

# Pediatrics teleECHO

## Early Onset Psychosis: Etiology and Treatment

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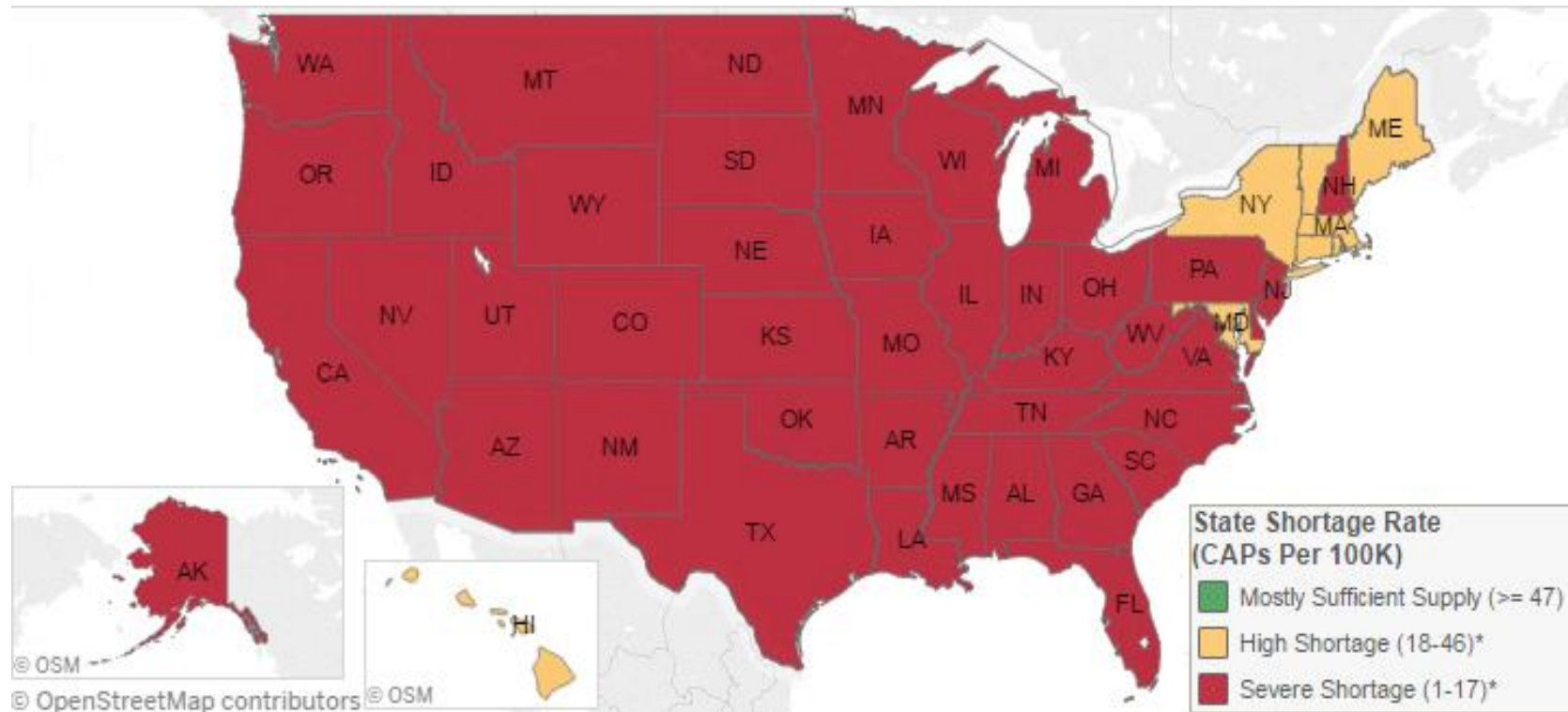
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# Child & Adolescent Psychiatrist Workforce Map by State (AACAP)



# Utah Workforce Distribution (AACAP)

## UTAH

### Child and Adolescent Psychiatrist (CAP) Workforce Distribution Map

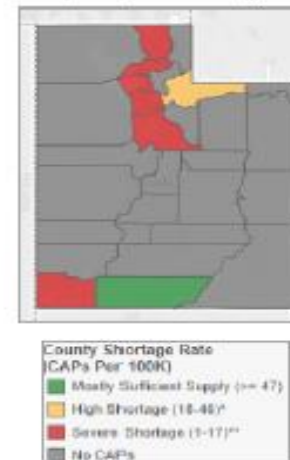
Practicing Child and Adolescent Psychiatrists by State 2015  
Rate per 100,000 children age 0-17



