THE ALARM OF EARLY PSYCHOSIS

PSYCHOSIS PART 1
In this video, you will learn

• The classification of Psychosis
• DSM-5 criteria of Schizophrenia
• Important differences between 1st & 2nd generation Anti-psychotic medications, and their side effect profiles
• Role of General Practitioner (GP) in the management of Psychosis in primary care clinic
Role of GP

• Keep high index of suspicion for Early Psychosis
• Refer for Multidisciplinary management
• Co-manage stable patients in partnership with psychiatrist
• Monitor & detect early relapse
• Monitor efficacy & side effects of medications
• Reinforce compliance to medications & psychosocial intervention
Misunderstanding of Psychosis

• It is a split-personality
• No matter what is done, psychotic patients will go downhill rapidly
• Anti-psychotics do more harm than good
• All patients will need Anti-psychotics for life
What is Psychosis?

A Severe Mental Disorder where the individual 
LOSES TOUCH WITH REALITY
Clinical significance of Psychosis

• 3% of general population experience psychotic symptoms
  ◦ 20% of which seek help at primary care

• 1% of population develops schizophrenia
  ◦ Peak age of onset: adolescence to young adulthood
  ◦ For age 15-44, Schizophrenia is ranked top 3 as the leading cause of disease burden locally (2004) & top 8 worldwide (2001)

• Disproportionately high social & economic costs

• Disproportionately high mortality

• 1 in 10 schizophrenia patients dies of suicide
Classification of Psychosis

**Psychosis**

- **Functional**
  - Brief Psychotic Disorder (<1 month Duration)
  - Schizophreniform Disorders (<6 months Duration)
  - Schizophrenia (>6 months Duration)
  - Schizoaffective Disorder
  - Delusional Disorders

- **Organic Causes**
  - Brain/ Intracranial
    - Head Injury with intra or extra cranial bleed
    - Brain Neoplasms
    - Epilepsy
  - Infection
    - Encephalitis
    - Meningitis
    - Septicaemia
    - Pneumonia
    - HIV
    - Neurosyphilis
  - Metabolic
    - Renal Failure
    - Hepatic Failure
    - Cardio-respiratory Failure (Hypoxia)
    - Hypo/ Hyperthyroidism
    - Cushing/ Addison’s disease
    - Any Electrolyte abnormality eg
      - Hypo/HyperNa
      - Hypokalemia
      - Hypo/ Hyperglycaemia
  - Endocrine
    - Any Electrolyte abnormality eg
      - Hypo/ HyperNa
      - Hypokalemia
      - Hypo/ Hyperglycaemia
  - Autoimmune
    - SLE
    - Hashimoto’s thyroiditis
    - Sarcoidosis
  - Vitamin Deficiency
    - Thiamine (B1) deficiency
    - (Korsakoff's psychosis)
    - Niacin (B3) deficiency
    - B12 deficiency

- **Drug/Substance Induced**
  - Illicit Drugs
  - Alcohol
  - Medications
    - Antibacterial:
      - Cefalexin
      - Ciprofloxacin
      - Gentamicin
    - Antituberculous:
      - Isoniazid
    - Anticonvulsants:
      - Sodium valproate
      - Bromocriptine
      - Corticosteroids
    - Hallucinogens:
      - LSD
      - Magic mushrooms
      - Ecstasy (MDMA)
      - Cannabis (in high doses)
      - Dissociative Drugs:
        - Ketamine
        - Dextromethorphan
      - Stimulants:
        - Amphetamines, ICE
## Mental State Examination (MSE)

| **Attitude, Appearance & Behaviour** | 25 years old Chinese female, alert, oriented to person, time and place  
No clouding of sensorium; loose, hanging hair, neat clothing, calm, little eye contact |
| **Affect** | Blunted, inappropriate expression of emotions |
| **Mood** | Mildly depressed |
| **Thought Process** | Loosened association, no flight of ideas |
| **Thought Content** | Delusions |
| **Perceptual Disturbances** | Mainly auditory hallucination |
| **Speech** | Not pressured, no poverty |
| **Cognitive Function** | Attention, concentration, memory, understanding  
Using abbreviated mental test (AMT) ≥ 9/10 |
| **Insight** | Lacks understanding of her illness, though recognises need for medicine |
| **Suicide/ Aggression** | Nil |

