MED441
KING SAUD UNIVERSITY

BH
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REVIEWED BY

Psychopharmacology

By Dr Ali Bahathig "Make sure to check out the cases at the end"

Objectives:

- Discuss classification of main psychotropic medications
- Know Mechanism of action of psychotropic medications
- Know common & dangerous adverse effects
- Choose a psychotropic medication rationally
- Manage failure of response to a therapeutic trial

Color index:

- Important
- Golden
- Textbook
- Old notes (439/438)
- New notes (441)
- Extra

Introduction

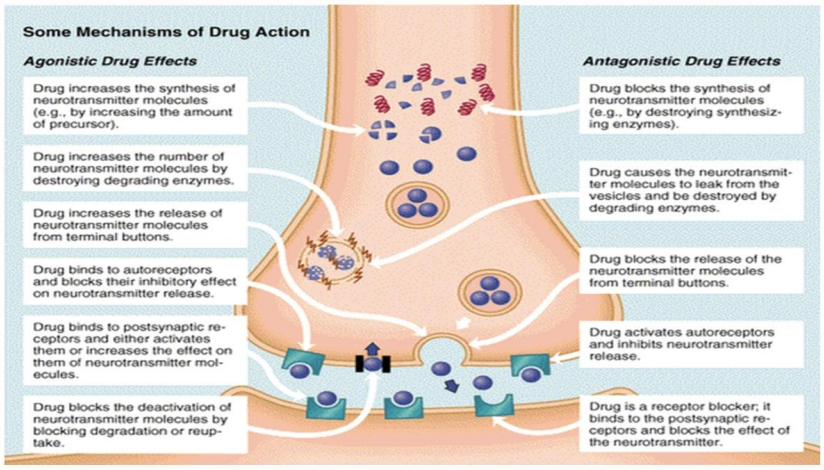
Why medications?

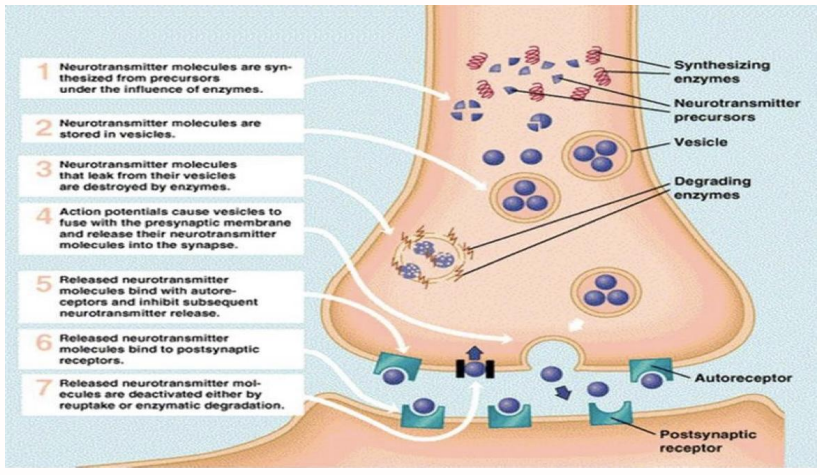
- Dopaminergic theory of Schizophrenia
- Monoaminergic theory of Mood Disorders

Neurotransmitters Go through 7 steps *"No Qs here"*

1. Synthesis.
2. Storage.
3. Enzymatic destruction if not stored.
4. Exocytosis.
5. Termination of release via binding with autorecptors.
6. Binding to receptors.
7. Inactivated either by **reuptake** or **degradation**.

Drugs are developed that address these actions as an **AGONIST** (mimic the NT) or **ANTAGONIST** (block the NT).





Psychopharmacologic Drugs work over A Spectrum

Antipsychotics — Mood stabilizers — Antidepressants — Anxiolytics / sedative — Stimulants

TOP 10 THERAPEUTIC CLASSES
In Canada, 2014

Rank / Class	Total Prescriptions (000s)
Cardiovasculars	87,553
Psychotropics	80,295
Gastrointestinal	46,021
Cholesterol Agents	40,556
Analgesic	33,488
Diabetes therapy	29,277
Neurological agents	28,358
Hormones	27,151
Anti-Infectives	24,614
Diuretics	19,193

Source: IMS Brogan
Excludes hospitals

Psychotropics are one of the most prescribed drugs but this chart is outdated

Antipsychotics

Antipsychotics
"They work on Dopamine"

Functions of Dopamine	• Attention • **Motivation & Reward** • Prolaction inhibition • involuntary movements • Energy • Nausea • Psychosis (it's not a function but high dopamine cause it)

