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Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcus (PANDAS) Pediatric Acute Neuropsychiatric Syndrome (PANS)

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Module 1: OCD

ulsive ... I will not be obsessive compulsive ...
ulsive ... I will not be obsessive compulsive ...
ulsive ... I will not be obsessive compulsive ...
ulsive ... I will not be obsessive compulsive ...
ulsive ... I will not be obsessive compulsive ...



Psychiatry Academy
Massachusetts General Hospital

Can You Catch Obsessive-Compulsive Disorder?



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Research suggests that strep throat can cause O.C.D. in certain children — prompting yet another debate about the connection between physical illness and psychological disorder. By Lisa Belkin

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Pediatric
Autoimmune
Neuropsychiatric
Disorders
Associated with
Streptococcal infection



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Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcus (PANDAS): Diagnostic Features

- OCD and/or a tic disorder
- abrupt symptom onset or exacerbation vs. insidious
- pre-pubertal onset (age 3-12)
- episodic course vs. chronic
- temporal association of symptom onset or exacerbation in association with **Group A Beta hemolytic streptococcus (GABHS)**
- choreiform movements present
- *(Swedo, Leonard, et al. Am J Psych 1998)*



Evidence for PANDAS:

Association Between Streptococcal Infection and Obsessive-Compulsive Disorder, Tourette's Syndrome (TS), and Tic Disorder

(Mell, L. Davis, R. Owens, R.

Pediatrics 2005;116:56 DOI: 10.1542/peds.2004-2058)

- Objective. Using population-based data from a large West-Coast health maintenance organization, assessment of whether streptococcal infection was associated with increased risk for OCD, TS, or tic disorder.
- Methods. Case-control study of children age 4- 13 receiving their first diagnosis of OCD, TS, or tic disorder between 12/92-12/99 at outpatient facilities. Cases were matched to controls by birth date, gender, primary physician, and propensity to seek health care.

TABLE 3. Association of GABHS Infection and Risk for Disease

	Cases, n (%)	Controls, n (%)	OR	95% CI	TS ITAL ADEMY
All cases					
GABHS within 3 mo of onset					
Any	10 (6.9)	19 (3.1)	2.50	1.09, 5.70	
≥2	10 (6.9)	12 (2.0)	3.46	1.75, 11.1	
GABHS within 1 y of onset					
Any	24 (17)	57 (9.4)	1.81	1.17, 3.43	
≥2	10 (6.9)	12 (2.0)	3.46	1.75, 11.1	
OCD					
GABHS within 3 mo of onset					
Any	2 (6.1)	2 (1.6)	3.81	0.70, 35.5	
≥2	1 (3.0)	2 (1.6)	2.32	0.21, 25.6	
GABHS within 1 y of onset					
Any	4 (12)	17 (13)	0.99	0.31, 3.20	
≥2	1 (3.0)	2 (1.6)	2.32	0.21, 25.6	
TS, no OCD					
GABHS within 3 mo of onset					
Any	3 (7.3)	4 (2.2)	3.05	0.58, 16.2	
≥2	6 (15)	11 (6.0)	2.60	0.83, 8.12	
GABHS within 1 y of onset					
Any	6 (15)	2 (1.1)	13.6	1.93, 51.0	
Tic disorder only					
GABHS within 3 mo of onset					
Any	5 (7.1)	13 (4.4)	1.87	0.62, 5.66	
≥2	3 (4.3)	8 (2.7)	1.78	0.44, 7.18	
GABHS within 1 y of onset					
Any	14 (20)	29 (9.7)	2.06	1.19, 5.14	
≥2	3 (4.3)	8 (2.7)	1.78	0.44, 7.18	



Association Between Streptococcal Infection and Obsessive-Compulsive Disorder, Tourette's Syndrome, and Tic Disorder

(Mell, L. Davis, R. Owens, R.

Pediatrics 2005;116:56 DOI: 10.1542/peds.2004-2058)

- Results: Patients with OCD, TS, tics were more likely than controls to have had prior streptococcal infection (OR: 2.22; 95% CI: 1.05, 4.69) in 3 months before onset date. Risk was higher in children with multiple streptococcal infections within 12 months (OR: 3.10; 95% CI: 1.77, 8.96).
- Having multiple infections with group A B-hemolytic streptococcus within a 12- month period was associated with an increased risk for TS (OR: 13.6; 95% CI: 1.93, 51.0)
- Conclusion: PANDAS may arise as a result of a post-infectious autoimmune phenomenon induced by childhood streptococcal infection.

