



# TREATMENT AND MANAGEMENT of Psychiatric disorders

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# Content/Learning Outcomes



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## 1. Antipsychotics

1. Psychosis  
(Schizophrenia)  
Haloperidol, Risperidone

## 2. Antidepressants

1. Depression –
2. Anxiety disorders  
(Panic, Generalized anxiety disorder, OCD),

## 3. Mood Stabilizers

Mania  
Lithium, Sodium valporate

## 4. Benzodiazepines

Insomnia, anxiety, agitated



should be able

1. to give a few examples of drugs in each category.
2. To know side-effects related certain drugs
3. Know the principles of management & treatment in psychiatry
4. Pharmacokinetic & Pharmacodynamic of medications in psychiatry



# How do you manage the patient?

12/26/2017

1. **Bio- psycho-social & spiritual model**
2. **Reasons to admit patients in Ward:**
  1. May cause danger to the patient or to someone else
  2. Depression ; suicidal,
  3. Psychosis or mania ; aggressive and danger to others
3. **Management = Investigation\*\*\*\*\* + Treatment**

# Not responding? 5 Ds



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1. Drug compliance – partial compliance
2. Dose -inadequate
3. Duration -
4. Dual diagnoses
5. Diagnosis wrong



# 1) Antipsychotics

- ▶ Indications: for psychotic symptoms (Schizophrenia, Mania, Depression with psychotic symptoms)
- ▶ Routes; oral, depot (monthly), IV, IM, Drop

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**Old: Typical/conventional antipsychotic;** a lot of side effects, dopamine blockage > serotonin blockage

1. Phenothiazine group: Chlorpromazine CPZ (sedative, postural hypotension)
2. Butyrophenone group; Haloperidol (>EPS)
3. Thioxanthenes group; flupentixol



## New: Atypical (less side effects) > serotonin antagonism

1. Risperidone (risperidal) 2mg bd (0.5 mg bd)
2. Olanzapine (Zyprexa) 10 mg ON = X obesity
3. Quetiapine (Seroquel) 200mg tds = very sedative
4. Ziprasidone, Aripiprazole (Abilify), Paliperidone, Zydys
5. Clozapine = treatment resistance schizophrenia  
Bone marrow suppression (agranulocytosis)  
FBC (WBC) monitoring





## Recommended CLOZARIL® dosage titration at start of therapy<sup>2</sup>

Week 1	am (mg)	pm (mg)	Total (mg)	Week 2	am (mg)	pm (mg)	Total (mg)
Day 1	12.5	12.5*	12.5-25	Day 8	50	100	150
Day 2	25	–	25	Day 9	100	100	200
Day 3	25	25	50	Day 10	100	100	200
Day 4	25	50	75	Day 11	50	200	250
Day 5	50	50	100	Day 12	50	200	250
Day 6	50	75	125	Day 13	100	200	300
Day 7	50	100	150	Day 14	100	200	300

Additional Subsequent dosage increments should be made no more than once or twice weekly, in increments not to exceed 50mg - 100 mg.