(Focused Physical Examination is also performed to exclude organic causes and metabolic diseases)
## First Rank symptoms of Schneider

(Strongly suggestive of Schizophrenia when present) (adapted)\(^5\)

<table>
<thead>
<tr>
<th>Auditory Hallucinations</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Voices discussing the patient in third person</td>
</tr>
<tr>
<td>• Voices commenting on the patient’s thoughts or actions</td>
</tr>
<tr>
<td>• Hearing one’s own thoughts being spoken out aloud</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Delusions of Thought Interference</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Thought insertion:</td>
</tr>
<tr>
<td>o The experience of having thoughts put into one’s mind by another person, or thinking someone else’s thoughts</td>
</tr>
<tr>
<td>• Thought withdrawal:</td>
</tr>
<tr>
<td>o The experience of one’s own thoughts being removed from one’s mind</td>
</tr>
<tr>
<td>• Thought broadcasting:</td>
</tr>
<tr>
<td>o The experience that one’s thoughts escape into the outside world and are experienced by others</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Delusion of Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Delusions of Control:</td>
</tr>
<tr>
<td>o The experience that one’s thoughts, emotions, impulses or actions are imposed or controlled by an external agent</td>
</tr>
<tr>
<td>• Somatic passivity:</td>
</tr>
<tr>
<td>o The belief that sensation(s) are being imposed upon one’s body by an external agent</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Delusional Perception</th>
</tr>
</thead>
<tbody>
<tr>
<td>• A primary delusion in which a normal perception is infused with a unique and idiosyncratic delusional meaning which does not have any apparent link between the perceived object and the delusion</td>
</tr>
</tbody>
</table>
## Laboratory investigations if clinically indicated (adapted)\(^5\)

<table>
<thead>
<tr>
<th>Investigations</th>
<th>Rationale/Medical Conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Full Blood Count, Fasting blood glucose &amp; lipids, Renal function test, Calcium, Magnesium, Liver function test, Urine for drug screening</td>
<td>Screening for Infection &amp; Anaemia Monitor haematological &amp; Baseline assessment for metabolic diseases before starting antipsychotics Electrolytes abnormalities Alcoholic consumption</td>
</tr>
<tr>
<td>Vitamin B12, Folate</td>
<td>Nutritional encephalopathies, Dementia</td>
</tr>
<tr>
<td>Thyroid Function Test</td>
<td>Hyperthyroidism, Hypothyroidism</td>
</tr>
<tr>
<td>HIV, VDRL/TPHA</td>
<td>HIV opportunistic infections, Neurosyphilis</td>
</tr>
<tr>
<td>Brain CT</td>
<td>Brain tumour, Head injury</td>
</tr>
<tr>
<td>If necessary, screen for</td>
<td>Epilepsy, Cushing’s Disease, SLE, Hashimoto’s encephalopathy Anti-NMDA receptor encephalitis, Wilson’s Disease Inborn errors of Metabolism</td>
</tr>
</tbody>
</table>
Jane fulfils the DSM-5 Diagnostic Criteria of Schizophrenia (simplified)\(^1\)

<table>
<thead>
<tr>
<th>A. Two or more symptoms:</th>
<th>Delusions</th>
<th>√</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hallucinations</td>
<td>√</td>
</tr>
<tr>
<td></td>
<td>Disorganised (bizarre) speech</td>
<td>√</td>
</tr>
<tr>
<td></td>
<td>Disorganised (bizarre) behaviour</td>
<td>√</td>
</tr>
<tr>
<td></td>
<td>Negative symptoms (emotional blunting, apathy, avolition, poverty of speech, asocialisation, anhedonia, inattention)</td>
<td>√</td>
</tr>
<tr>
<td>B. Duration</td>
<td>1 month of constant, characteristic symptoms</td>
<td>√</td>
</tr>
<tr>
<td></td>
<td>6 months of continual symptoms</td>
<td>√</td>
</tr>
<tr>
<td>C. Exclusion Criteria</td>
<td>Exclude schizoaffective disorder, mood disorder, autism spectrum disorder, organic psychosis or substance use disorder</td>
<td>√</td>
</tr>
<tr>
<td>D. Function</td>
<td>Social / Occupational Dysfunction</td>
<td>√</td>
</tr>
</tbody>
</table>
For Jane