MONDAY
NOVEMBER 28



"I'd like to put you through a comprehensive stress test, which involves listening to my mother-in-law, balancing a checkbook, and babysitting a red-headed two year old."



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Evidence Against PANDAS

(Kurlan, R. and Kaplan, E.; *Pediatrics*; 2004; 113; 883-886)

- GABHS infection is very common in the school age period
- Rates of asymptomatic carriers are high
- Tics and OCD worsen during times of stress and can be worsened by other precipitants (fatigue, anxiety, etc.)
- For SC, choreoathetoid movements appear 3-5 months after GABHS; Swedo et al initially suggested infection up to 9 months before symptom onset may be acceptable for PANDAS diagnosis
- Most non-PANDAS TD patients have onset before puberty
- Clinical course: 53% of one series of 80 consecutively referred TS patients had sudden, explosive worsening or onset of tics (*Singer; Ped Neurol*, 2002)



Streptococcal Infection and Exacerbations of Childhood Tics and Obsessive Compulsive Symptoms: A Prospective Blinded Cohort Study (Kurlan R, Johnson D, Kaplan E, TSSG. Pediatrics; 2008;121:1188-1197)

- Study Design: 2-year NIMH prospective cohort study
- N = 40 PANDAS, 40 TD/OCD
- Subjects were systematically evaluated with office visits every 3 months; monthly throat cultures for 24 months
- Subjects were re-evaluated clinically within 3 days of clinical exacerbation; investigators were blind to infection status
 - Results: There were more infections and exacerbations in the PANDAS group compared to controls. Only 5/ 64 exacerbations were associated with strep infection (within 4 weeks), and all were in cases.
 - **But less than 25% of the exacerbations in PANDAS group were precipitated by strep infections!**
 - Conclusion: For children with clear-cut features of PANDAS, a low threshold for obtaining culture/titers with fever, sore throat and/or acute, explosive exacerbation of tics/OCD may be reasonable
 - Antibiotic treatment of acute streptococcus infection is indicated only for positive throat culture or rapid strep test

Streptococcal Upper Respiratory Tract Infections and Exacerbations of Tic and Obsessive-Compulsive Symptoms: A Prospective Longitudinal Study.

Leckman, J. King, R. Gilbert, D. Coffey, B. Singer, H. Dure, L. Grantz, H. Katsovich, L. Lin, H. Lombroso, P. Kawikova, I. Johnson, D. Kurlan, R. and Kaplan, E.
Journal of the American Academy of Child and Adolescent Psychiatry; 2011; Volume 50; (2); 108-118.



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Method: Prospective longitudinal design; N=31 PANDAS and 53 non-PANDAS subjects. Clinical symptoms and laboratory were evaluated regularly over 25 months. Additional testing occurred at the time of any tic or OCD exacerbation. Lab personnel were blind to clinical status, and investigators were blind to lab results.

Results: No group differences were observed in number of clinical exacerbations or number of new onset GABHS infections.

On only 6 occasions of a total of 51 (12%), a newly diagnosed GABHS infection was followed, within 2 months, by a tic or OCD exacerbation. In each case, this occurred in the non-PANDAS group.

Conclusion: This study provides no evidence for a temporal association between GABHS infections and tic/OCD exacerbations in children who meet published diagnostic criteria for PANDAS.