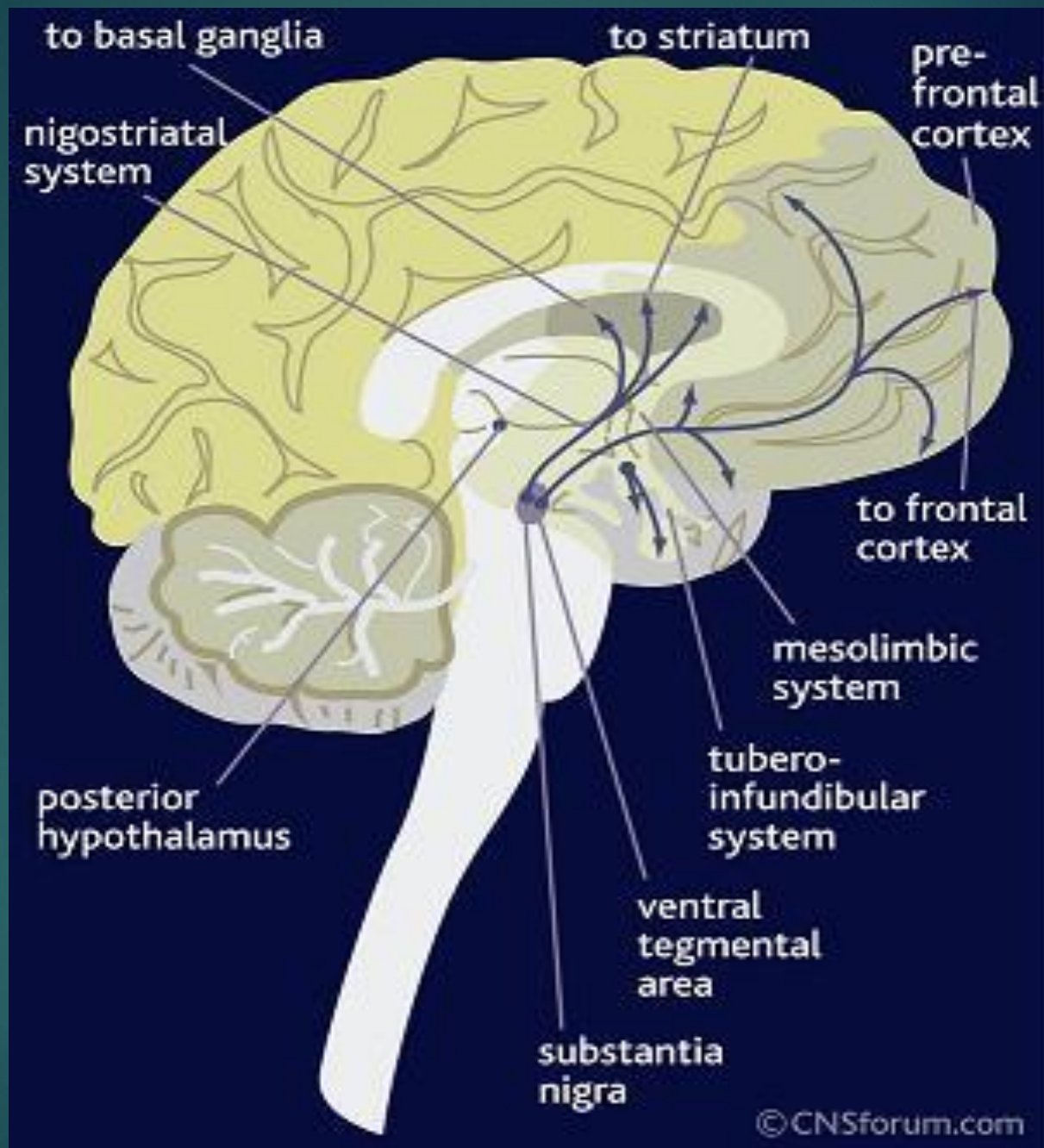


# Side Effects of Antipsychotics:

Dopamine blockage:

1. **Mesolimbic-mesocortical pathway**= reduce positive symptoms
2. **Nigro-striatal pathway**= EPS
3. **Tubero-infundibular pathway** = high prolactin - - amenorrhoea

Why Atypical antipsychotic has less EPS?





# EPS Extra pyramidal Side effects

1. **Acute dystonia** ; immediate side effect > drug naive patients, - hours  
---- sudden muscle contraction,  
neck; torticolis,  
trunk; opisthotonus  
eye; oculogyric crisis  
laryngeal dystonias ; result of suffocation
2. **Parkinsonism (days)** ; tremor, rigidity, stiffness  
Dopamine blockage
3. **Akathesia** : restlessness
4. **Tardive dyskinesia** : abnormal involuntary movements > mouth; chewing  
= supersensitivity of dopamine receptors  
= irreversible



1. **Neuroleptic Malignant Syndrome** ;  
idiosyncratic reaction, fever, stiffness,  
disorientation
2. **Anticholinergic** SE  
Constipation, dryness of mouth, blurred  
vision, urinary retention.
3. **Hormonal** : elevated prolactin  
(galactorrhoea), amenorrhoea, sexual side  
effects
4. **Antihistamine** ; sedation
5. **Weight gain** (Clozapine 4.5kg, Olanzapine 4kg,  
Risperidone 2 kg Ziprasidone 0.04kg; Allison et al)



- ▶ **Metabolite** : metabolite syndrome, syndrome X; diabetes, impaired glucose, hypercholesterolemia,
- ▶ **CVS; anti adrenergic**; postural hypotension, QT prolongation
- ▶ **Sexual dysfunction**



