7TH ANNUAL CHAIR SUMMIT
Master Class for Neuroscience Professional Development
September 11 – 13, 2014 | Westin Tampa Harbour Island
Case Challenge: Schizophrenia

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Disclosures

- **Research/Grants:** AstraZeneca Pharmaceuticals LP; Otsuka America Pharmaceutical, Inc.; Myriad Genetics Inc./Rules-Based Medicine, Inc.
- **Consultant:** Eli Lilly and Company
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Disclosures

- **Research/Grants:** Otsuka America Pharmaceutical Inc. - PI Forum - (PI Clinical Trials Funding Deposited at the University)
- **Speakers Bureau:** Janssen Pharmaceuticals, Inc.; Lundbeck; Novartis Corporation; Otsuka America Pharmaceutical Inc.; Sunovion Pharmaceuticals Inc.
- **Consultant:** Boehringer Ingelheim; Merck & Co., Inc.; Otsuka America Pharmaceutical Inc.; Teva Pharmaceuticals; Sunovion Pharmaceuticals Inc.
Learning Objective 1

Individualize treatment for patients with schizophrenia by balancing the unique experiences of each patient with side effects, medical comorbidity, and medication adherence history.
Review the current data on treatment resistance in schizophrenia and consider all evidence-based pharmacological treatment options, even those that may require careful monitoring to improve patient care.
Learning Objective 3

Devise a treatment plan with patient participation that includes measurement-based care including regular symptom assessment and metabolic monitoring for patients diagnosed with schizophrenia.
Albert Duncan

- 15 year old male referred by primary care clinician
- Chief Complaint: “Not functioning well”
- Patient describes anxiety, often when he is alone but primarily when he is out of the house among people
- He elaborates that what he feels is a tense, high, or somewhat unreal feeling
- It frightens him
Patient describes an anxious, “chaotic feeling. “I have to put on a fake front to keep people from seeing that I am scared of them.”

“I have to work really hard at trying to look normal when I am falling apart.”

“There’s just a lot going on in my head.”

“I just want to be a normal kid and have friends and hang out and do stuff.”
Symptoms Continue

- When alone in room, occasionally has self-harm ideas and has to restrain himself by holding his arm, but no specific target or history of action
- He reveals that he has been worrying that others can hear/read his thoughts, but acknowledges this is not possible
Albert Duncan

- Recent fall-off of most friendships, switched to online schooling because he “doesn’t like being around people”
- Occasionally feels “down,” denies hopelessness/helplessness, suicidal ideation, guilt
- Mother reports functional decline: grades, family, social
Normal Control vs. Child High Risk HVLT-R t-score Group Mean Comparison

Presented at ICOSR, 2013. Orlando, Florida
a. Baseline Independent Samples t-test (2-tailed)*: $p = .095$, $t = -1.75$, $df = 25$

b. Exit Independent Samples t-test (2-tailed): $p = .155$, $t = -1.48$, $df = 20$

*Baseline Independent Samples t-test $H_0 \neq H_a$ $p < .05$ (sig.1-tailed), $t = -1.75$, $df = 25$
Cognitive Impairment in Adolescents with Schizophrenia

- **Objective**: To assess adolescent subjects with schizophrenia using an objective neuropsychological battery
- **Methods**: Adolescent patients (N = 17) were compared to controls (N = 17) utilizing an age-appropriate neuropsychological battery
- **Results**: Patients were impaired on nearly all measures with their greatest difficulty seen in working memory and attention.
- **Conclusions**: The subjects had a generalized cognitive dysfunction with greatest difficulties in attention and working memory.

The authors have utilized these findings to plan clinical treatments in day hospital and outpatient clinic.

Neuropsychologic Test Results of Adolescents

Discussion Points

● Can the “prodrome” be accurately identified using symptoms, biomarkers, family history (or genes)?

● Are there ways to specify the direction of “prodromal” symptoms in order to apply specific treatments?