Demographics and Clinical Characteristics at Baseline



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Variable	n	PANDAS Patients (n = 31)	n	Non-PANDAS Patients (n = 53)
Age (years), mean \pm SD (range)*	31	9.6 \pm 1.9 (6.0-13.2)	53	10.5 \pm 1.8 (6.6-13.9)
Girls (%)	31	19%	53	26%
Caucasian (%)	31	100%	53	94%
Parent education (years), mean \pm SD	30	15.5 \pm 2.5	53	15.1 \pm 2.7
Primary diagnoses (%)				
TS (including chronic tics)	26	84	49	92
OCD	22	71	35	66
Age of onset (years), mean \pm SD (range)				
TS (including chronic tics)	26 ^a	5.8 \pm 2.1 (2-9)	49 ^a	6.1 \pm 1.9 (3-10)
OCD	22 ^b	6.6 \pm 2.2 (2-10)	35 ^b	6.6 \pm 1.8 (3-10)
Baseline symptom severity by diagnosis, mean \pm SD				
TS (including chronic tics) ^c	26 ^a	18.5 \pm 9.1	49 ^a	17.5 \pm 8.8
OCD ^d	22 ^b	10.9 \pm 8.4	35 ^b	12.2 \pm 5.9
Other DSM-IV diagnoses (%)				
ADHD	31	42	53	53
Separation anxiety	31	13	53	11
Specific phobia	31	3	53	11
Major depression	31	6	53	11
Symptom severity, mean \pm SD				
ADHD rating scale ^e	31	18.6 \pm 13.9	53	22.2 \pm 14.3
ASQ-P ^f	31	8.7 \pm 7.4	53	10.5 \pm 8.2
CDI ^g	31	5.8 \pm 6.5	53	5.8 \pm 6.3
MASC ^h	31	46.4 \pm 14.1	53	46.7 \pm 19.4
CGAS-Investigator ⁱ	31	77 \pm 12.9	53	75.2 \pm 12.9
Positive family history ^j (%)				
Tics	31	37	53	42
OCD	31	40	53	38
ADHD	31	40	53	37
Anxiety disorder	31	52	53	42
Major depression	31	60	53	38
Rheumatic fever	31	20	53	8

Clinical Exacerbations of Tic and/or Obsessive Compulsive Symptoms (OC)

	PANDAS (n = 31)	Non- PANDAS (n = 53)	Total
Total number of exacerbations	25	34	59
Number of subjects with exacerbations	16	20	36
Number of subjects with multiple exacerbations	6	7	13
Maximum number of exacerbations per subject	3	5	5
Tic exacerbations	14	18	32
Number of subjects with tic exacerbations	10	16	26
OC exacerbations	8	14	22
Number of subjects with OC exacerbations	6	8	14
Combined tic + OC exacerbations	3	2	5
Number of subjects with tic + OC exacerbations	3	2	5

Note: PANDAS = pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections.

Relative Risk for Newly Diagnosed Group A β Hemolytic Streptococcal (GABHS) Infections Controlling for Age

PANDAS/Non-PANDAS	Relative Risk	95% CI
Relative risk for definite GABHS infections	0.50	0.20-1.22
Relative risk for possible GABHS infections	1.19	0.54-2.65
Relative risk for definite + possible GABHS infections	0.81	0.45-1.43

Note: None of the relative risks were statistically significant. CI = confidence interval; PANDAS = pediatric autoimmune disorders associated with streptococcal infections.



Clinical Factors Associated with PANDAS

(Murphy, T. Storch, E. Lewin, A. Edge. P. Goodman, W. Journal of Pediatrics, 2011, in press)

- Objective: To explore associated clinical factors in children with Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal infections (PANDAS).
- Design: Children with tics, obsessive-compulsive disorder, or both (N = 109) were examined with personal and family history, diagnostic interview, physical examination, medical record review, and measurement of baseline levels of streptococcal antibodies.

Table 1. Subject demographics by group classification

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	PANDAS			Without PANDAS		
	Total (%)	M (%)	F (%)	Total (%)	M (%)	F (%)
Subjects enrolled	41	28 (68)	13 (32)	68	38 (56)	30 (44)
Ethnicity						
Hispanic	2 (5)	2 (7)	0	5 (7)	4 (10)	1 (3)
Asian	0	0	0	3 (4)	3 (8)	0
African American	1 (2)	1 (4)	0	0	0	0
Caucasian	38 (93)	25 (89)	13 (100)	60 (88)	31 (82)	29 (97)
Diagnosis						
OCD, no tics (n = 22)	8 (20)	5 (18)	3 (23)	14 (21)	4 (11)	10 (33)
Tic, no OCD (n = 19)	5 (12)	3 (11)	2 (15)	14 (21)	10 (26)	4 (13)
OCD+tic (n = 68)	28 (68)	20 (71)	8 (62)	40 (59)	24 (63)	16 (53)
ADHD (n = 56)	25 (61)	18 (64)	7 (54)	31 (46)	20 (53)	11 (37)
Affective instability	24 (59)	15 (54)	9 (69)	42 (62)	24 (63)	18 (60)
Psychotic symptoms	5 (12)	4 (14)	1 (8)	6 (9)	3 (8)	3 (10)
Separation anxiety	12 (29)	8 (29)	4 (31)	15 (22)	7 (18)	8 (27)
Duration of illness, years*	2.8	2.8	2.7	3.9	3.8	4.0
Age at onset, years	5.9	5.8	6.1	5.6	5.8	5.5
Ratings						
CYBOCS	21.8 ± 7.3	21.2 ± 7.6	22.8 ± 6.7	20.6 ± 9.6	19.9 ± 10.1	21.3 ± 8.9
YGTSS	21.7 ± 9.9	19.56 ± 9.7	21.2 ± 10.8	17.2 ± 9.9	18.2 ± 10.3	15.5 ± 9.2



