The Psychosis Prodrome
Neural Diathesis-Stress Model of Psychotic Disorders

- **Inherited Constitutional Factors**
- **Acquired Constitutional Factors** e.g. Prenatal Events
- **Stress** e.g. Life events/EE
- **Neuromaturational Processes**
- **Constitutional Vulnerability**
- **Psychotic Outcome**
Empirical Evidence is Needed to Support A Neurodevelopmental Theoretical Framework

Prodromal signs are subclinical manifestations of the perceptual, ideational and behavioral symptoms of psychosis and decline in functioning.

- It is estimated that at least 70% of schizophrenia patients manifest premorbid behavioral dysfunction during adolescence (Cannon, et al., 1999).

Complex interactions between genes, environment, and development characterize this period, and our knowledge of these processes is both limited and largely theoretical.
Predicting Schizophrenia Requires a “Close-in” Approach
Symptoms
Positive Symptoms

- Perceptual Aberrations

- Confusion about what is real and what is imaginary; feeling like your mind is playing tricks on you

- Feeling that people are taking special notice of you or singling you out; paranoid thinking

- Feeling that your ideas or behaviors are being controlled by outside forces

- Unrealistic ideas of special identity or abilities

- Preoccupation with the supernatural (telepathy, ghosts, UFOs)
Negative Symptoms

• Feeling like something (emotions, thoughts, behavior) has been taken away or removed

• Wanting to spend more time alone

• Not feeling motivated to do things

• Trouble understanding conversations or written materials

• Difficulty identifying and expressing emotions

• Initially difficult to distinguish from depression
  – Longitudinal perspective is important
Disorganized Symptoms

- Trouble with attention
- Neglect of personal hygiene
- Odd appearance or behavior
- Laughing at odd or inappropriate times
- Problems with communication: vague, confused, muddled, racing or slowed speech, difficulty staying on track or getting to the point
Functional and Social Deterioration
Social Deterioration

• Social Deterioration is a key aspect of the prodrome
• If there is no social deterioration it is questionable whether the prodrome is present
• “Decay” not “drift” - social deterioration follows symptoms
Onset of Social Disabilities (from IRAOS scale)

-Dysfunctional general behaviour

-Dysfunctional behaviour in social / occupational roles

1st positive symptom

60  50  40  30  20  10  0

months before first admission

51 Self-care
52 Leisure activity
53 Speed of coping with daily activities
54 Communication/social withdrawal
55 Lack of consideration and friction
56 Behaviour in emergencies
57 Participation in family life
58 Marriage or equiv. - emotional
59 Marriage or equiv. - sexual
60 Parental role
61 Sexual role behaviour
62 Work relationships
63 Interest in work place
64 General responsibility / interest
Course of the Prodromal Period

- Roughly 25 - 35% of high-risk individuals convert to psychosis within two-years.

Cannan., et al., Arch Gen Psychiatry, 2008.

Cumulative survival distribution function modeling time to conversion in 291 high-risk (prodromal) participants and 134 healthy controls.
Treatment
Typical Intervention during the Prodrome/First Episode

• School intervention
  – Individualized Education Program (IEP)
  – Non-Public Schools (NPS)
• Psychiatric Consultation/Treatment
• Psychoeducational Multi-Family Group & Skills Groups
• Stress Management and Coping Enhancement.
• Individual Therapy and Individual Family Therapy as Needed
Treatment Benefits with Significant Side Effect Profile

- Low dose antipsychotics
- 60 prodromal cases randomly assigned to Olanzapine (5-15 mg) vs. placebo for 8 weeks
- Olanzapine was associated with significant symptom reduction at 8 weeks, but also with significant weight gain (9.9 lbs).

Cognitive Therapy for Prevention

- Randomized controlled trial:
  - cognitive therapy was provided to 37 prodromal patients
  - monitoring/case management to 23 patients over 6 months.
  - Then diagnostic status was followed for one year.

- 26 sessions over 6 months, based on Beck’s general principals:
  - problem oriented
  - time-limited
  - education
  - using guided discovery and homework task
  - encourage collaborative empiricism

- Results:
  - 6% of the cognitive therapy group converted, whereas 26% of the monitoring group did.
  - The cognitive therapy reduced:
    - the likelihood of making progression to psychosis
    - the likelihood of being prescribed an antipsychotic medication.

- Trouble with attrition (42/58 finished), masking was compromised, number of participants was small, observation period was limited.

Despite an impressive halving of the rate of progression to psychosis in the drug-treated group, the study was inconclusive because of a high dropout rate—nearly half the subjects leaving the study during the year-long treatment phase.

