Schizophrenia in Adolescents/Physician Suicide

From the 22nd Annual National Psychopharmacology Update, presented by the Nevada Psychiatric Association

Diagnosis and Treatment of Schizophrenia in Adolescents

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Diagnosis of schizophrenia: patient may have delusions, hallucinations, disorganized and catatonic behavior, social and occupational dysfunction, and poor school function; 6 mo of symptoms required to make diagnosis; clinician should exclude medical problems; signs include lack of age-appropriate interpersonal, academic, or occupational functioning; onset of psychosis before 13 yr of age rare; peak time of onset late adolescence to young adulthood; sex ratio 2:1 in favor of males; age of onset 5 yr earlier in males

Clinical signs: patients may withdraw from outside world and become disorganized; written communications may not make sense; prominent symptoms in adolescents include hallucinations, bizarre thoughts, and difficulty making and keeping friends; they may have family history of schizophrenia; flat affect typical in early-onset schizophrenia

Prevalence: schizophrenia affects 1% of population; children and adolescents frequently misdiagnosed with bipolar, schizoaffective, or obsessive-compulsive disorder, or with developmental syndrome; risk increases 5- to 20-fold if first-degree relative has schizophrenia; risk increased 5% to 15% if sibling has schizophrenia; velocardiofacial syndrome associated with schizophrenia; neuroanatomic studies show increased ventricle size, decreased gray matter, and cortical thinning

Evaluation: should include toxicity screen and evaluation for lesion of central nervous system; neurology consultation required if concerned about Wilson disease, lupus erythematosus, or N-methyl-D-aspartate encephalitis

Management: American Academy of Child and Adolescent Psychiatry (AACAP) recommends that every psychiatric assessment should include screen for psychosis, that adult criteria be used for diagnosis, and that antipsychotic drugs should be primary treatment, focusing on medications approved by Food and Drug Administration (FDA); long-term treatment required to prevent relapse; adjunctive medications such as benztropine used for dystonia; although clozapine not approved for patients <18 yr of age, it may work in treatment-resistant cases; laboratory values and abnormal movement rating scales should be monitored; cognitive behavioral therapy may help patient to ignore voices and paranoid delusions; families need education and support; AACAP considers electroconvulsive therapy to be option for treatment-resistant patients

Positive trials

Aripiprazole: Findling et al studied 302 patients 13 to 17 yr of age with schizophrenia; they received placebo, 10 mg aripiprazole daily, or 30 mg daily; at 6 wk, mean reductions on Positive and Negative Syndrome Scale (PANSS) 22 points (placebo group), 30 points (10-mg group), and 31 points (30-mg group); study led to approval of drug; in hospitalized children, rapid upward titration often best for controlling symptoms

Olanzapine: placebo-controlled study used flexible dose of olanzapine (2.5 to 20 mg/day; mean dose 11 mg/day); primary outcome change in score on Brief Psychiatric Rating Scale; effect size for olanzapine 0.63; however, drug associated with weight gain of 4.5 kg at 6 wk

Comparison of agents: Sikich et al evaluated patients on spectrum (with schizoaffective or schizoaffective disorder or schizophrenia); study compared olanzapine (2.5 to 20 mg/day), risperidone (0.5 to 6 mg/day), and molindone (10 to 140 mg/day); antipsychotic agents given with benztropine to maintain blinding; positive response defined as 20% reduction in psychotic symptoms and score of “much improved” or “very much improved” on Clinical Global Impression (CGI) scale at 8 wk; response rates 34% in olanzapine group, 46% in risperidone group, and 50% in molindone group; study concluded that second-generation drugs not superior to molindone; however, molindone not available in United States; endpoints from study occurred earliest in olanzapine group; risperidone had lowest dropout rate; every drug effectively reduced psychotic symptoms (reduction in symptoms similar among groups); rate of weight gain highest in olanzapine and risperidone groups; largest increase in prolactin level seen in risperidone group; largest increase in insulin level seen in olanzapine group; every drug changed metabolic parameters

Risperidone: 2 trials conducted (one vs placebo, other comparing high and low doses of risperidone); response defined as 20% improvement on PANSS; reduction in PANSS scores significantly greater in both risperidone groups; long-term trial of

Educational Objectives

The goals of this program are to improve management of schizophrenia and promote prevention of physician suicide. After hearing and assimilating this program, the clinician will be better able to:

1. Describe signs of early-onset schizophrenia in adolescents.
2. Outline the results of major clinical trials leading to the approval of currently used antipsychotic medications for children with schizophrenia.
3. Treat a child with schizophrenia based on individual response to medications and side effects.
4. Recognize signs of physician burnout and other risk factors for physician suicide.
5. Manage a physician at risk for suicide.