State CAPs per 100,000 children age 0-17



Practicing Child and Adolescent Psychiatrists by County 2015  
Rate per 100,000 children age 0-17



\*Council on Graduate Medical Education, Re-examination of the Academy of Physician Supply made in 1980 by the Graduate Medical Education National Advisory Committee for selected specialties, Bureau of Health Professions in support of activities of the Council on Graduate Medical Education, 1990, Cambridge, ABT Associates.

\*\*Kim WL, American Academy of Child and Adolescent Psychiatry Task Force on Workforce Needs. Child and adolescent psychiatry workforce: A critical shortage and national challenge. Acad Psychiatry. 2003;27:273-82.

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# Pediatric Behavioral Health Issues. . .

- Approximately 1 in 5 children in the U.S. suffer from a mental illness
- Yet 80% never receive treatment
- 75% of the children who do have psychiatric disorders are normally seen in their primary care clinic
- 85% of prescribing is done by the primary care physician
- Pediatricians and primary care doctors are on the front line. . .



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# Psychosis

- “Psychosis is defined as the severe disruption of thought and behavior resulting in the loss of reality testing. The diagnosis of psychosis is based on overt changes in a person’s behavior and functioning, with evidence of disrupted thinking evident on mental status examination” – AACAP Practice Parameter
- The diagnostic assessment of psychotic symptoms in youth presents unique developmental concerns. Misdiagnosis is common, often as bipolar disorder or severe depression with psychotic features, personality disorders, OCD, and developmental syndromes.
- Most children who report hallucinations do not meet criteria for schizophrenia, and many do not have a psychotic illness.
- Normative childhood experiences, including overactive imaginations and vivid fantasies, can be misinterpreted as psychosis.

# Overview

- Our duty to take a good history and evaluate MSE carefully
- Psychotic symptoms can present in a variety of disorders
  - Affective Disorders with psychotic features such as MDD or Bipolar Disorder are more common than youth having primary psychotic disorders
- 40-60% of youth with bipolar disorder have psychotic features
- 15-35% of youth with depression can have psychotic symptoms
- Between the ages of 13-19 years, prevalence of schizophrenia is approximately 0.54%
- Lifetime prevalence is estimated at 0.3% - 0.7%; male-to-female ratio is approximately 1.4:1
- Peak age of onset is 15-25 years in men and 20-30 years in women

# Overview. . .

- 50% of cases are diagnosed before the age of 25 years.
- Childhood Onset Schizophrenia (COS) is diagnosed before the age of 13 and carries a poor prognosis. COS is quite rare, with an incidence lower than 1 in 10,000 children
- Incidence of Early Onset Schizophrenia (EOS) is less clear but up to 5% of adults became ill before 14 yrs of age and up to 20% of adults before the age of 18
- More males than females experience EOS/COS, 2:1
- About 3% of first episode cases can be attributed to a medical condition
- Consider substance induced and the role of Cannabis in the duration and the onset of symptoms
  - Earlier age at onset of cannabis use is associated with an earlier age of onset of psychosis

# Overview. . .

- Diagnostic criteria for COS and EOS are the same as those used for adults in DSM V, except psychotic symptoms present before the age of 13 in COS and 18 in EOS
- Many youth have difficulty recognizing their symptoms as abnormal and may not complain about the hallucinations spontaneously
- Youth with COS/EOS show:
  - Problems with attention, socialization compared to adult onset
  - Communication problems is a predictor of outcome in youth at high risk for psychosis – monitor poverty of speech and subtle communication disturbances during interviews
  - Also see cognitive impairment and social withdrawal
    - Impaired memory, attention, verbal processing, and executive function which correlate with loss of function in school, community and social relationships