Table III. Titer assessments by groups

	PANDAS (n = 39)*	Without PANDAS (n = 60)*		
	n (%)	n (%)	χ^2	P value
Elevated ASO	23 (59)	22 (37)	4.7	.03
Elevated anti-DNaseB	19 (49)	24 (40)	.73	.39
Elevated anti-Acho	14 (36)	15 (25)	1.4	.24
No elevations	0 (0)	22 (37)	40.1	<.0001
1 titer elevations	16 (41)	16 (27)	2.2	.13
2 titer elevations	21 (54)	19 (32)	4.8	.03
3 titer elevations	2 (5)	3 (5)	t	.66



Clinical Factors Associated with PANDAS

(Murphy, T. Storch, E. Lewin, A. Edge, P. Goodman, W. Journal of Pediatrics, 2011, in press)

- Results: Significant group differences were found on several variables, such that children in whom PANDAS (vs. without PANDAS) were more likely to have had
 - dramatic onset
 - definite remissions
 - remission of neuropsychiatric symptoms during antibiotic therapy
 - history of tonsillectomies/adenoidectomies
 - evidence of group A streptococcal infection
 - clumsiness
- Conclusion: Identification of clinical features associated with PANDAS should assist in delineating risks for this subtype of obsessive-compulsive disorder/tics.

Hierarchy of Pediatric Acute Onset Neuropsychiatric Syndrome (Swedo et al. *Pediatr Therapeut* 2012; 2:2. 100011)



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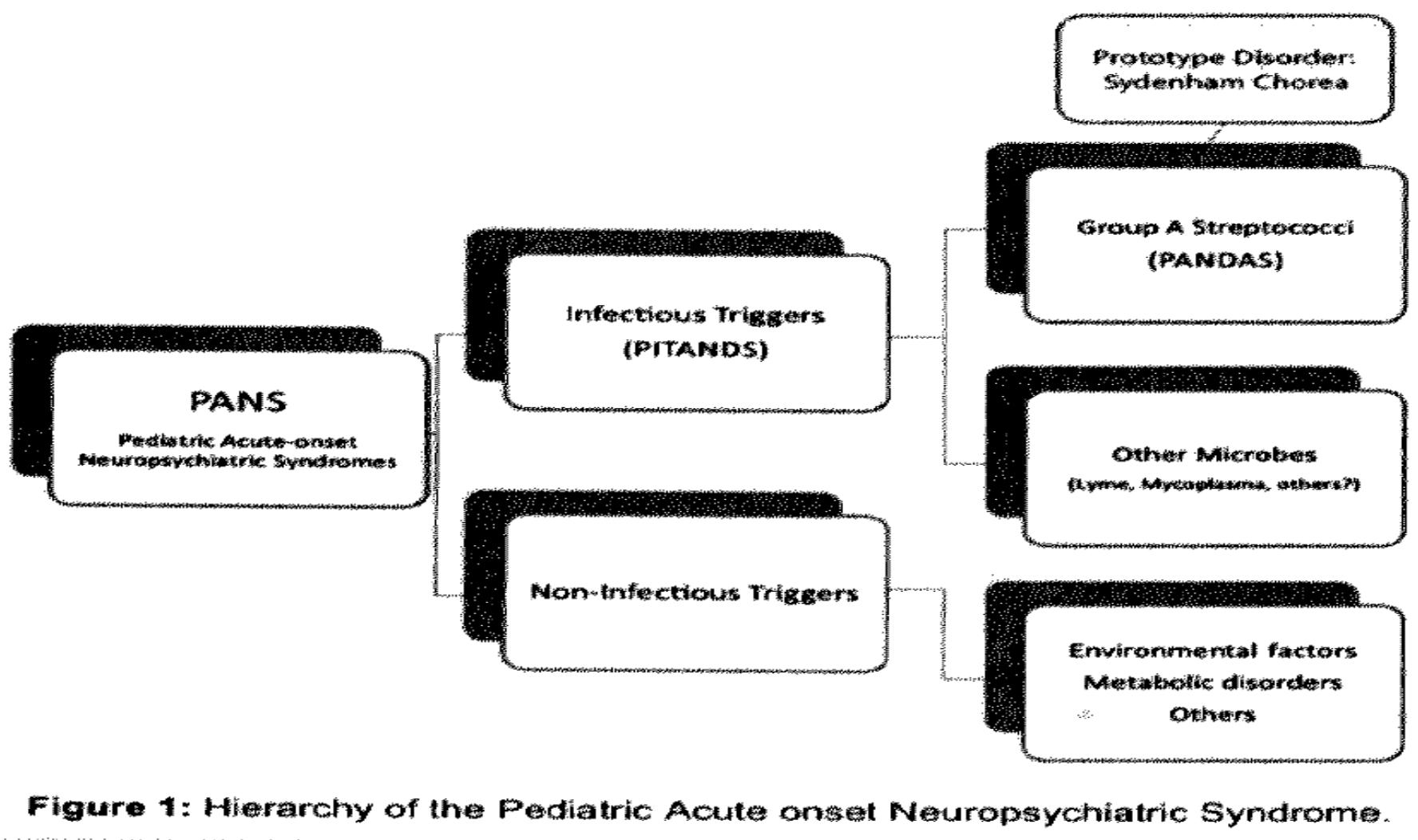


