3 weeks x3 treatments
- Objective improvement based on CGI and CYBOCS scores, mother estimates him to be '90 percent' better



# Conclusion

- PANS/PANDAS is a treatable condition
- Requires a diverse team
- Families are very stressed
- UA/Banner CPAE team is available to telehealth consultation to providers.
- We do need to see patients in person initially if we are going to provide direct care.

## Team

- Michael Daines, MD (immunology)
- Sydney Rice MD, MS (developmental pediatrics)
- Pawel Kiela DVM, PHD (microbiome and mice)
- Andrew Gardner, PHD, BCBA (psychology)
- Chelsea Carr, PHD, BCBA (psychology)
- Fayez Ghishan, MD (GI)
- Jessica West, RN
- Linnette Ortiz, MPH
- Joann Schultz
- Many students, residents, fellows

Connections

- <u>CPAE@bannerhealth.com</u>
- Jessica West, RN
- https://peds.arizona.edu/cpae