# Differential Diagnosis. . .

- Hallucinations **do not equal** “psychosis”
- Medical Conditions - including CNS infections, delirium, brain neoplasms, endocrine disorders, genetic syndromes (e.g., velocardiofacial [22q11] syndrome), encephalitis, autoimmune disorders, and toxic exposures.
- Drugs of abuse - dextromethorphan, LSD, hallucinogenic mushrooms, psilocybin, peyote, cannabis, stimulants, and inhalants. Prescription drugs - corticosteroids, anesthetics, anticholinergics, antihistamines, and amphetamines
- Schizoaffective Disorder
- Affective Disorders – Bipolar Disorder, Major Depressive Disorder
- Anxiety Disorders and OCD can present with intrusive thoughts/hallucinations

# Differential Diagnosis. . .

- Differentiating EOS and COS from other mental health conditions is very important
- Patients with bipolar disorder can experience hallucinations and delusions but also has clinical characteristics of mania, disorganized behaviors, depression or dysregulated moods. Followed longitudinally can clarify diagnosis
- Trauma may have trauma-related hallucinations associated with PTSD, nightmares, dissociations, trance like states and these symptoms can improve with psychotherapeutic and/or social interventions.
- Children with ASD may have odd beliefs, few friends, language delay, social awkwardness, concrete thoughts and difficulty interacting with other children
- Normative experiences – vivid fantasy play, magical thinking, hallucinations with falling asleep (hypnogogic) and awaking (hypnopompic), cultural beliefs, young children with fevers can be prone to hallucinations

# Prodromal onset. . .

- Most patients experience some degree of functional deterioration before the onset of psychotic symptoms, including social withdrawal and isolation, idiosyncratic or bizarre preoccupations, unusual behaviors, academic failure, deteriorating self-care skills and/or dysphoria.
- These changes may be associated with depression, anxiety, aggressive behaviors, or other conduct problems, including substance abuse, which can often confuse the diagnostic picture.
- The prodromal phase may vary from an acute marked change in behavior to a chronic insidious deterioration. — Practice Parameter AACAP

# Presenting Symptoms. . .

- Most common include hallucinations, delusions, impaired functioning, flattened affect, and social withdrawal.
- Parents more likely to report these problems to the clinician, as children often minimize, misinterpret, or avoid mentioning their symptoms.
- Early on kids may show nonspecific, but irregular or unusual, social and cognitive development, social withdrawal, avoidance, eccentric, or suspicious behavior.
- Patients may be incoherent, loose associations or tangential, overinclusive, thought-blocking, echolalia, or neologisms.
- Affect can be flat or blunted, it may also be silly, goofy, or labile.
- Children rarely have insight into the significance of their symptoms, lack judgment and can have poor impulse control
- Youth may manifest either a decreased or increased rate of eye blinking, as well as paroxysmal saccadic eye movements (inability to follow an object with smooth eye movements)



# Poor Long-Term Outcome . . .

- Moderate to severe impairment across the life span
- Predicted by low premorbid functioning, insidious onset, higher rates of negative symptoms, childhood onset, and low intellectual functioning
- Youth with EOS have greater social deficits, more unemployment and a lower likelihood to live independently
- 5% of individuals with EOS die by suicide or by accidental death directly because of behaviors influenced by psychotic thinking
- Adults with schizophrenia are at higher risk of other co-morbidities, such as heart disease, obesity, HIV, hepatitis, and diabetes – AACAP Practice Parameters

# Psychopharmacology of Early Onset Psychosis

- There have been 3x as many trials conducted with 2<sup>nd</sup> generation antipsychotics in youth compared with 1<sup>st</sup> generation medications
- Six studies were published between 1960-1990's using 1<sup>st</sup> generation agents
- Only a few studies done in the 90's using SGA's. . .
- Multiple studies have been completed since then. . .
- With “less” side-effects than conventional antipsychotics, their use has dramatically increased, especially in children . . . Yet at the time, there was no FDA indication for their use in children. First use was for autism related aggression (Risperdal)

# FDA Approved Medications

## Antipsychotic Medications Approved for Schizophrenia in Youth:

- **2<sup>nd</sup> Generation:**
  - Aripiprazole (> 13 yrs)
  - Risperidone (> 13 yrs)
  - Quetiapine (> 13 yrs)
  - Olanzapine (> 13 yrs)
  - Lurasidone (>13 yrs)
  - Paliperidone (> 12 yrs)
  - Clozapine (> 10 yrs) – treatment resistant