Figure 1: Hierarchy of the Pediatric Acute onset Neuropsychiatric Syndrome.

Swedo et al 2012; Diagnostic Criteria Proposed for Pediatric Acute-onset Neuropsychiatric Syndrome (PANS)



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Criterion	Description
I	Abrupt, dramatic onset of obsessive-compulsive disorder or severely restricted food intake
II	Concurrent presence of additional neuropsychiatric symptoms, with similarly severe and acute onset, from at least two of the following seven categories (see text for full description): 1. Anxiety 2. Emotional lability and/or depression 3. Irritability, aggression and/or severely oppositional behaviors 4. Behavioral (developmental) regression 5. Deterioration in school performance 6. Sensory or motor abnormalities 7. Somatic signs and symptoms, including sleep disturbances, enuresis or urinary frequency
III	Symptoms are not better explained by a known neurologic or medical disorder, such as Sydenham chorea, systemic lupus erythematosus, Tourette disorder or others.
	Note: The diagnostic work-up of patients suspected of PANS must be comprehensive enough to rule out these and other relevant disorders. The nature of the co-occurring symptoms will dictate the necessary assessments, which may include MRI scan, lumbar puncture, electroencephalogram or other diagnostic tests.



TABLE 1. OVERVIEW OF PANS EVALUATION

- Family history
- Medical history and physical examination
- Psychiatric evaluation
- Infectious disease evaluation
- Assessment of symptoms and history that points to need for further evaluation of immune dysregulation (autoimmune disease, inflammatory disease, immunodeficiency)
- Neurological assessment
- Assessment of somatic symptoms, including possible sleep evaluation
- Genetic evaluation

PANS, pediatric acute-onset neuropsychiatric syndrome.

Clinical Evaluation of Youth with PANS: Recommendations from the 2013 Consensus Conference. Chang, K. et al. JCAP; DOI:10.1089/cap.2014.0084

Clinical
Evaluation of
Youth with PANS:
Recommendation
s from the 2013
Consensus
Conference.
Chang, K. et al.
JCAP;
DOI:10.1089/cap.
2014.0084

TABLE 2. DIFFERENTIAL DIAGNOSIS FOR YOUTH WITH PANS

- Obsessive compulsive disorder
- Anorexia nervosa
- Avoidant/restrictive food intake disorder (ARFID)
- Tourette syndrome
- Transient tic disorder
- Bipolar disorder
- Sydenham chorea
- Autoimmune encephalitis
- Systemic autoimmune disease^a
- Wilson's disease^a

^aRelatively rare conditions.

PANS, pediatric acute-onset neuropsychiatric syndrome.

