SCHIZOPHRENIA and PSYCHOSES

Schizophrenia is a diagnosis which includes psychoses symptoms.
Greek - Skhizen (to split) Phren (mind)
Splitting of the mind or its function – NOT a split personality.
Psychoses can be a descriptive term for a group of symptoms characterised by thoughts and emotions which are disconnected from reality.

Outline
- Epidemiology
- Aetiology
- Clinical features
- Treatment
- Prognosis

Epidemiology
- Incidence/prevalence
  - Life time risk 1%
  - Annual incidence 15-20/100,000
  - Prevalence 0.5 -1%
- Similar statistics across all cultures WHO 1973
- Peak onset
  - Men: 15-25 years
  - Women 25-35 years
  - Similar rates in men and women

Aetiology: Gene-environment threshold hypothesis

Several susceptibility genes
Early environment events (Obstetric, paediatric effects on brain)
leads to increased vulnerability (neuromotor delay, cognitive impairment, social anxiety)

Psychosis
Drug misuse

Genetics –cont–
- Rate of schizophrenia in adopted away children higher if had biological parent with Schizophrenia
- Children raised by an adoptive parent with schizophrenia do not have an increased rate
- Polygenic mode of transmission
Aetiology: Peri-natal exposure
- Higher rates of pregnancy and birth complications in people who develop schizophrenia
  - Maternal infection
    - Higher rates in winter births
    - Exposure to influenza epidemics in 2nd trimester may increase risk (Small studies, highly controversial)
  - Obstetric complications
    - Low birth weight
    - Prematurity
    - Subtle hypoxic-ischaemic CNS / neuronal damage?
  - A neuro-developmental disorder?

Brain abnormalities
- Not diagnostic for Schizophrenia
- Reduced whole brain volume
- Enlarged lateral and third ventricle
- Bilateral reduction hippocampal and amygdala volume
- Abnormal cerebral blood flow
- Aberrant connectivity between synapses and dendrites “disconnectivity syndrome”
- Dopamine theory
  - Imbalance of serotonin-dopamine in pre-frontal cortex
  - Glutamate deficiency (Dopamine imbalance)
- EEG abnormalities especially after evoked potentials

Epidemiology: Social factors
- More people with SCZ in lower socio-economic class
- Social adversity in childhood may increase risk of SCZ
- Higher rate of admission with SCZ in urban areas
- Higher rates of schizophrenia in those born in urban areas
  - Social drift versus social causation hypothesis

Ventricular size

Epidemiology: Social factors
- Higher incidence in recent immigrants (e.g. 2nd generation African-Caribbean immigrants)
  - Selective migration of vulnerable individuals
  - Related to lower socio-economic status
  - Exposure to risk factors in early life
  - Possible racial discrimination

Aetiology: Social factors
- Adverse life events trigger illness onset and relapse, but are not causal
- High expressed emotions can lead to relapse (critical comments, hostility, over-involvement)
- Drug misuse
  - Cannabis component cause but not sufficient alone
  - Most illicit drugs increase serotonin and dopamine and can give symptoms of psychosis short-term
**Pathophysiological Theory**

Hyperactive mesolimbic pathways

VTA → Nucleus accumbens

Responsible for positive symptoms

Hypactive mesocortical pathways

VTA → frontal cortex

Responsible for negative symptoms

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**Symptoms**

<table>
<thead>
<tr>
<th>Premonial</th>
<th>Prodromal</th>
<th>Positive</th>
<th>Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subtle motor, linguistic and social dysfunction Jones et al 1994</td>
<td>Functional decline, odd ideas, eccentric interests, changes in affect, unusual speech and bizarre perceptual experiences</td>
<td>Delusions, hallucinations, thought disorder, bizarre behaviour</td>
<td>Flattening of affect and volition, amotivation, anhedonia and attentional impairment</td>
</tr>
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</table>

**Definition F20 Schizophrenia  ICD 10**

Symptoms lasting for at least one month (at some time during most of the days)

At least one of the following:

- Thought echo/insertion / withdrawal, or thought broadcasting
- Delusions of control / passivity phenomena, delusional perception
- Hallucinatory voices giving running commentary or discussing patient between themselves (3+ persons), or other types of hallucinatory voices coming from some part of the body
- Persistent delusions of other kinds that are culturally inappropriate and impossible

Or at least two of the following:

- Persistent hallucinations in any modality when accompanied by delusions (which may be fleeting or half-formed) without clear affective content, or when accompanied by persistent over-valued ideas
- Neologisms, breaks or interpolations in the train of thought, resulting in incoherence or irrelevant speech
- Catatonic behaviour
- "Negative" symptoms (Flattening of affect and volition, amotivation, anhedonia and attentional impairment)