# How to overcome?

**Parkinsonism** ; tremor,  
rigidity, stiffness, salivation

T. Artane  
Reduce antipsychotic dose  
Change antipsychotic

**Acute dystonia**

IM Kemadrin (10mg), BZD

**Akathesia**; restlessness

benzodiazepine,  
propanolol

**Tardive dyskinesia** :  
involuntary movements >  
mouth; chewing

change to  
Clozapine/Quetiapine





# Evolution in treatment approach

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1960

- Positive symptoms reduction

1980

- Negative symptoms focus

1990

- Cognitive deficits
- QoL & Subjective Well-being

2000

- Remission/recovery
- Long-term treatment



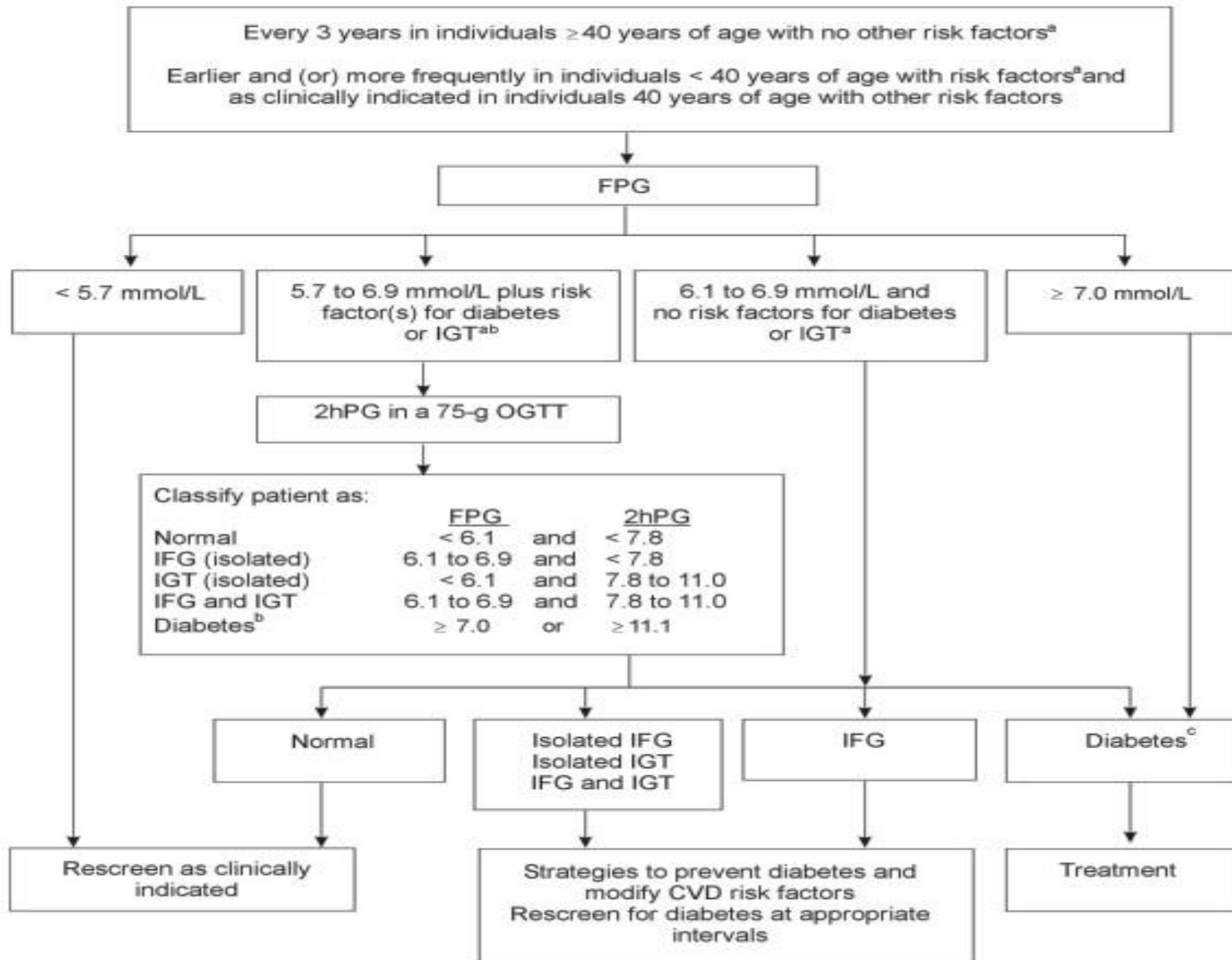
# Metabolic syndrome

**Table 2. Screening and monitoring for cardiovascular risk factors in first 6 months of atypical antipsychotic use.<sup>72,73</sup>**

Baseline screening					
History:	Cardiovascular and diabetes risk factors, family history, diet, exercise				
Physical exam:	BMI, waist circumference				
Investigations:	Fasting plasma glucose, fasting lipids, electrolytes (potassium, magnesium), ECG				
Monitoring*					
	Clozapine	Olanzapine	Quetiapine	Risperidone	Ziprasidone
<b>BMI</b> at 1, 3, and 6 months	✓	✓	✓	✓	
<b>Fasting plasma glucose</b> at 1, 3, and 6 months	✓	✓	✓	✓	
<b>Fasting lipids</b> at 6 months	✓	✓			
<b>Electrolytes</b> monthly			✓	✓	✓
<b>ECG</b> monthly			✓	✓	✓
<b>Cardiac troponin I*</b>	✓				

\*More rigorous monitoring is needed in cases involving higher dosage and polypharmacy.

<sup>†</sup>May be measured with other blood work at 1, 3, and 6 months OR if signs/symptoms suggest myocarditis or pericarditis.