• Her short-term prognosis depends on response to treatment
• Her long-term prognosis appears fair
  
  She has a long duration of about 5 years of undiagnosed psychosis, with negative symptoms
• Predisposing factor: positive family history
• Precipitating factor: exam stress in university
• Perpetuating factor: family’s belief in spiritual possession (for family counselling), inadequate insight
• Protective factor: good premorbid function, cheerful & outgoing personality, above average IQ, not cognitively impaired, supportive family

When adequately treated, 50% of patients are able to maintain satisfying quality of life in the community despite symptoms.⁶
PSYCHOSIS
PHARMACOTHERAPY
AT A GLANCE
History of Antipsychotics

1st generation antipsychotics:
- Electroconvulsive Therapy (ECT)
- Chlorpromazine
- Fluphenazine
- Trifluoperazine
- Haloperidol

2nd generation antipsychotics:
- Clozapine
- Risperidone
- Olanzapine
- Quetiapine
- Ziprasidone
- Aripiprazole

Timeline:
- 1940
- 1950
- 1960
- 1970
- 1980
- 1990
- 2000
<table>
<thead>
<tr>
<th>Comparison</th>
<th>1&lt;sup&gt;st&lt;/sup&gt; generation AP</th>
<th>2&lt;sup&gt;nd&lt;/sup&gt; generation AP</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dopamine Antagonists</strong></td>
<td>+++</td>
<td>++</td>
</tr>
</tbody>
</table>
| **Mechanism of action**                         | Non-selective for Dopamine (D2) receptors:  
- at 60% D2 occupancy, mesolimbic/cortical tract exerts antipsychotic effect  
- at 70% D2 occupancy, nigrostriatal tract exerts EPSE side effect  
- at 80% D2 occupancy, tuberoinfundibular tract increase prolactin secretion side effect | Selective for D2 receptors in mesolimbic system, result in lesser EPSE side effect  
5HT2A receptors Antagonists |
| **Efficacy on positive symptoms**               | ++                           | ++ similar efficacy |
| **Efficacy on negative symptoms**               | -                            | +                           |
| **Extrapyramidal Side Effects (EPSE) & Neuroleptic Malignant Syndrome (NMS)** | +++                          | +                          |
|                                                  | (except Risperidone at high dose ++) | (except Aripiprazole, Lurasidone) |
| **Metabolic side effects**                      | +                            | +++                         |
|                                                  | (except Aripiprazole, Lurasidone) |                             |
| **Sexual Dysfunction**                          | ++                           | +                           |
|                                                  | (except Risperidone at high dose ++) |                             |
| **Cost**                                        | +                            | +++                         |
| **Also use in mania, depression, aggression**   | +                            | +                           |
| **Available in injections**                     | Haloperidol decanoate (Haldol depot*), Flupenthixol decanoate (Fluanxol depot*) Zuclopenthixol decanoate (Clopixol depot*) | Risperidone (Risperdal Consta® q2w) Paliperidone (Invega Sustenna® q1m, or Trinza®q3m) Aripiprazole (Abilify Maintena*) |

*Haldol depot®, Fluanxol depot®, Clopixol depot*, Risperdal Consta®, Invega Sustenna®, Trinza®, Abilify Maintena*
Figure 1. The Four Dopamine Pathways relevant to Antipsychotic Pharmacology. DA: dopamine; EPS: Extrapyramidal Syndrome; TD: Tardive Dyskinesia; VTA: ventral tegmental area.