As with the other trial, fatigue and significant weight gain were major adverse side effects.

The hazard of conversion to psychosis for the placebo-treated patients was 2.5 times that for the olanzapine-treated patients ($p=0.09$).

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Second Generation Antipsychotics

Weight gain

Sedation

Metabolic Syndrome

Extrapyramidal Side Effects

Prolactin Elevation
Complications with Medications:

• Increased activation from SSRI’s
• Increased withdrawal dyskinesias from neuroleptics
• Increased disinhibition from benzodiazepines
Tasks of Adolescent Development

- Completing school and finding meaningful work
- Preparing for independent living
- Developing a clear sense of self
- Developing supportive relationships with friends and family
Maintain a delicate balance between too much and too little stimulation.

Normative Tasks of Adolescent Development

Too Little Stress: Boredom, Preoccupation with Symptoms, Stagnation

Too Much Stress: Symptoms, Overwhelmed, Need to Withdraw
Life Events

Joseph Ventura, Keith H. Nuechterlein, David Lukoff, and Jean Pederson Hardesty
Department of Psychiatry and Biobehavioral Sciences
University of California, Los Angeles

In this prospective, longitudinal study, 11 recent-onset schizophrenic outpatients who met criteria for psychotic relapse or significant psychotic exacerbation during a 1-year period of standardized maintenance medication, and 19 patients who did not relapse during this follow-up period, were interviewed monthly regarding life events. As hypothesized, for relapsing patients, a significantly higher number of independent life events (those not the result of symptomatology or personal influence) occurred in the month preceding relapse. This increase was apparent relative to either the analogous month of a “nonrelapse” period in the same patient or the average number of independent events per month during a 1-year standardized medication period for nonrelapsing patients. The methodological advances of this design as well as the consistency of these findings with those of previous retrospective studies supports the hypothesis that life events may sometimes “trigger” schizophrenic episodes.

Stress Management: Enhanced Coping

• Fortify ability to tolerate feelings

• Fortify ability to solve problems
Stress Management: Enhanced Coping

Observe and Describe Emotions

Reduce Vulnerability to Negative Emotions

Build Positive Experiences

Self Soothe the Five Senses
Adolescent/Young Adult Skills Group

• Every 2 weeks for 90 minutes

• 1st meeting: introductions, self-definition, and goal setting

• 2nd meeting on: skills training - stress identification and management, problem solving, relaxation training, pleasant events scheduling, emotion regulation and distress tolerance, communication skills, etc.
Skill Enhancement

• Stress Identification and Reduction
• Problem Solving Techniques
• Coping Skills Enhancement
• Social Skills Enhancement
• Self-Esteem and Self-Definition
• Distress Tolerance
• Cognitive Restructuring
Problem Solving Techniques

- Clearly Identify Problem
- Generate Possible Solutions
- Evaluate Pros and Cons of Solutions
- Select Best Strategy
- Troubleshoot
- Implement Plan
• This **Expressed Emotion (EE)** research and Family Therapy is also relevant to psychosis in adults, but due to time, I will discuss it in the context of the prodrome. Family therapy is a highly effective for Psychosis.

Implications:

• Adoptees at genetic risk are more sensitive to problems in the adoptive family.

• There may be a protective effect in having been reared in a “healthy” adoptive family.
Multifamily Group Meetings

- Every 2 weeks for 90 minutes
- 1st meeting: “Getting to know you”
  - Share personal information and begin to develop a sense of who family members are as people
- 2nd meeting: “Experience with symptoms”
  - Share personal stories re: impact of symptoms
  - Continue to build relationships
MFG: Structure of Sessions 3 on

- Socializing with families 15 minutes
- A “go around” reviewing the week’s events 20 minutes
- Selection of a single problem 5 minutes
- Formal problem solving 45 minutes
- Socializing with families 5 minutes
Main Treatment Goals for Prodrome

• Get everyone in the family on the same (or a similar) page.
• Reduce the amount of stress in a vulnerable individual’s life.
• Develop a broad array of coping strategies for individuals and families.
• Consider using medications to reduce biological risk.
While treatments are showing progress in reducing symptoms, ameliorating the course, and potentially preventing illness onset, there are significant issues relating to side-effects & drop-out, and cost.

The nature of prodromal populations (e.g., socially anxious, avoidant, paranoid) make treatment adherence costly and difficult.

High-risk individuals have a conversion rate of 35% but we have no idea which of the group fits into this category.