Clinical Evaluation
of Youth with
PANS:
Recommendations
from the 2013
Consensus
Conference.
Chang, K. et al.
JCAP;
DOI:10.1089/cap.2
014.0084

General laboratory studies

All patients meeting PANS criteria should have the following:

- Complete blood cell count with manual differential
- Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP)
- Comprehensive metabolic panel
- Urinalysis (to assess hydration) and to rule out inflammation for children with urinary complaints; clean-catch urine culture for those with pyuria
- Throat culture, anti-streptolysin O (ASO) and anti-DNAse B



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Pediatric Acute Neuropsychiatric Syndrome (PANS)

*Murphy, T. Patel, P. McGuire, J. Kennel, A. et al Characterization of the
Pediatric Acute-Onset Neuropsychiatric Syndrome Phenotype*

*Journal of Child and Adolescent Psychopharmacology; DOI:
10.1089/cap.2014.0062*

TABLE 1. FREQUENCY OF CLINICAL SYMPTOMS

	n (%)
Anxiety	43 (100)
Panic/Somatic ^a	15 (35)
Generalized anxiety disorder (GAD) ^a	20 (47)
Separation anxiety disorder (SAD) ^a	33 (77)
Social phobia ^a	12 (28)
School avoidance ^a	20 (47)
Mood and behavioral symptoms	43 (100)
Emotional lability and/or increased irritability	43 (100)
Anxious/Depressed ^b	19 (46)
Withdrawal/Depression ^b	10 (24)
Somatic complaints ^b	9 (22)
Social problems ^b	2 (5)
Thought problems ^b	21 (51)
Attention problems ^b	8 (20)
Rule-breaking behavior ^b	3 (7)
Aggressive behavior ^b	12 (29)
Suicidality (n=33)	10 (30)
Behavioral regression	36 (84)
Deterioration in school performance	36 (88)
Sleep disturbance	36 (84)
Tics	30 (70)
Simple	30 (70)
Complex	12 (28)
Sensory abnormalities	26 (61)
Urinary problems	24 (56)
Frequent urination (pollakiuria)	19 (44)
Enuresis	11 (26)
Handwriting deterioration in youth ages 7-14 years (n=30)	17 (57)

Food restriction	20 (47)
ADHD diagnosis	20 (47)
Inattention ^c	11 (26)
Impulsivity/hyperactivity ^c	14 (33)
Oppositionality ^c	11 (26)
Irrational thinking and/or psychotic symptoms	12 (28)
Visual hallucinations	5 (12)
Olfactory hallucinations	4 (9)
Auditory hallucinations	3 (7)
Mydriasis	10 (23)
Choreiform movements	9 (21)
Anorexia (not caused by PANS-OCD)	5 (12)
Visuospatial/Motor impairment (n=42) ^d	28 (67)
Obsessive compulsive symptoms	
Harm to self and/or others	39 (91)
Ordering and/or arranging, symmetry	30 (70)
Contamination	29 (67)
Sexual and/or religious	16 (37)
Collecting and/or hoarding	14 (32)

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TABLE 2. FREQUENCY OF INFECTIOUS TRIGGERS AND ILLNESSES
BASED ON PARENT REPORT AND MEDICAL RECORD REVIEW

	n (%)
Infectious triggers	
Group A streptococcus (GAS)	25 (58)
<i>Mycoplasma pneumoniae</i>	5 (12)
Upper respiratory infection (URI)	16 (37)
Lyme	1 (2)
No infectious trigger	4 (9)
Other ^a	5 (12)
Medical history	
Frequent strep/Tonsillitis	31 (72)
Frequent URIs	25 (58)
Frequent ear infections	5 (12)
Pneumonia	5 (12)
Premature birth	6 (14)
Pregnancy complications ^b	5 (12)
Immune-based illness	22 (51)
Kawasaki's disease	2 (5)
Allergies	9 (21)
Asthma	7 (16)
Hashimoto's thyroiditis	1 (2)
Psoriasis	1 (2)
Neutropenia	1 (2)
Henoch-scholein purpura	1 (2)

^aUrinary tract infections, gastrointestinal illnesses, exposure to undiagnosed illness in sibling.

^bPre-eclampsia, induction, prenatal exposures, postnatal complications, abnormal Apgar scores.