## 2) Mood Stabilizers



- ▶ Indications:
  - ▶ Bipolar, major depressive disorder,
  - ▶ Schizophrenia with depressive symptoms
  - ▶ Schizoaffective disorder



# 1) Lithium

## ▶ Pharmacokinetics

Absorb = GIT

Not protein bind

Not metabolize in liver

Excrete by kidneys

Half-life 20hrs

- ▶ Has teratogenic SE (x pregnant, breast feeding women)
  - 1<sup>st</sup> trimester (Ebstein's anomaly (10-20x RR), anencephaly, cranio-facial abn)
  - 3<sup>rd</sup> trimester (neonatal goiter, cardiac arrhythmia)
- ▶ Blood monitoring baseline investigations
  - 0.8-1.2 mmol/L acute
  - 0.4-0.8 maintenance (therapeutic level),



# Side effects of Lithium

Immediate = metallic taste, dry mouth, constipation, wgt gain, fine tremor, acne,

Long term = Renal (polyuria, minimal glomerulonephritis, renal failure)

Thyroid (hypothyroidism)

Cardiac (T wave flattening, sinus dysrhythmias)

Toxicity symptoms:  $>1.5$  mmol/L coarse tremor, ataxia, GIT symptoms  
 $>2.0$  seizure, disorientation, coma,  
 $> 3.0$  peritoneal dialysis @ HD; death



# Adverse Effects



<b>GIT</b>	<b>Nausea &amp; vomiting; Decreased appetite; Diarrhea (Li citrate); Weight gain (Li – induced oedema)</b>
<b>NS</b>	<b>Tremor; Dysphoria, lack of spontaneity, slowed reaction times, impaired memory; Mild parkinsonism, ataxia, dysarthria,</b>
<b>Renal</b>	<b>Polyuria &amp; polydipsia; Nonspecific interstitial fibrosis (10 years); Renal failure; Nephrotic syndrome</b>
<b>Thyroid</b>	<b>Benign transient diminution of circulating TH, Goiter; benign reversible Exophthalmos; Hyperthyroidism &amp; Hypothyroidism</b>
<b>CVS</b>	<b>ECG – T wave flattening/inversion; Sinus dysrhythmias, Heart block, Syncopal episodes; Ventricular arrhythmias, CHF</b>
<b>Skin</b>	<b>May be dose dependent; Acneiform, Follicular, Maculopapular eruptions; Pretibial ulcerations; worsening of Psoriasis; Alopecia</b>



## 2) Sodium Valproate = Epilim

- Blood monitoring (therapeutic level),
- Has teratogenic SE (x pregnant, breast feeding women)  
Neural tube defect, septal defect
- Metabolize in liver
- Protein bind

## 3) Carbamazepine = Tegretol

- Blood monitoring (therapeutic level),
- Has teratogenic SE (x pregnant, breast feeding women)
- Metabolize in liver
- Protein bind
- Side effects: dizziness, ataxia, tremor, blood (agranulocytosis, aplastic anaemia, leucopenia, thrombocytopenia), rash

## 4) Lamotrigine = new



- ▶ Lamotrigine (Lamictal): This medication appears to be most useful for the depressed phase of bipolar disorder.
- ▶ Topiramax (Topamax)



# Antipsychotic Monotherapy for Bipolar Mood disorder

- ▶ Olanzapine (Zyprexa): This medication is approved for treatment of both acute mania and maintenance once the symptoms are under control.

This medication may be used in combination with an antidepressant for treatment of depression in bipolar disorder.

This medicine may be safer in pregnant women.

- ▶ Risperidone (Risperdal): At higher doses, this medicine may cause restlessness, tremor, or other EPS symptoms.
- ▶ Quetiapine (Seroquel): The most common side effects are sedation and dry mouth.



# 3) Antidepressants

## Indications

1. Major Depressive Disorder
  2. Panic Disorder
  3. Generalized anxiety disorder
  4. Obsessive Compulsive Disorder
- ▶ Bipolar in Depressive state