Faculty Disclosure

In adherence to ACCME Standards for Commercial Support, Audio Digest requires all faculty and members of the planning committee to disclose relevant financial relationships within the past 12 months that might create any personal conflicts of interest. Any identified conflicts were resolved to ensure that this educational activity promotes quality in health care and not a proprietary business or commercial interest. For this program, the following has been disclosed: Dr. Robb is on advisory panels for Ironshore Pharmaceuticals & Development (a wholly owned subsidiary of Highland Therapeutics), Pfizer, Rhodes Pharmaceuticals, and Tris Pharma; is a consultant for Aevi Genomic Medicine, Allergan, Bracket Global, H. Lundbeck A/S, Neuronetics, and Takeda Pharmaceutical Company; is on data and safety monitoring boards for Aevi Genomic Medicine and Neuronetics; has received grant/research support from Allergan, H. Lundbeck A/S, Pfizer, SyneuRx, and Takeda Pharmaceutical Company; has received honoraria from Bracket Global; is a stockholder/shareholder in Eli Lilly and Company, GlaxoSmithKline, Johnson & Johnson, and Pfizer, and has received travel support from Allergan, H. Lundbeck A/S, Rhodes Pharmaceuticals, Takeda Pharmaceutical Company, and Tris Pharma. Dr. Myers reported nothing to disclose. The planning committee reported nothing to disclose. In her lecture, Dr. Robb presents information related to off-label or investigational use of a therapy, product, or device.
open-label risperidone included 390 children who completed these trials; 279 continued treatment for 6 mo and 111 for 1 yr; median dose ≈4 mg/day; 50% of patients still in trial at 12 mo; every group had continued reduction in psychotic symp- toms; helpful for children and parents to know that continued improvement likely after child released from hospital Paliperidone: trial included 201 adolescents; dose based on weight; 3 mg most effective dose, although some children need up to 12 mg; trial compared paliperidone with aripiprazole and placebo; children on paliperidone started at 3 mg/day and titrated to maxi- mum dose of 9 mg/day; children on aripiprazole started at 2 mg/ day and titrated to maximum dose of 15 mg/day; 75% of children completed 8-wk trial; drugs equally effective but had different side effects; paliperidone associated with akathisia, headache, somnolence, tremor, and weight gain; aripiprazole associated with worsening of schizophrenia and sleepiness; extrapyramidal symptoms (EPS) more frequent in paliperidone group; both drugs reduced symptoms by ≈25 points from baseline Lurasidone: 6-wk double-blinded trial included 112 patients on placebo, 110 on 40 mg/day and 104 on 80 mg/day; based on reduction in PANSS, both doses of lurasidone superior to placebo (effect sizes 0.48 and 0.51); results for CGI similar Clozapine: often used when FDA-approved drugs ineffective, but carries several black box warnings

**Negative trials:** ziprasidone — Findling et al compared 40 to 160 mg/day with placebo and found no differences between groups at 6 wk; asenapine — trial in adolescents with schizophrenia did not confirm efficacy of asenapine; study included 3 arms and twice-daily treatment with 2.5 mg, 5 mg, or placebo; extension study reported similar findings

**Side effects:** atypical antipsychotics associated with akathisia, cognitive issues, changes in glucose and lipids, impaired memory, sedation, sexual dysfunction, tardive dyskinesia, and weight gain; ziprasidone has smallest effect on weight but not effective in adolescents

**Management algorithm:** aripiprazole — may be used as first-line drug; patient takes 2.5 mg for 2 days, then 5 mg for 3 days, then 10 mg/day; dose may be increased to 30 mg as needed; 30 mg associated with faster onset of relief of symptoms than 10 mg; aggressive titration appropriate for inpatients; risperidone — good second choice; patient begins with 0.5 mg per day and titrates to 1 mg at 1 wk; maximum dose 6 mg/day; prolactin levels should be monitored; patients may develop amenorrhea, breast tenderness, and EPS; quetiapine — also effective; olanzapine — because of metabolic issues, other drugs such as paliperidone and lurasidone should be tried first

**Manifestations of schizophrenia:** adolescents may have positive and negative symptoms; negative symptoms may be failure in school and loss of friends; patient may have paranoid thoughts about other people at school; obtaining information from school and family may be important

**Clozapine:** treatment of last resort; warnings include agranulocytosis and cardiac collapse; clozapine only drug shown to reduce rate of suicide (compared with placebo) in patients with schizophrenia