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TABLE 3. CHARACTERISTICS OF YOUTH WITH PANS AND A COMPARISON BY TIC PRESENCE

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	Total sample (n=43) n (%)	Youth with tics (n=30) n (%)	Youth without tics (n=13) n (%)	χ^2	p value
Male	24 (56)	19 (63)	5 (38)	2.28	0.13
Comorbid ADHD	20 (47)	16 (53)	4 (31)	1.86	0.17
Comorbid non-OCD anxiety disorder	43 (100)	30 (100)	13 (100)	–	–
Elevated laboratory results					
Anti-DNAse B (n=42)	30 (71)	21 (70)	9 (69)	0.05	0.83
Anti-streptolysin O (ASO) (n=43)	16 (37)	12 (40)	4 (31)	0.33	0.57
Anti-nuclear antibodies (n=19)	1 (5)	1 (3)	0	0.49	0.49
Mycoplasma immunoglobulin M (IgM) (n=42)	9 (21)	5 (17)	4 (31)	1.41	0.23
Mycoplasma immunoglobulin G (IgG) (n=42)	27 (64)	20 (67)	7 (54)	0.64	0.42
Lyme screen (n=42)	5 (12)	5 (17)	0	2.27	0.13
Western blot confirmation (n=5)	0	0	0	–	–
Raji cell (n=42)	14 (33)	11 (37)	3 (23)	0.53	0.47
Low IgG (n=42)	2 (5)	2 (7)	0	0.94	0.33
Low IgA (n=42)	6 (14)	6 (20)	0	3.15	0.08
Low IgM (n=42)	0	0	0	–	–
Elevated IgE (n=42)	13 (31)	8 (27)	5 (38)	0.50	0.48

ADHD, attention deficit hyperactivity disorder; OCD, obsessive compulsive disorder; PANS, pediatric acute-onset neuropsychiatric syndrome.

**Lack of Association of Group A Streptococcal Infections and Onset of Tics:
European Multicenter Tics in Children Study**

Neurology 2022 Mar 15;98(11):e1175-e1183.

doi: 10.1212/WNL.0000000000013298. Epub 2022 Feb

Schrag,A, Martino,D et al. European Multicentre Tics in Children Study (EMTICS)



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Background and objectives: The goal of this work was to investigate the association between group A streptococcal (GAS) infections and tic incidence among unaffected children with a family history of chronic tic disorders (CTDs).

Methods: In a prospective cohort study, children with no history for tics who were 3 to 10 years of age with a first-degree relative with a CTD were recruited from the European Multicentre Tics in Children Study (EMTICS) across 16 European centers. Presence of GAS infection was assessed with throat swabs, serum anti-streptolysin O titers, and anti-DNAse titers blinded to clinical status. GAS exposure was defined with 4 different definitions based on these parameters. Cox regression analyses with time-varying GAS exposure were conducted to examine the association of onset of tics and GAS exposure during follow-up. Sensitivity analyses were conducted with Cox regression and logistic regression analyses.

Results: A total of 259 children were recruited; 1 child was found to have tic onset before study entry and therefore was excluded. Sixty-one children (23.6%) developed tics over an average follow-up period of 1 (SD 0.7) year. There was a strong association of sex and onset of tics, with girls having an \approx 60% lower risk of developing tics compared to boys (hazard ratio [HR] 0.4, 95% confidence interval [CI] 0.2-0.7).

However, there was **no statistical evidence to suggest an association** of any of the 4 GAS exposure definitions with tic onset (GAS exposure definition 1: HR 0.310, 95% CI 0.037-2.590; definition 2: HR 0.561, 95% CI 0.219-1.436; definition 3: HR 0.853, 95% CI 0.466-1.561; definition 4: HR 0.725, 95% CI 0.384-1.370).

Discussion: These results do not suggest an association between GAS exposure and development of tics

PANDAS and PANS: *Summary*



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- There is mixed data regarding the diagnosis of PANDAS in children with OCD and tic disorders.
- Streptococcus may be one of several precipitants of explosive OCD/tic onset or exacerbations, particularly in those with fever, and/or sore throat or recent exposure.
- Positive cultures and rising antibody titers can be confirmatory.
- It is not unusual for tics to become “explosive” or onset acutely, but it is unusual for this to occur in pediatric OCD.
- Non-strep infectious and non-infectious triggers can be associated with acute onset OCD symptoms.
- If there is suspicion of an infectious trigger, a workup for inflammatory origin is recommended. Antibiotic treatment of the infectious agent is indicated.
- Long-term use of antibiotics, NSAIDS, steroids and/or immunomodulatory treatment is not established currently.