## Types

- ▶ Old : TCA, MAOI > Side effects
- ▶ New : SSRI, SNRI, NASSA, RIMA



# Antidepressant drug treatment



## Classification and pharmacodynamics of the antidepressants

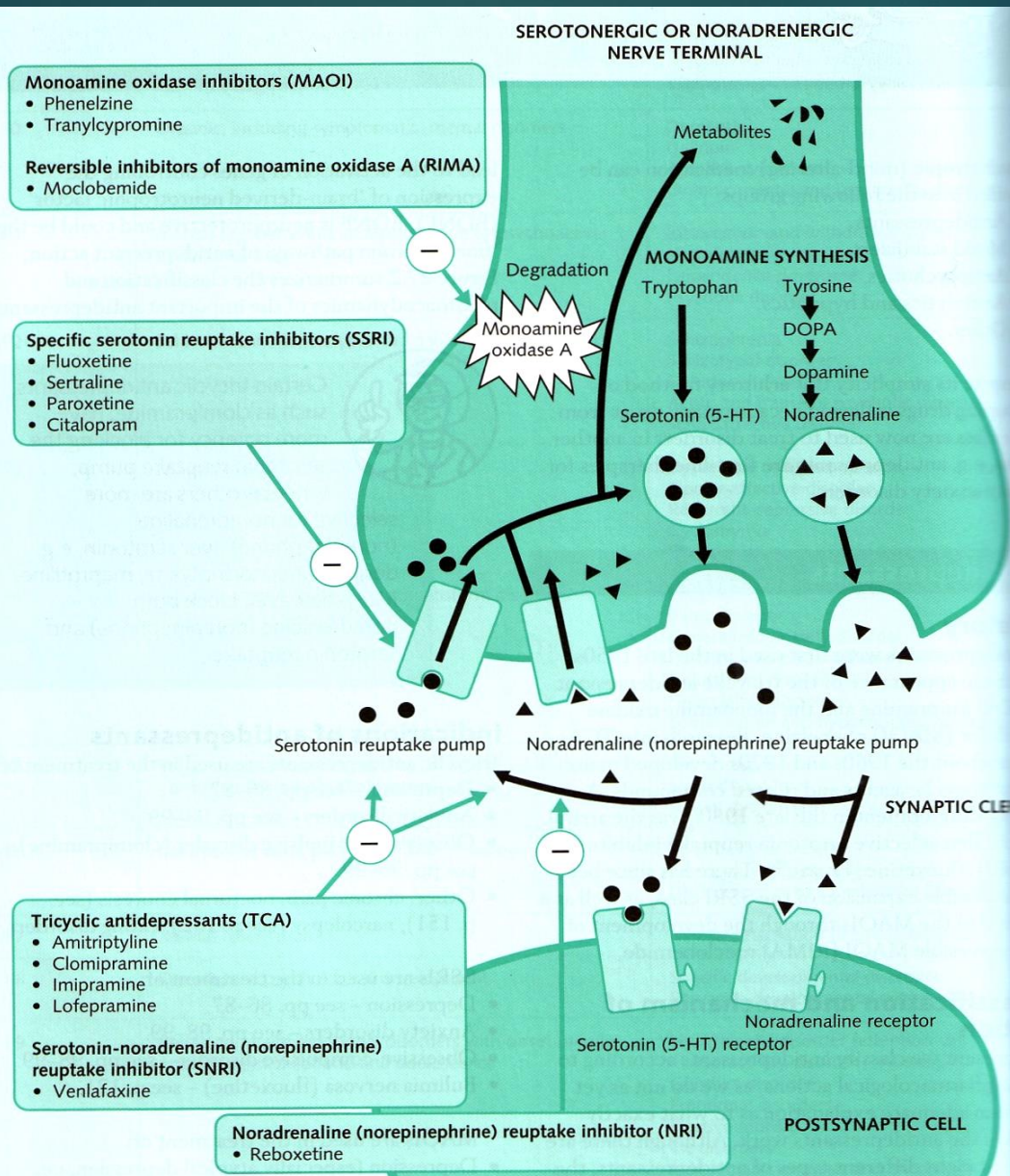
Class of antidepressant	Examples	Mechanism of action
Tricyclic antidepressant (TCA)	Amitriptyline, dosulepin (dothiepin), lofepramine, clomipramine, imipramine	Presynaptic blockade of both noradrenaline (norepinephrine) and serotonin reuptake pumps (to a lesser extent – dopamine) Also blockade of muscarinic, histaminergic and $\alpha$ -adrenergic receptors
Selective serotonin reuptake inhibitor (SSRI)	Fluoxetine, sertraline, paroxetine, citalopram, fluvoxamine	Selective presynaptic blockade of serotonin reuptake pumps
Serotonin-noradrenaline (norepinephrine) reuptake inhibitor (SNRI)	Venlafaxine	Presynaptic blockade of both noradrenaline (norepinephrine) and serotonin reuptake pumps (also dopamine in high doses) but with negligible effects on muscarinic, histaminergic or $\alpha$ -adrenergic receptors (in contrast to TCAs)
Monoamine oxidase inhibitor (MAOI)	Phenelzine, tranylcypromine, isocarboxazid	Non-selective and irreversible inhibition of monoamine oxidase A and B
Reversible inhibitor of monoamine oxidase A (RIMA)	Moclobemide	Selective and reversible inhibition of monoamine oxidase A
Noradrenergic and specific serotonergic antidepressant (NaSSA)	Mirtazapine	Presynaptic $\alpha_2$ receptor blockade (results in increased release of noradrenaline (norepinephrine) and serotonin from presynaptic neurons)
Noradrenaline (norepinephrine) reuptake inhibitor (NRI)	Reboxetine	Selective presynaptic blockade of noradrenaline (norepinephrine) reuptake pumps

Others:

Tetracyclic antidepressants: mianserin, maprotiline

Serotonin 2A antagonist/serotonin reuptake inhibitor (SARI): nefazodone and trazodone





Note: the serotonin and noradrenaline (norepinephrine) pathways are presented together for convenience; they do not occur in the same nerve terminal

Fig. 27.1 Mechanism of action of antidepressants at the synaptic cleft.