**Adherence:** by 18 mo, 75% of youths with schizophrenia stop their medication; in TEOSS study that followed adolescents over long term, only 12% of children continued treatment; to improve adherence and outcomes, families and youth need education about schizophrenia; difficult for children to learn in school while dealing with cognitive side effects and hearing voices; side-effect burden may be greater in adolescents, including weight gain; use of intramuscular (IM) antipsychotics improves adherence, but not currently approved for children <18 yr of age; many community clinics not staffed to give depot medication, but child may get IM medication from another practitioner or through adult clinic

**Suggested Readings**


**Physicians at Risk for Suicide: Assessment and Intervention**

Michael Myers, MD, Professor of Clinical Psychiatry, State University of New York Downstate Medical Center, Brooklyn

**Overview:** 50% of US physicians experience burnout; speaker conducted semistructured interviews with 75 family members, friends, and colleagues of 45 physicians who committed suicide; many never received care from physician, counselor, or psychiatrist; families interviewed by speaker expressed wish for changes within profession to make it easier for physicians to seek help

**Epidemiology:** 300 to 400 physicians die by suicide each year in United States; rate higher in physicians than general population; 85% to 90% of people who commit suicide (including physicians) have psychiatric illness; associated conditions include substance abuse (common in physicians), posttraumatic stress disorder, personality disorders, double depression, medical comorbidities, anxiety disorders, bipolar illness, and adjustment disorders

**Risk factors:** physician may not be forthcoming with medical history; risk factors include previous history of depression or attempt at suicide, family history of mood disorder or suicide, lawsuits, investigation of medical licensure, poor adherence with treatment (often because of stigma), and treatment-refractory psychiatric illness; primary care practitioner should refer physician to psychopharmacologist if improvement not observed; undiagnosed bipolar illness should be considered; rapid cycling possible in patients with mixed mood disorders

**Comorbid conditions:** include impulsivity, unrecognized attention-deficit disorder, and unrecognized emergent psychosis; severe sleep deprivation may be risk factor; physicians with mood disorders who seem stable may decompensate if they undergo changes in circadian rhythms; Joiner et al described individuals who become dangerously suicidal within minutes or hours; such patients usually in agitated state with severe insomnia, convictions that border on delusions, and hopelessness; it may be difficult to reason with them

**Factors specific to physicians:** higher suicide rates may be related to greater knowledge about ways to commit suicide; clinician should ask carefully about suicidal plans; stigma is key factor in physician suicide; clinicians should be mindful of transference and countertransference issues when treating physi- cians; even mental health professionals often carry residual, internalized stigma despite training

**Culture of medicine:** improving, but atmosphere still difficult; some trainees feel bullied; factors related to personality may contribute to desperate thinking; excessive perfectionism
should be addressed during therapy; physicians tend toward altruism and may be unaccustomed to putting themselves first.

**Triad:** in theory of suicidal behavior, Joiner (2005) described triad of perceived burdensomeness (patients feel like burden to family and believe they no longer serve purpose), failed belongingness (patients no longer feel they belong [in this case, to medical profession] and feel unworthy), and learned fearlessness (losing fear of death increases risk for suicide); Joiner believes that similar level of pain and fear might be associated with such disparate experiences as mountain climbing, performing surgery, fighting in wars, and being afflicted with anorexia; physicians who have thereby flirted with death or who care for patients with massive injuries may lose fear of death; surgeons may be especially vulnerable.

**Role of mentors:** two interns committed suicide in 2014 within days of one another; supervisors and mentors of young doctors should set example by sharing their own insecurities, unmasking their own humanity, and disclosing their own psychiatric treatment; doing so creates atmosphere of kindness and affirms that supervisors care; public humiliation or shame may be last straw that drives person toward suicide.

**How clinicians can help:** clinician may offer to speak at grand rounds about physician burnout and depression, offer in-service training, write about problem, work with planning committee for continuing medical education to invite speakers, promote physician wellness program, and volunteer to serve on physician health program.

**Management:** history — to detect suicidal thinking and planning, clinician must thoroughly assess risk; documentation should be careful and timely; clinician should ask about stockpiled medications; toxic medications available on internet; hospitalization — safety main reason for hospitalizing physician; if unsure, clinician should seek second opinion; clinician should not inappropriately hospitalize physician (physician may respond by avoiding psychiatric care); many physicians greatly relieved after sharing their frightening thoughts and suicidal plans; patients must be followed carefully after discharge; old records — essential to learn how other professionals have diagnosed and treated patient; if records no longer available, attempt to call treating clinician; adjunctive care — clinician should work closely with physician health program and employ biopsychosocial model of treatment; family members should be involved, split care — communication between clinician and others treating patient essential; clinician should maintain standard of care (treat patient in same way as nonphysician); cognitive behavioral therapy — many suicide-specific forms of therapy available, including dialectical behavior therapy and collaborative assessment and management of suicidality; approach — should be kind and compassionate, but also firm and parental at times; self-report may be unreliable (patients who do not report suicidal thinking may be at risk); passive suicidal thinking no less risky than active suicidal thinking.