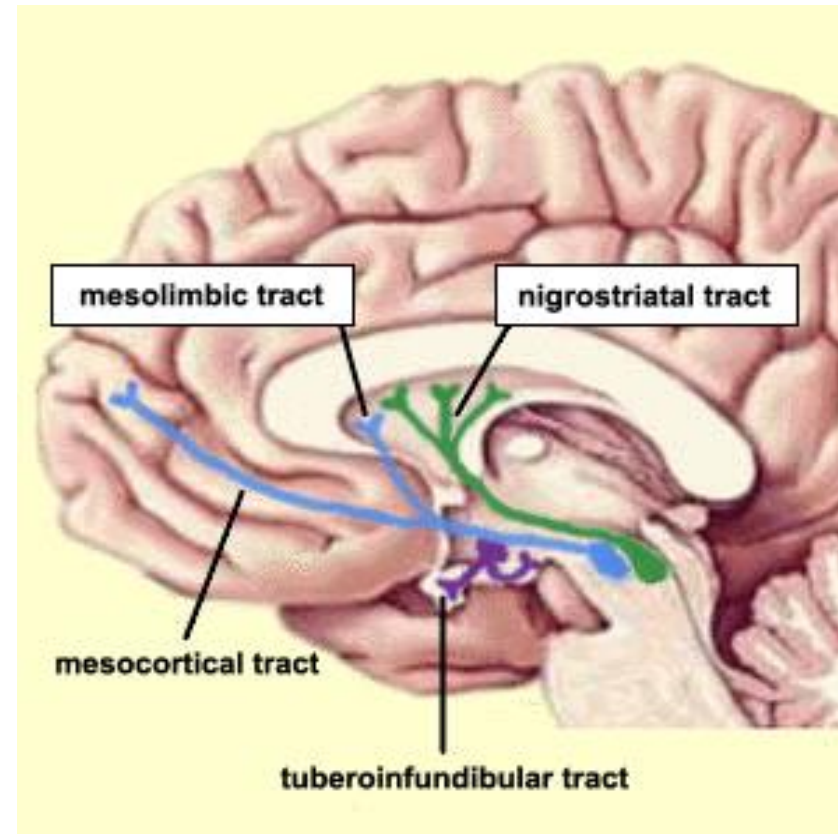
# 2nd Generation Antipsychotics/Dopamine Modulators

- Have a high affinity for Serotonin (5HT) receptor subtypes
  - Goal is to block 70% of D2 and enough 5-HT2A to alter DA binding
- Blocking 5-HT2A has different results depending on the pathway
  - Mesolimbic – where positive symptoms reside
  - Nigrostriatal – EPS, Parkinsonian symptoms
  - Mesocortical – treats negative symptoms, cognition
  - Tuberoinfundibular – modulates prolactin secretion



# Major Dopamine Pathways

- Blocking 5-HT<sub>2A</sub> has different results depending on the dopamine (D<sub>2</sub>) pathway
  - Mesolimbic – + positive sx's; no effect on D<sub>2</sub> blockade
  - Nigrostriatal – EPS, reverses D<sub>2</sub> blockade, increases D<sub>2</sub> activity
  - Mesocortical – negative symptoms, cognition, reverses D<sub>2</sub> blockade
  - Tuberoinfundibular – prolactin secretion; reverses DA blockade to reduce hyperprolactinemia



# Evidence for 2<sup>nd</sup> Generation Antipsychotics

- 2<sup>nd</sup> Generation have become more frequently used than 1<sup>st</sup> Generation medications because of reportedly lower risk for Tardive Dyskinesia, but more concerns related to metabolic issues and weight gain
- Approvals for 2<sup>nd</sup> generation antipsychotics have only occurred in the past 10-12 years
  - Risperdal and Abilify were approved in 2007 for youth with schizophrenia
  - Zyprexa and Seroquel were approved in 2009 for youth with schizophrenia