# Side Effects of Antidepressions:

## 1. **Anticholinergic SE**

1. Constipation, dryness of mouth, blurred vision

## 2. **Antihistamine** ; sedation

## 3. **Anti adrenergic, CVS**; postural hypotension, QT prolongation

## 4. **Lower seizure threshold**

## 5. **Weight gain**

## 6. **Sexual dysfunction**

## 7. **Serotonin Syndrome ;**



# Psychoeducation on antidepressants

- ▶ Minimum of 2 weeks onset
- ▶ Common side effects
  - ▶ GIT upset etc.
  - ▶ Paradoxical effects



# 4) Benzodiazepines (sedative & hypnotics)

## Properties:

1. Sedation = aggressive, agitated patients
2. Hypnotics = insomnia
3. Muscle relaxant = anesthesia, pre-med
4. Antiepilepsy
5. Anxiolytic = Anxiety disorders

Short-acting benzodiazepines > tolerance and dependence and withdrawal effects

- ◉ Withdrawal symptoms
  - headache
  - mild anxiety
  - insomnia , irritability
  - hand tremors, increased tone
  - periods intense anxiety
  - hypersensitivity to sensory stimuli
  - disturbed sleep, concentration
  - mild paranoia / headache
  - facial numbness





TABLE 1

**BENZODIAZEPINES APPROVED FOR THE TREATMENT OF ANXIETY AND INSOMNIA<sup>2,4\*</sup>**

<b><i>Benzodiazepines</i></b>	<b><i>Dose Equivalence (mg) †</i></b>	<b><i>Effective Dose Range (mg)</i></b>
<i>Short elimination half-life (&lt;12 hrs)</i>		
Alprazolam <sup>‡</sup>	.25	.5–1 TID/QID
Oxazepam	30	10–30 TID/QID
Temazepam	15	7.5–30 at bedtime
Triazolam <sup>§</sup>	.5	.25–.5 at bedtime
<i>Intermediate elimination half-life (12–24 hrs)</i>		
Alprazolam XR	.5	1–4 QD
Lorazepam	1	2–10 divided 2–3 times per day
Estazolam <sup>§</sup>	2	1–2 at bedtime
<i>Long elimination half-life (&gt;24 hrs)</i>		
Chlordiazepoxide	25	5–25 TID/QID
Chorazepate	3.75	15–60 divided 2–3 times per day
Clonazepam <sup>‡</sup>	.25	.5–2 BID
Diazepam	5	2–10 BID to QID
Halazepam	40	20–40 TID/QID
Flurazepam <sup>§</sup>	15	15–30 at bedtime
Quazepam <sup>§</sup>	15	7.5–30 at bedtime

\* Based largely on 2007 *Physician's Desk Reference*.<sup>4</sup> Duration of action is based on mean half-life of all active metabolites. Midazolam is not included as it is indicated only for the induction of general anesthesia and has no role in the treatment of anxiety.

† Others have reported different dose equivalence<sup>2</sup>: alprazolam (0.5 mg); oxazepam (15 mg); temazepam (30 mg); triazolam (0.25 mg); chlordiazepoxide (10 mg); chorazepate (7.5 mg); flurazepam (15 mg); quazepam (15 mg).



## **ADVERSE EFFECTS OF BENZODIAZEPINES**

### **1. Over-sedation**

Depressed psychomotor performance, poor memory, ataxia contribute to car accidents, shoplifting

Most marked in the elderly, may produce mental confusion contribute to falls and fractures