Adapted from http://tmedweb.tulane.edu/pharmwiki/doku.php/rx_of_schizophrenia
Extrapyramidal Side Effects (EPSE) of Antipsychotics²,⁵

<table>
<thead>
<tr>
<th>EPSE</th>
<th>Duration of onset</th>
<th>Signs</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute dystonia (occurs in 10% of patients, especially in young males)</td>
<td>Hours to days</td>
<td>Fixed muscle postures with spasm (oculogyric crisis, torticollis, opisthotonos)</td>
<td>• Diazepam or Anticholinergics (benzhexol/ benztropine)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Supportive</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Switch to 2nd generation</td>
</tr>
<tr>
<td>Parkinsonism (occurs in up to 90% of patients)</td>
<td>Days to weeks</td>
<td>Tremors, rigidity, bradykinesia, mask-like facies, festinating gait</td>
<td>• Anticholinergics</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Reduce dose</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Switch to 2nd generation</td>
</tr>
<tr>
<td>Akathisia (occurs in 20% of patients, esp. middle aged females)</td>
<td>Hours to weeks</td>
<td>Subjective feelings of restlessness &amp; objective motor restlessness (swinging of legs, pacing, rocking)</td>
<td>• Reduce dose (distinguish from worsening psychosis which requires increase dose)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Propranolol or benzodiazepine</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Switch to 2nd generation</td>
</tr>
<tr>
<td>Tardive Dyskinesia (TD) (Occurs in 5-60% of patients, esp. elderly female with mood disorders)</td>
<td>Months or years</td>
<td>Orofacial dyskinesia, lip smacking, tongue rotating, choreoathetoid movements of head, neck &amp; trunk</td>
<td>• Prevention: Use the lowest possible dose for the shortest possible time</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Benzodiazepine, propranolol, vitamin E</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Use of anticholinergic increases risk of TD</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Switch to 2nd generation</td>
</tr>
</tbody>
</table>
Neuroleptic Malignant Syndrome (NMS)

What it is
- Emergency with 10-20% mortality rate
  - occurs in <1% patients
- Idiosyncratic reaction, not related to dose
- Sympathetic hyperactivity

Management
- Admit to hospital - withdrawal of the offending AP
- Supportive care for hyperthermia, hydration
- Pharmacotherapy
  - Benzodiazepines
  - Dopamine agonists (e.g. bromocriptine)
  - IV muscle relaxants (e.g. dantrolene)

DSM-5 criteria for NMS¹
1. Use of neuroleptic
2. Elevated temperature
3. Severe muscle rigidity
   AND 2 of the following:
   - Diaphoresis
   - Dysphagia
   - Tremor
   - Incontinence
   - Changes in level of consciousness ranging from confusion to coma
   - Mutism
   - Tachycardia
   - Elevated or labile blood pressure
   - Leukocytosis
   - Laboratory evidence of muscle injury
### 2nd Generation Antipsychotics & Side-Effect Profile

<table>
<thead>
<tr>
<th>Drug</th>
<th>Target dose (mg/day)</th>
<th>Metabolic Effect (monitor weight, BMI, BP, fasting blood glucose &amp; lipids - baseline - 3 months - yearly)</th>
<th>EPSE</th>
<th>Prolactin secretion &amp; sexual dysfunction</th>
<th>Sedation</th>
<th>Anticholinergic (dry mouth, constipation, urinary retention, blurring of vision, precipitate glaucoma)</th>
<th>Hypotension &amp; reflex tachycardia (start low &amp; go slow esp for Quetiapine &amp; Clozapine)</th>
<th>Agranulocytosis (for Clozapine: mandatory to monitor absolute neutrophil count - weekly for first 6 months - biweekly for next 6 months - monthly for life)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quetiapine (Seroquel®)</td>
<td>150-800 (in 2 divided doses)</td>
<td>++</td>
<td>+/-</td>
<td>-</td>
<td>+++</td>
<td>+ (at high doses)</td>
<td>+++</td>
<td>-</td>
</tr>
<tr>
<td>Risperidone (Risperdal®)</td>
<td>2-6</td>
<td>++</td>
<td>+++</td>
<td>+++ (at high dose)</td>
<td>++</td>
<td>-</td>
<td>++</td>
<td>-</td>
</tr>
<tr>
<td>Aripiprazole (Abilify®)</td>
<td>10-30</td>
<td>+/-</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Ziprasidone (Geodon®)</td>
<td>40-160</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>++</td>
<td>-</td>
<td>+ (may prolong QTc)</td>
<td>-</td>
</tr>
<tr>
<td>Olanzapine (Zyprexa®)</td>
<td>10-20</td>
<td>+++</td>
<td>++</td>
<td>+</td>
<td>++</td>
<td>+ (at high dose)</td>
<td>+/-</td>
<td>-</td>
</tr>
<tr>
<td>Clozapine (Clozaril®)</td>
<td>200-450 (in 2 divided doses)</td>
<td>+++</td>
<td>+/-</td>
<td>+</td>
<td>+++</td>
<td>++</td>
<td>+++</td>
<td>+++</td>
</tr>
</tbody>
</table>
Algorithm of Approach in Management of Schizophrenia