Summary of Priorities and Challenges for Early Intervention:

- Identifying the subgroup of high-risk participants likely to convert in the immediate future can help to:
  - Focus limited resources and reduce false-positives (significant side-effects).
  - Reduce untreated time, improve course, and potentially prevent onset.
  - Train families to reduce EE, and provide psychoeducation in enlist member to help track symptoms.
  - Help to inoculate: prepare and protect the care takers.
Early Identification

• Helps improve course, delay onset, and may help to prevent onset.
Neurotoxicity of Psychosis

Enduring Effects of Untreated Psychosis

- Short DUP, N=31 (treatment <1 year after psychosis onset)
- Long DUP, N=22 (treatment ≥1 year after psychosis onset)

~40% Relapse
~80% Relapse

% Patients Relapse-Free

# Months after treatment entry

**Example: Perceptual Abnormalities**

**P. 4. DESCRIPTION: PERCEPTUAL ABNORMALITIES/HALLUCINATIONS**

a. Unusual perceptual experiences. Heightened or dulled perceptions, vivid sensory experiences, distortions, illusions.

b. Pseudo-hallucinations or hallucinations into which the subject has insight (i.e. is aware of their abnormal nature.)

c. Occasional frank hallucinations that may minimally influence thinking or behavior.

Anchors in each scale are intended to provide guidelines and examples of signs for every symptom observed. It is not necessary to meet every criterion in any one anchor to assign a particular rating. Basis for ratings includes both interviewer observations and patient reports.

<table>
<thead>
<tr>
<th>PERCEPTUAL ABNORMALITIES/HALLUCINATIONS</th>
<th>Severity Scale (circle one)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 Absent</td>
<td>1 Questionably Present</td>
</tr>
<tr>
<td>1 Questionably Present</td>
<td>2 Mild</td>
</tr>
<tr>
<td>2 Mild</td>
<td>3 Moderate</td>
</tr>
<tr>
<td>3 Moderate</td>
<td>4 Moderately Severe</td>
</tr>
<tr>
<td>4 Moderately Severe</td>
<td>5 Severe but Not Psychotic</td>
</tr>
<tr>
<td>5 Severe but Not Psychotic</td>
<td>6 Severe and Psychotic</td>
</tr>
</tbody>
</table>

| Minor, but noticeable perceptual sensitivity (e.g. heightened, dulled, distorted, etc.). | Unexpected, unformed perceptual experiences/changes that are puzzling but are not considered to be significant. | Repeated, unformed images (e.g., shadows, trails, sounds, etc.), illusions, or persistent perceptual distortions that may be worrisome or experienced as unusual. | Recurrent illusions or momentary hallucinations that are recognized as not real yet can be frightening or captivating, and may affect behavior slightly. Not sure of source of experiences. | Hallucinations that occasionally affect thinking or behavior, that are experienced as possibly external to self or possibly real. Skepticism can be induced. | Recurrent hallucinations perceived as real and distinct from the person's thoughts. Clearly influence thinking, feeling, and/or behavior. Skepticism cannot be induced. |
If only the first signs of severe mental illness were this easy to spot.

There are many ‘red flags’ that may signal the onset of psychosis, a form of mental illness. Recognizing these signs can be hard, but it’s key to helping young people at risk. The Portland Identification and Early Referral (PIER) program is here to help. Our goal is to identify and treat those at risk through family intervention, education, and medical therapy. In many cases, early treatment can stop psychosis in its tracks.

The PIER Program
“an ounce of prevention”

For more information, including a list of warning signs, please contact PIER at 1-877-880-3377.

Maine Medical Center
A health place like no place in Maine.
Young people outgrow many things, but not severe mental illness. Most cases develop after 12 and begin with the following warning signs:

- A drop in performance at school, work, or home
- Increasing social withdrawal and isolation
- Significant changes in behavior or thinking
- A change in how one thinks, feels, hears, or experiences the world

If you or your child show most of these symptoms, seek help as soon as possible. Treatment is available, and early intervention may prevent an illness.

What if it’s not “just a phase”?

For more information, call 1-877-880-3377.

The P.I.E. Program
“an ounce of prevention”

Maine Medical Center

The MaineHealth® Family
• Prodromal patients who convert to psychosis = 35% in two years (from being identified as prodromal)

• 75% of patients with schizophrenia show a prodromal syndrome first

• Recent decline Social and Cognitive function, and subtle psychotic symptoms define a prodromal state.

• Environmental Stressors include: a) Normal adolescent stressors, b) Stressful life events, and c) Expressed Emotion in the family- these factors contribute to the onset of illness, and are good targets for intervention.

• Interventions: Medicine (low dose antipsychotics), CBT, Social Skills training, Family therapy, stress training.

• Early Identification and treatment definitely improves course (less relapses & symptoms) and may..... prevent onset.
Links!

- http://vimeo.com/6609638