### **2. Additive effects with other CNS depressants**

e.g. alcohol, drug overdose

### **3. Disinhibition**

Aggressiveness ? Contribute to baby battering, wife beating

### **4. Depression, emotional blunting**

### **5. Cognitive impairment**

### **6. Adverse effects in pregnancy**

Neonatal depression

### **7. Abuse**

### **8. Tolerance, dependence, withdrawal effects**





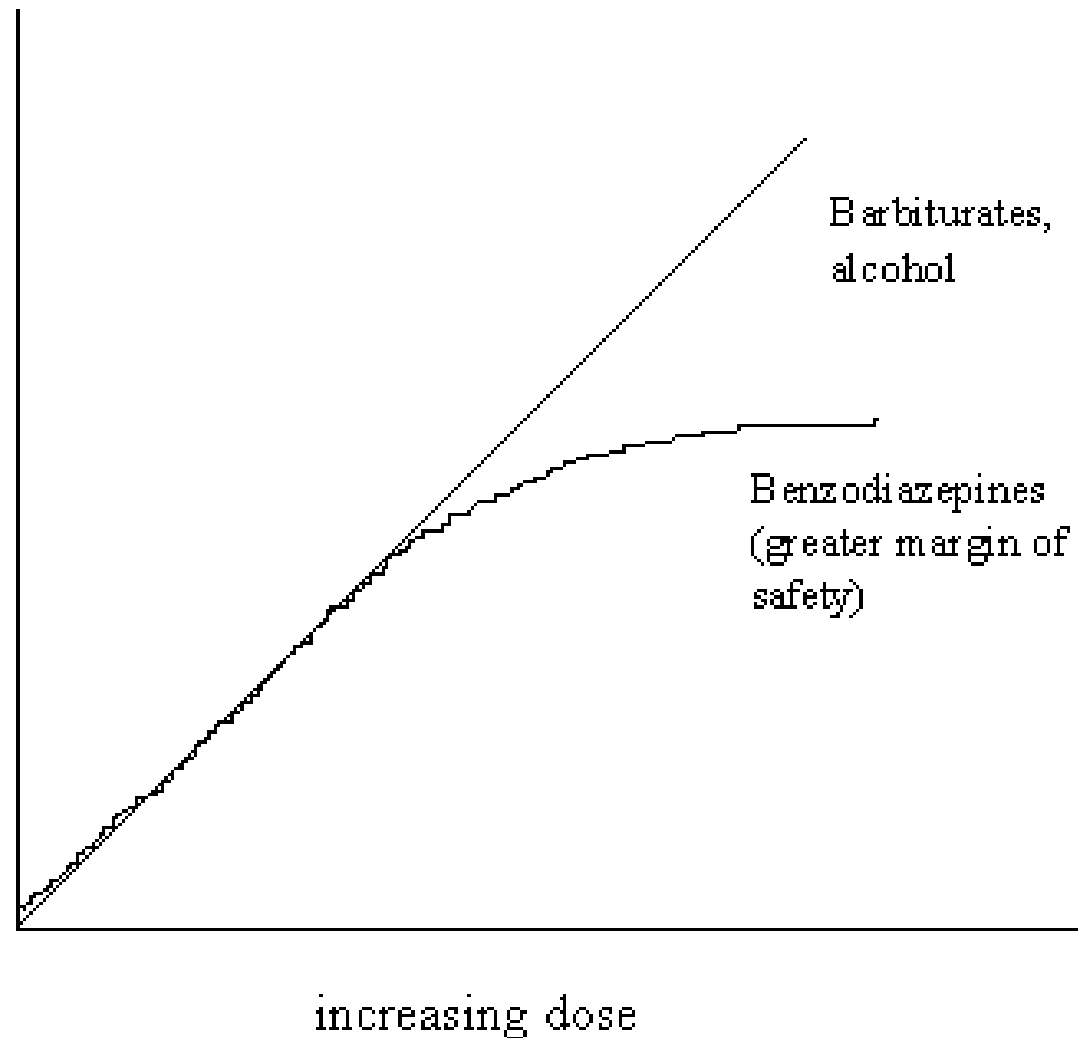
## CNS effects:

depression of medulla  
respiratory centers-  
coma

anesthesia—loss of  
body sensation

hypnosis

sedation





# Cholinesterase inhibitors

- ▶ **What are Cholinesterase Inhibitors (ChE-Is)?**
- ▶ Treatment for mild to moderate Alzheimer's disease.
- ▶ The three most commonly used ChE-Is are donepezil (Aricept, Eisai, Inc), rivastigmine (Exelon, Novartis Pharmaceuticals), and galantamine (Reminyl, Janssen Pharmaceuticals).



- ▶ Methylphenidate ; ADHD
  - ▶ Appetite retardation
  - ▶ Weight & height monitoring



# 5) Electro-Convulsive Therapy: ECT

- ▶ Induce seizure/ fits

## 1) Anesthesia Part =

- ▶ General Anesthetics = Methohexital, propofol
- ▶ Anticholinergic = atropine
- ▶ Muscle relaxants = succinylcholine

## 2) Electrical Stimulus = milicoulombs

# Indications of ECT



Not as first line treatment

1. Major Depressive Disorder
  - Failed medication trials
  - Severe depression with high suicidality
  - Present psychotic or melancholic symptoms
  - Stupor depression
2. Bipolar Affective Disorder (Manic episode)
  - Failed medications
  - Severe and very agitated
3. Schizophrenia
  - Failed medications
  - Marked positive and affective(mood) symptoms
  - Catatonic schizophrenia
4. Other Indications
  - Neuroleptic Malignant Syndrome
  - Intractable seizure disorders
  - Intractable Obsessive Compulsive Disorder