**Changes:** Association of American Medical Colleges is conducting symposia and designing programs in collaboration with Mayo Clinic.

**Supporting medical communities:** when medical community grieving suicide by physician, clinician can reassure others who feel guilt or blame themselves; anger and rage at deceased common; safe milieu should be created for physicians to talk; when supporting groups of physicians, clinician should emphasize confidentiality so that others feel safe sharing their thoughts; avoid judging others at meeting and facilitate group, rather than delivering lecture; such interventions may prevent other suicides.

**Suggested Readings**


**Acknowledgments**

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- Review Educational Objectives on page 1
  - Take pretest
  - Take posttest
  - Listen to audio program
  - Review written summary and suggested readings
  - Take posttest

- 5 minutes
- 10 minutes
- 60 minutes
- 35 minutes
- 10 minutes

- Total estimated time to complete the educational process: 2 hours.
SCHIZOPHRENIA IN ADOLESCENTS/PHYSICIAN SUICIDE

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To submit a test form by mail or fax, complete Pretest section before listening and Posttest section after listening.

1. Which of the following statements about diagnosis of schizophrenia in adolescents is NOT correct?
   (A) The onset of psychosis is rare before 16 yr of age
   (B) The time of onset of schizophrenia is typically earlier in males than in females
   (C) The first clinical signs may take the form of withdrawal from the outside world and a flat affect
   (D) Hallucinations are often prominent symptoms in adolescents

2. Which of the following was an outcome of the study that led to approval of aripiprazole for children with schizophrenia?
   (A) The mean reduction on the Positive and Negative Syndrome Scale (PANSS) was significantly greater in
      the 10-mg aripiprazole group than in the placebo group
   (B) The mean reduction on the PANSS was significantly greater in the 30-mg group than in the 10-mg group
   (C) The 30-mg dose of aripiprazole was not approved because of the severity of side effects

3. In a study that compared a flexible dose of olanzapine with placebo in children, which of the following was identified as
   an especially concerning side effect?
   (A) Akathisia (B) Fatigue (C) Hyperprolactinemia (D) Weight gain

4. A study compared treatment of adolescents on the schizophrenic spectrum with olanzapine, risperidone, and molindone. Which of the following did the study report?
   (A) The dropout rate at 8 wk was highest in the risperidone group
   (B) Only olanzapine was associated with changes in metabolic parameters
   (C) Response rates at 8 wk were highest in the molindone group
   (D) The study could not be effectively blinded because of the different side effects of these agents

5. In a placebo-controlled trial that included 201 adolescents with schizophrenia, what was the most effective daily dose of
   paliperidone?
   (A) 1.5 mg (B) 3 mg (C) 9 mg (D) 12 mg

6. In a study that compared paliperidone with aripiprazole in children with schizophrenia, which of the following side
   effects was more prominent in the aripiprazole group?
   (A) Akathisia (B) Sleepiness (C) Headache (D) Tremor

7. Which of the following drugs was found ineffective for treating children with schizophrenia in a clinical trial?
   (A) Clozapine (B) Lurasidone (C) Ziprasidone (D) Quetiapine

8. Which of the following statements about suicide by physicians in the United States are true?
   1. Half of physicians experience burnout
   2. Many physicians who commit suicide never received psychiatric care
   3. Most physicians who commit suicide have extenuating professional or personal circumstances but do not have
      a psychiatric illness
   4. 75 to 100 physicians die by suicide each year
   (A) 1,2 (B) 1,3 (C) 2,3 (D) 1,2,3,4

9. Factors that may contribute to higher rates of suicide by physicians in particular, compared to the general population, include all the following, EXCEPT:
   (A) Stigma attached to having a psychiatric illness
   (B) Having knowledge about ways to commit suicide
   (C) Perception of burdensomeness
   (D) Tendency toward perfectionism

10. A clinician is treating a physician with severe depression and is considering hospitalization to prevent suicide, but is
    unsure whether this action is warranted. The patient does not wish to be hospitalized. Which of the following should the
    clinician do?
    (A) Err on the side of caution and hospitalize the physician for safety reasons, because physicians often do not give
        an accurate history about their suicidal ideation
    (B) Do not hospitalize the physician, because if hospitalized, he or she may avoid psychiatric care in the future
    (C) Seek a second opinion from another psychiatric professional

Answers to Audio Digest Psychiatry Volume 46, Issue 07: 1-B, 2-C, 3-D, 4-A, 5-B, 6-C, 7-A, 8-B, 9-D, 10-B