Patient with Hallucination or Delusion

Exclude Organic Causes

Exclude Drug / Substance Abuse

Functional Psychosis

Fulfils DSM-5 for Schizophrenia

Use a single Antipsychotic (AP) 1st or 2nd generation according to side-effect profile & efficacy, 4-6 weeks

- Treatment of associated issues:
  - Depression or Anxiety (SSRI)
  - Mania (Mood stabilisers)
  - Agitation & Insomnia (Hypnotics)
  - Suicidal tendency (ECT)

- Maintain effective dose at least 6 months, continue for 2 years not lower than half of effective dose
- Life-long for patients with 2 episodes within 5 years

Does not fulfil DSM-5 for Schizophrenia

Evaluate

- Multidisciplinary team
- Psychosocial Intervention

Side effects → Inadequate response

Switch to another AP 1st or 2nd generation

- Clozapine +/- AP or ECT (managed by specialist)

Side effects → Inadequate response

VASECME@gmail.com

Mental health CME for primary care
When to refer$^{2,5}$

- To confirm diagnosis of Psychosis & initiate treatment
- Risk of harm to self & to others, or a public nuisance
- For multidisciplinary management
- Failed pharmacotherapy or complications from pharmacotherapy
- Special patient groups: obstetric, paediatric & geriatric
In IMH Mental Health-GP Partnership Program (IMH-GPPP)$^5$

Patients co-partnered with GP are those with:

- Stable psychiatric conditions
- Maintenance anti-psychotic medications, requiring minimum adjustments to dosage

Excluding those with:

- Suicide or aggression risk
- Disruptive Personality Disorder
- On Clozapine prescription
- Managed with Benzodiazepines only

IMH-GPPP is ongoing, those interested, please contact IMH-GPP@imh.com.sg
Natural history of schizophrenia

Adapted From Slideshare: Update on Schizophrenia
CAN PSYCHOSIS BE PREVENTED OR DELAYED?

...SEE PSYCHOSIS PART 2 ON “THE INSIDIOUS ONSET OF AT-RISK MENTAL STATE”
REFERENCES


ACKNOWLEDGEMENT

Authors (VASE Team)

• Dr Charity Low
  (Peace Family Clinic (WL 832), GDMH 18/19)
• Dr Roy Teow Kay Leong
  (United Health Family Clinic & Surgery, GDMH 16/17)
• Dr Paul Ang (Zenith Medical Clinic, GDMH 16/17)
• Dr Eugene Chua
  (Family Physician in public institute, GDMH 18/19)
• Dr Lim Choon Guan (Senior Consultant and Deputy Chief, Dept of Developmental Psychiatry, IMH)
• Dr Kumi Mehara (Japan Green Clinic, GDMH 18/19)
• Dr Siti Aishah (Polyclinic, GDMH 16/17)
• Dr Nyein Nyein (Clinical Psychologist, Thrive Family)
• Mr Ng Boon Tat (Pharmacist)

Actors

• Dr Eugene Chua as The General Practitioner
• Choy Yu (Staff Nurse, KTPH) as Jane
• Jackie Low as The Mother

Contributors

• Dr Tommy Chan Chun Ting (Consultant, EPIP, IMH)
• Dr Chan Keen Loong (Senior Consultant, Department of Psychological Medicine, KTPH)
• Dr Zheng Shushan (Associate Consultant, EPIP, IMH)
• Psalms Chia (Student)

Venue of filming

• IMH clinic consultation room

IMH grant
DISCLAIMER

The information in this video is correct to the best of our knowledge at the point of circulation. It is by no means exhaustive. Please refer to the above references & other materials to consolidate your appreciation of the subject. The authors disclaim any liability in connection with the use of this information.

All rights reserved. No part of this video may be reproduced, distributed or transmitted in any form by any means without the permission of the authors.