Exclusion criteria (Differential diagnosis)

- Manic or depressive episode
- Organic brain disease or alcohol- or drug-related

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**Schizophrenia Sub-types**

<table>
<thead>
<tr>
<th>Paranoid schizophrenia</th>
<th>Delusions or hallucinations prominent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hebachipic schizophrenia</td>
<td>Flattening, shallowness, incongruity or inappropriateness of affect</td>
</tr>
<tr>
<td>Behaviour which is aimless and disjointed</td>
<td></td>
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</table>

**Thought disorder**

**Catatonic Schizophrenia**

For a period of at least two weeks one or more of the following psychomotor disturbances:

1. Stupor or mutism
2. Excitement
3. Posturing
4. Negativism
5. Rigidity or (6) Waxy flexibility
6. Command automatism

**Simple schizophrenia**

Riddiculous but progressive negative symptoms

No overt psychotic symptoms prior

**Residual**

Negative symptoms with clear cut positive symptoms in the past

**Undifferentiated**

Criteria for Schizophrenia but none of the above sub-types

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**Differential Diagnosis**

- Organic syndromes.
- Drug induced states.
- Mood disorders with psychotic features.
- Delusional disorders.
- Personality disorders.

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**Prognosis**

- ~ 22% of patients have one episode only (complete remission)
- ~ 32% episodic remittent
- ~ 8% impairment after first episode (stable deficit)
- ~ 38% impairment increasing after each episode
- Relapse 60-80% in 5 years
- ~ 10% commit suicide
- Reduced life span by 10 years
Management

- Physical
- Psychological
- Social
- Rehabilitation & Recovery

Treatment: Medication

- Medication effects (and side effects)
  - Blockage of different receptor types
  - To target positive and negative symptoms, cognitive performance and non-specific symptoms and behaviour
    - Dopamine D2 receptors (extra pyramidal side effects)
    - Muscarinic-anticholinergic receptors (Constipation, drowsiness, dry mouth, blurred vision)
    - Alpha 1 adrenergic receptors (hypotension, dizziness)
    - Histaminic receptors (weight gain, drowsiness)
  - Oral or injection (short or long acting)

- Adjunctive medication
  - Anti depressants, mood stabilizers, tranquilizers

PET image showing dopamine receptor binding in the basal ganglia

Treatment: Medication and other medical

<table>
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<tr>
<th>Medication</th>
<th>Examples</th>
<th>Some Side effects</th>
</tr>
</thead>
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<tr>
<td>Typical antipsychotics</td>
<td>Haloperidol, Flupenthixol, Fluphenazine, Pipothiazine, Zuclopenthixol</td>
<td>Extra pyramidal, Sexual side effects, Weight gain</td>
</tr>
<tr>
<td>Atypical new generation antipsychotics</td>
<td>Risperidone, Olanzapine, Aripiprazole</td>
<td>Less EPS, Metabolic syndrome, Some weight gain</td>
</tr>
<tr>
<td>Treatment resistance</td>
<td>Clozapine (Blocks more selective)</td>
<td>Agranulocytosis, Myocarditis, Cardiomyopathy, Pulmonary embolism, Sexual side effects, Weight gain</td>
</tr>
</tbody>
</table>

In life threatening situations or extreme treatment resistance: ECT

NICE GUIDELINES - Acute episode

- Decide antipsychotic with the service user and carer if appropriate.
- Most suitable medication - consider the relative potential of individual antipsychotics to cause extra pyramidal side effects (such as akathisia), metabolic side effects (such as weight gain), and other side effects (including unpleasant subjective experiences).
- Trial of the medication at optimum dosage for 4–6 weeks.

NICE GUIDELINES

- Offer CBT and family intervention.
- High risk of relapse if medication is stopped in 1–2 years.
- Offering depot/long-acting injectable antipsychotics - service users prefer -avoiding covert nonadherence
NICE GUIDELINES

Symptoms have not responded adequately to treatment:
- review the diagnosis
- adherence to antipsychotic medication
- psychological treatments
- other causes of non-response, for example co-morbid substance or alcohol misuse, concurrent use of other prescribed medication, or physical illness.

Treatment –cont.-:
Comprehensive multi-disciplinary approach

- Social
  - Integrated care plan approach (person-centred)
  - Care co-ordinator, individual care plan, recovery plan
  - Occupational therapy
- Psychological
  - Psycho education and relapse signature
  - CBT
  - Family work
  - Art therapy
- Rehabilitation
  - Social skills training
  - Carer’s assessment
  - Monitor physical health

References
- NICE guidance Schizophrenia Updated March 2009
- McDonald C. and Murray R. Early and late environmental risk factors for schizophrenia. Brain Research Reviews 2001;35:7