Side effect reversible retrograde and antrograde amnesia

Complications of anathesia





# Psychological Aspects

## Psychotherapy:

- ▶ Psychoeducation = pt and his/her family
- ▶ Counseling,
- ▶ CBT; Cognitive Behavioral Therapy,
- ▶ Psychodynamic psychotherapy,
- ▶ Interpersonal therapy.
- ▶ Behavioral Therapy

Rehabilitation: supported employment,  
occupational therapy

# Social Aspects



1. Family therapy
2. Family counseling
3. Minimize adverse life events e.g. Financial Aids, confiding relationship, resolve marital conflicts
4. Welfare department



# Alternative Medicine

- ◉ Acupuncture
- ◉ Aromatherapy
- ◉ Diet & Nutrition = vitamin & supplementations
- ◉ Environmental Medicine
- ◉ Homeotherapy
- ◉ Herbal Medicine
- ◉ Meditation
- ◉ Yoga
- ◉ Tai Chi



# Lubuk Yu rescuer seeks help of bomoh

By T.N. Alagesh  
news@nst.com.my

**MARAN:** The health authorities may have confirmed that 19 people involved in the rescue operation in Lubuk Yu here last month were infected with melioidosis and leptospirosis, but this has not stopped some in the search party from seeking treatment from traditional healers.

Shahrin Shukor, 31, came down with fever on July 10 after diving into the water to search for the victim. He was subsequently warded at the Sultan Haji Ahmad Shah Hospital in Temerloh from June 12 to 14.

The odd-job worker from Bandar Jengka, after finding out that six members of the search party had died, sought alternative treatment as soon as he was discharged from hospital.

"I believe in both modern and traditional treatment, so I sought the help of a bomoh who said that the site was *keras* (haunted) and my sickness was due to evil spirits.

"He performed some rituals and I later had a special cleansing bath. I was still feeling weak at

the time but now I feel much better.

"I used to visit the waterfall and bathe there but this is the first time I got sick. I don't plan on going there again."

Shahrin claimed that the supernatural beings, who safeguarded the waterfall, were furious with picnickers, especially youngsters who arrived in big groups during the weekends and also at night.

"Besides the heaps of rubbish, some of the youths consume alcohol and indulge in immoral activities. Visitors can find empty alcohol bottles and packets of used condoms in the vicinity of the waterfall."

Felda settler, Mohd Asim Manan, 58, paid a heavy price for his curiosity when he had to be warded at the Jengka 3 Hospital on June 11 after showing flu-like symptoms and severe headaches.

Asim, who visited the waterfall with three other friends during the second day of the search and rescue operation, said he was not part of the operation and was just visiting.

"Since the weather was not promising, we decided to return home after spending some



The Lubuk Yu waterfall site is off-limits to visitors.

two hours at the waterfall. It was crowded with people at that time.

"Upon returning home, I began to feel unwell and my condition worsened on June 11 forcing my family members to rush me to the hospital's emergency ward."

Asim said he felt very weak and had no appetite to eat. He took some herbal medicine but it did not help.

"My family members were worried especially when I could not sleep at night. Now I feel much better. Perhaps there is a mystery surrounding the waterfall."

Tan Eng Seng was in the hospital for 10 days but this has not dampened the spirit of the volunteer fireman.

The 46-year-old vegetable farmer from Kampung Sungai Jerik in Maran, Pahang, was among the 20 people who came down with the severe fever after taking part in the five-day search. He developed chills and severe body aches a day after the end of the operation.

Tan sought treatment at Bandar Jengka Hospital but when his condition worsened, his family decided to send him to a private hospital in Kuantan where he is still being warded.

"This is the most challenging experience I've encountered since I registered to join as a volunteer fireman 20 years ago.

"I knew some of the victims who died and when I heard about their deaths, I actually thought I was going to suffer the same fate as our symptoms were similar."

He said the fire and rescue volunteer team was called in on July 27 and was given fibreglass boats to search for the victim.

"During the five-day search operation, we would arrive early in the morning and only leave the site near midnight.

"The Fire and Rescue Department had arranged for a caterer to deliver meals to the site and usually after a tiring day at work, we would just eat whatever was available there and return home to rest."

# Summary



## EPS

- ▶ **Acute dystonia ; Parkinsonism;**
- ▶ **Akathesia** : restlessness
- ▶ **Tardive dyskinesia**
- ▶ **Metabolite dysfunction**

**Biopsychosocial-spiritual**

**Level monitoring**

**Side effects of Lithium**





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12/26/2017

THANK YOU

Video