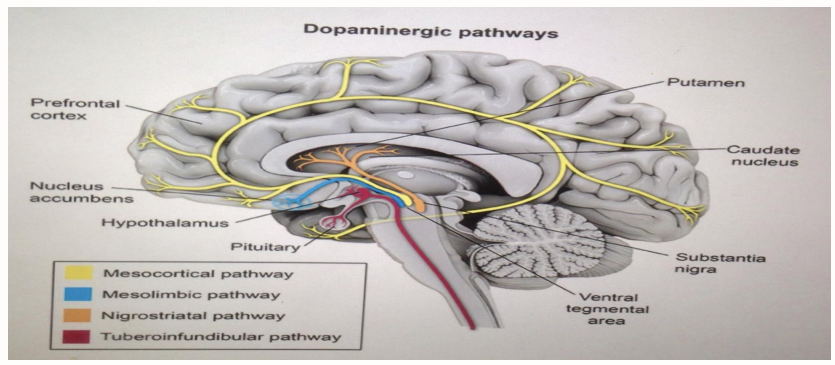
Antipsychotics and dopamine system *"No Qs here but understand it"*

→ Mesocortical pathway functions: **Motivation**, **Attention**, cognitive.

→ Mesolimbic pathway is the **reward area**, high dopamine in this area will cause **psychosis** so we want to close it.

→ Nigrostriatal pathway functions: involuntary **movement**.

→ Tuberoinfundibular pathway functions: **Prolaction inhibition** (posterior pituitary).



Indications for use *"Psychotic Symptoms"*	• **Schizophrenia** • **Schizoaffective disorder** • Bipolar disorder- for mood stabilization and/or when **psychotic features** are present • Delirium (small doses) • Psychotic depression • Augmenting agent in treatment resistant depression or anxiety disorder • Dementia (psychotic symptoms or aggressive behavior) • Trichotillomania

Typical 1st generation (conventional)	Atypical 2nd generation
Treat psychotic symptoms, regardless of the illness, remember Psychosis is a Sx not a diagnosis. Requires about one month for significant antipsychotic effect.	
Dopamine (D2) **receptor antagonists** Effective against: Positive symptoms > Negative symptoms (makes **negative symptoms worse** but treats positive symptoms)	**Serotonin-dopamine antagonists** Effective against both Positive and Negative symptoms
Chlorpromazine fluphenazine **Haloperidol** **loxapine** molindone **trifluoperazine** **perphenazine** pimozide prochlorperazine thiothixene thioridazine	aripiprazole **Clozapine** **Olanzapine** paliperidone quetiapine **Risperidone** **Ziprasidone** almost all of them are important :)

Antipsychotics

Antipsychotics

Typical 1st generation	Atypical 2nd generation

Side effects

- ★ **ExtraPyramidal Symptoms (EPS):**
  - **Stiffness** and shakiness **(Dystonia)**.
  - **Uncomfortable restlessness (Akathisia)**.
  - **(Pseudoparkinsonism)**.
  - Long-term use can produce **movements of the face (Tardive Dyskinesia)** and, rarely, of the arms or legs.
- Feeling **sluggish**, slow in thinking, apathy, low motivation **(Negative symptoms)**.
- Problems with breast swelling or tenderness and (**Galactorrhea**). *"↑ Prolactin levels"*
- Some can affect blood pressure and make patient feel dizzy.
- Decrease Libido.
- **Lowers seizure threshold, worsens QTc interval.**

"These side effects depend on the potency and dose of the drug used"

- Sleepiness and slowness.
- **Weight gain**.
- **Increased chance of developing diabetes and ★Metabolic Syndrome**.
- Decrease Libido.
- Some can affect blood pressure and make patient feel dizzy.
- In **high doses**, some have the same **EPS** and **Parkinsonian side-effects** as the older medications (stiffness of the limbs) but less than typical.
- Problems with breast swelling or tenderness and (Galactorrhea) but less than typical.
- **Lowers seizure threshold, worsens QTc interval.**

"Atypicals still can cause EPS but less than the typicals"

Important Note,
★All Antipsychotics have these effects:
1- **EPS** → Typical > Atypical, High potency > Low potency.
2-**QTc Prolongation**.
3-**Lowers seizure threshold**.
4-↑ **Prolactin** levels.
5-Can cause **NMS** (Neuroleptic Malignant Syndrome).

First generation antipsychotics	*Second generation antipsychotics*	*Clozapine*
Extrapyramidal effects Dystonia Pseudoparkinsonism Akathisia Tardive dyskinesia	Olanzapine Weight gain Sedation Glucose intolerance and frank diabetes mellitus Hypotension	Sedation
Sedation		Hypersalivation
Hyperprolactinaemia	Risperidone Hyperprolactinaemia Hypotension EPS at higher doses Sexual dysfunction	Constipation
Reduced seizure threshold		Reduced seizure threshold
Postural hypotension	Amisulpiride Hyperprolactinaemia Insomnia Extrapyramidal effects	Hypo & hypertension
Anticholinergic effects Blurred vision Dry Mouth Urinary Retention	Quetiapine Hypotension Dyspepsia Drowsiness	Tachycardia
Neuroleptic malignant syndrome		Pyrexia
Weight gain		Weight gain
Sexual dysfunction		Glucose intolerance and diabetes mellitus
Cardio-toxicity (including prolonged QTc)		Nocturnal enuresis
		Rare serious side effects Neutropaenia 3% Agranulocytosis 0.8% Thromboembolism Cardiomyopathy Myocarditis Aspiration pneumonia

