Summary of Treating Early Onset Schizophrenia by Jon McLellan, MD

Schizophrenia is a neurodevelopmental disorder characterized by severe disruptions in thought, perceptions and behavior. Early onset schizophrenia (EOS), defined as onset prior to age 18 years, is diagnosed using the same criteria as in adults (AACAP, 2013). Individuals with EOS typically suffer long-term symptomatic and functional impairment, with significant social, occupational and cognitive difficulties. Early detection and the initiation of comprehensive effective treatment are imperative for addressing the potential lifelong morbidity associated with the illness.

Schizophrenia occurs in approximately 1 percent of the general population worldwide. Males are more likely than females to have the disorder (ratio of 1.4 to 1) (McGraff and Susser, 2009). The typical age of onset of schizophrenia ranges from 15 to 30 years, and commonly first presents during adolescence. Onset prior to age 12 years is rare. The validity of the diagnosis has not been established for young children less than 6 years of age) (AACAP, 2013).

Schizophrenia and other psychotic illnesses have characteristic symptom presentations, courses of illness and mental status findings. For youth presenting with acute psychosis, the differential diagnosis includes psychotic mood disorders and medical conditions, e.g., acute intoxication, neurological conditions, autoimmune disorders or delirium. Comprehensive medical evaluations, including toxicology screens, neuroimaging studies, genetic and laboratory testing, and expert consultation should be considered as indicated based on clinical presentation and history.

The diagnostic assessment must also take into account developmental variations in symptom reports. The diagnosis of schizophrenia requires overt evidence of disrupted thinking and behavior. In general population surveys, children and adolescents commonly describe experiences suggestive of psychosis (Kelleher and Cannon, 2011). Youth with trauma histories, developmental lags or autism spectrum disorders often report unusual perceptions or cognitions. Yet, most reports of psychotic-like experiences in juveniles are not associated with clinically significant disruptions in mental status or functioning, and never progress to a true psychotic illness (McClellan, 2011). An accurate diagnostic assessment is essential for insuring appropriate effective treatment.

There is substantial evidence demonstrating the efficacy of antipsychotic medications for schizophrenia in adolescents and adults (AACAP, 2013; Lehman et al., 2004). Second generation agents ("atypical antipsychotics) are the most widely used in community settings, although the superiority of atypical antipsychotics, as compared to traditional neuroleptics, has not been established in either adults (Lieberman et al., 2005) or juveniles (Sikich et al., 2008). The only antipsychotic medication with established superiority for treatment refractory cases is clozapine, which is not considered a first-line agent given the risk of serious side effects, including neutropenia and seizures. At this time, first-line antipsychotic medication choice for schizophrenia and other psychotic illnesses is primarily based on side effect profile, patient and family preference, and cost (AACAP, 2013).

Several randomized controlled trials have demonstrated the efficacy of antipsychotic agents for reducing symptoms of EOS (AACAP, 2013). Risperidone, aripiprazole, quetiapine, paliperidone, and olanzapine are FDA approved to treat schizophrenia in adolescents age 13 years and older. Olanzapine is generally considered a second-line treatment given significant risks for weight gain and metabolic problems (Sikich et al., 2008). Ziprasidone is FDA approved to treat adults with schizophrenia; however a large unpublished industry sponsored randomized placebo-controlled trial of ziprasidone for EOS was terminated early by the data safety monitoring board due to lack of efficacy (clinicaltrials.gov). Overall, there are less data available examining first generation antipsychotics for EOS; haloperidol, perphenazine and thiothixene are FDA approved for treating schizophrenia in youth ages 12 years and older.

Systematic side effect monitoring in needed for all youth taking antipsychotic medications. Children and adolescents are particularly vulnerable to weight gain and metabolic adverse events (Correll et al., 2009), yet metabolic functions are not routinely assessed for most youth prescribed these agents in community settings (Raebel et al., 2014). Guidelines for adverse event monitoring have been established, and should be incorporated into standard practice (AACAP, 2013),

Adjunctive medications are often used in clinical settings to address potential side effects (e.g., antiparkinsonian agents for extrapyramidal side effects), or associated psychopathology (e.g, mood stabilizers for mood instability or aggression; antidepressants for depression or negative symptoms; benzodiazepines for anxiety,

insomnia, akathisia or catatonia). The use of adjunctive psychotropic agents has not been systematically studied in EOS, and care is needed to avoid unnecessary polypharmacy (AACAP, 2013).

Finally, comprehensive psychosocial interventions are important for youth with schizophrenia. Patients and their families generally require psychoeducation regarding diagnostic issues, treatment options, safety planning, medication adherence and relapse prevention. Case management and intensive community support services, including special education and/or vocational or occupational programs, are often indicated. There are a number of psychotherapeutic interventions that have been found to be helpful for improving functioning and reducing symptoms in adults with schizophrenia, including cognitive remediation and cognitive-behavioral therapies, social skills training, and family interventions (AACAP, 2013). Although these treatments have not been well studied in EOS, the therapeutic strategies are readily extrapolated to a pediatric population.

References

American Academy of Child and Adolescent Psychiatry (AACAP), McClellan J, Stock S, Practice parameter for the assessment and treatment of children and adolescents with schizophrenia. *J Am Acad Child Adolesc Psychiatry*. 2013;52(9):976-90.

Correll CU, Manu P, Olshanskiy V, Napolitano B, Kane JM, Malhotra AK. Cardiometabolic risk of second-generation antipsychotic medications during first-time use in children and adolescents. *JAMA*. 2009;302(16):1765-73.

Kelleher I, Cannon M. Psychotic-like experiences in the general population: characterizing a high-risk group for psychosis. *Psychol Med*. 2011;41:1-6.

Lehman AF, Lieberman JA, Dixon LB, McGlashan TH, Miller AL, Perkins DO, Kreyenbuhl J; American Psychiatric Association; Steering Committee on Practice Guidelines. Practice guideline for the treatment of patients with schizophrenia, second edition. *Am J Psychiatry*. 2004;161(2 Suppl):1-56.

Lieberman JA, Stroup TS, McEvoy JP, Swartz MS, Rosenheck RA, Perkins DO, Keefe RS, Davis SM, Davis CE, Lebowitz BD, Severe J, Hsiao JK; Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) Investigators. Effectiveness of antipsychotic drugs in patients with chronic schizophrenia. *N Engl J Med*. 2005;353(12):1209-23.

McClellan J. Clinically relevant phenomenology: the nature of psychosis. *J Am Acad Child Adolesc Psychiatry*. 2011;50(7):642-4.

McGrath JJ, Susser ES. New directions in the epidemiology of schizophrenia. *Med J Aust*. 2009;190(4 Suppl):S7-9.

Raebel MA, Penfold R, McMahon AW, Reichman M, Shetterly S, Goodrich G, Andrade S, Correll CU, Gerhard T. Adherence to Guidelines for Glucose Assessment in Starting Second-Generation Antipsychotics. *Pediatrics*. 2014;epub PMID:25287454
.