# TEOSS (Treatment of Early Onset Schizophrenia Spectrum Disorders Study) – JAACAP, 2010

- Designed to study treatment of youth with COS/EOS between the ages of 8-19 yrs (similar study in adults, CATIE)
  - CATIE study showed that 1<sup>st</sup> generation and 2<sup>nd</sup> generation antipsychotics were comparably effective but were associated with high rates of discontinuation, side effects or failure to control symptoms
  - TEOSS set out to compare the efficacy and safety of 2<sup>nd</sup> generation antipsychotics (Olanzapine and Risperidone) with a 1<sup>st</sup> generation antipsychotic (Molindone)
- Double blind multi site trial, randomly assigned youth to Olanzapine (2.5-20 mg ), Risperidone (0.5-6 mg ) or Molindone (10-140 mg)
- Primary outcome was defined by CGI-I score of 1 or 2 and 20% reduction in PANSS total score after 8 weeks of treatment

# TEOSS (Treatment of Early Onset Schizophrenia Spectrum Disorders Study)

- 116 children were in the study
- No significant differences in efficacy were found among treatment groups (Molindone 50%, Olanzapine 34%, Risperidone 46%)
- No significant differences in symptom reduction between treatment arms, all 3 meds were essentially equal
- Investigators noted that safety findings were what differentiated the treatments
  - Weight gain was big concern in the Olanzapine arm
  - Coupled with CATIE results, 1<sup>st</sup> generation antipsychotics are just as likely to work well clinically as the SGA's in youth with schizophrenia

# TEOSS (Treatment of Early Onset Schizophrenia Spectrum Disorders Study)

- TEOSS also had an extension phase, lasted up to 44 weeks
- Only youth who were responders (20% reduction in PANSS plus CGI-I score < 2) could continue

**54 youth started extension phase, only 14 completed the study**

Side-effects or lack of efficacy (weight gain main reason)

There were **no differences among the 3 treatment** arms in terms of symptoms reduction on the PANSS or CGI-I

All treatment groups showed statistically significant weight gain

EPS, akathisia, seen more in Molindone arm

No significant differences in neurocognitive outcomes

12% of those originally enrolled in TEOSS completed 12 months of treatment with their original medication

**\*\*Evidence from the TEOSS suggests that none of the agents worked that well and all had potential problems with side effects**

# Therapeutic Interventions

- There are very few studies of psychosocial treatments for youth with schizophrenia.
- Psychoeducation, including parent seminars, problem-solving sessions, milieu therapy, reintegrating the subjects back into their schools and communities, associated with lower rates of rehospitalization.
- 3-month trial of cognitive remediation therapy, in comparison with standard therapy, was associated with improvements in planning ability and cognitive flexibility in adolescents with schizophrenia.
- Can benefit from adjunctive psychotherapies designed to remediate morbidity and promote treatment adherence.
- Strategies for the patient include psychoeducation and treatment options, social skills training, relapse prevention, basic life skills training, and problem-solving skills or strategies.
- Psychoeducation for the family is also indicated to increase their understanding of the illness, treatment options, and prognosis and to develop strategies to cope with the patient's symptoms.

# Weight Gain and Metabolic Effects

- No generally accepted definition of clinically significant weight gain during development, despite a growing concern about obesity in childhood
- Proposal by Christoph Correll M.D.
  - (Correll et al., 2006a JAACAP)
- Requires monitoring and “extra” work on the part of providers

# Weight Gain. . .

- In a naturalistic study, youth naive to antipsychotic therapy (n = 272, 4–19 years old) gained on average 4.4 kg on aripiprazole, 5.3 kg on risperidone, 6.1 kg on quetiapine, and 8.5 kg on olanzapine over approximately 12 weeks of treatment.
- A comparison group of psychiatrically ill youth not receiving an antipsychotic agent (n = 15) gained only 0.2 kg over the same time period. Significant increases in cholesterol and/or triglycerides were noted in subjects taking olanzapine, quetiapine and risperidone.
  - AACAP Practice Parameters



# Proposed Monitoring Guidelines for Children & Adolescents

- BMI at each visit (check height/weight)
- Blood pressure at each visit
- Quarterly measurements of waist circumference
  - **Abdominal obesity** is most correlated with metabolic syndrome – questioned now for youth, not as reliable
- Baseline fasting lipids/glucose
  - At 3 months, then every 6 months
  - Ask about weight loss, polyuria, polydipsia which could signal diabetes
  - Fasting Trig:HDL ratio; want less than 3.5 mg/dL; could signal insulin resistance

# Comments/Questions? . . .



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