● Is there adequate data to recommend treatment approaches to the “prodrome”?

● In other branches of medicine, there are concerns of over diagnosis of early stages of illness. How can such concerns be dealt with in the “prodrome”? 
Multiple Issues Lead to Duration of Untreated Psychosis (DUP)

**Why is Duration of Untreated Psychosis So Long?**

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<td>• Wishful thinking</td>
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Initial Anticholinergic Prophylaxis for Neuroleptic-Induced Extrapyramidal Syndromes

- Incidence of extrapyramidal syndromes (EPS) for prophylaxis and no-prophylaxis groups by age decade. Individual syndromes are shown as insets. Asterisk indicates $p < .001$; dagger, $p < .05$.

- Note high risk for EPS in the 10-19 year old age group

Cardiometabolic Risk of Second-generation Antipsychotic Medications During First-time Use in Children and Adolescents

- **Introduction**: Authors note concern of cardiometabolic effects of second-generation antipsychotics, but note little data in the literature.

- **Methods**: In the SATIETY study, patients from age 4-19 were followed (N = 205); subjects had mood or schizophrenia spectrum diagnoses.

- **Results**: Weight gain was significant for all 4 medications assessed, ranging from 4.4Kg-8.5Kg over 10 weeks. Weight gain in an untreated group was 0.2Kg. Metabolic measures increased for olanzapine and quetiapine, but only for triglycerides for risperidone. There was no difference between aripiprazole and untreated subjects.

- **Conclusions**: Weight gain was seen for each second-generation group while there were differences across the group for metabolic measures.

Objective: To assess the safety and efficacy of two atypical antipsychotic medications compared to a first-generation compound (plus an anticholinergic medication).

Method: Pediatric patients were assigned to either olanzapine, risperidone or molindone plus benztropine in the 8-week trial. The primary measures were CGI and PANSS.

Results: One hundred nineteen subjects were entered in the study and 70 completed the 8-week trial. The 3 groups had equivalent outcome on rating scales. The olanzapine arm was terminated early because of weight gain. Both atypicals showed significant weight gain and increased akathisia was associated with molindone.

Conclusions: Risperidone and olanzapine did not show superiority. Adverse effects varied between the medications. The authors note that the findings bring into question the high use of second-generation antipsychotics.

Underutilization of Clozapine

- “Two clear antipsychotic trial failures warrant initiation of clozapine, and long delays in clozapine treatment should be avoided.”
- 1999 data from Novartis (manufacturer of clozapine) estimated 160,000…received a trial of clozapine…
- Using percentages of non-responders, it appears that only 25% of non-responders ever received clozapine.

Early Use of Clozapine for Poorly Responding First-Episode Psychosis

- The investigators note that a sub-group of first-episode patients have ongoing psychotic symptoms.
- Patients in the CAMH program followed a medication algorithm. Seventy-six percent of the 123 patients who agreed to try clozapine were compared to those who refused.
- The clozapine treated group had a 19-point reduction in BPRS scores (53-34) while the other patients had a two-point increase.
- The authors note reluctance to use clozapine early in the illness and suggest that clozapine may have an important role in early stage patients.

CAMH = Center for Addiction & Mental Health
Response Rates for Antipsychotic Trials 1 and 2 (Olanzapine or Risperidone) Followed by Trial 3 (Clozapine)

Clinical Connections

- Individualize treatment for patients with schizophrenia by considering their uniqueness, history of side effects, medical comorbidity, and past adherence to treatment.
- Review the current data on treatment resistance in schizophrenia and consider all evidence-based pharmacological treatment options, even those that may require careful monitoring to improve patient care.
- In approaching the “middle-aged” patient with schizophrenia, there are now approaches not only to treat the diagnosis, but for addressing domains of the illness.
- Further, treatments to address cognition and other domains are now combining with exploratory medications.
- Finally, the middle age patient group has a number of non-responders to first-line treatment and attention to this issue remains crucial.