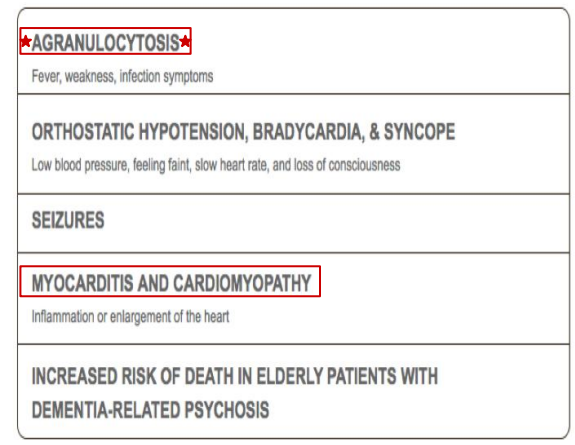
TABLE
RECEPTOR BLOCKADE AND ANTIPSYCHOTIC SIDE EFFECTS[2]

Receptor Type	*Side Effects*
D_2	EPS, prolactin elevation
M_1	Cognitive deficits, dry mouth, constipation, increased heart rate, urinary retention, blurred vision
H_1	Sedation, weight gain, dizziness
α_1	Hypotension
$5\text{-}HT_{2A}$	Anti-EPS (?)
$5\text{-}HT_{2C}$	Satiety blockade

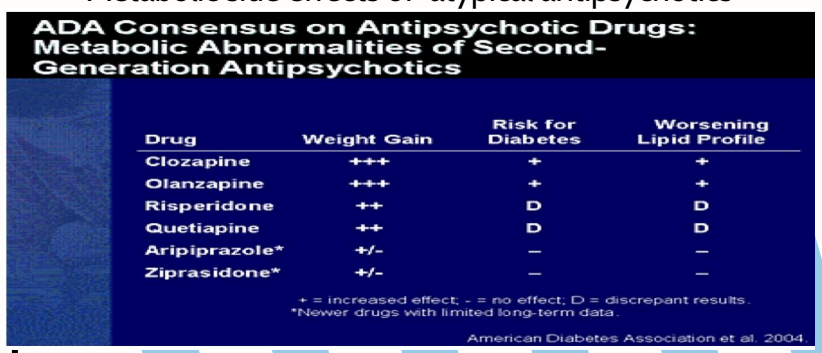
D=dopamine; EPS=extrapyramidal symptoms; M=muscarine; H=histamine; 5-HT=serotonin.
Robinson DS. *Primary Psychiatry.* Vol 14, No 10. 2007.

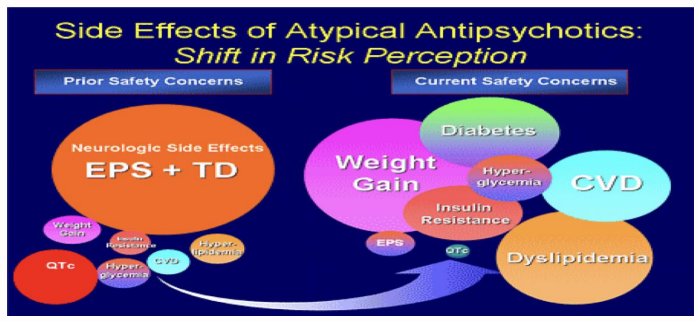
High Potency typical antipsychotics: **Neurological** side effects
Low Potency typical and atypical antipsychotics: many **other** side effects

Clozapine



Metabolic side effects of atypical antipsychotics





Antipsychotics

These two drug cause worst metabolic side effects

Worst in QT interval

TABLE 2
ANTIPSYCHOTICS: SAFETY AND TOLERABILITY[1]

Item	Typical Neuroleptic	Clozapine	Risperidone	Olanzapine	Quetiapine	Ziprasidone	Aripiprazole
EPS	+ to +++	±	± to +++*	± to +*	±	± to +*	± to +
TD	+++	±	± to ++	± (?)	± (?)	± (?)	± (?)
Somnolence	± to +++	+++	±	++	++	±	±
Prolactin	+++	±	+++	±	±	±	±
Weight	± to ++	+++	+	+++	++	±	±
Dyslipidemia	± to +	+++	+	+++	++	±	±
DM	± to +	+++	+	+++	++	±	±
QTc	+	++	+	+	+	++	±
Orthostatic BP↓	± to +++	+++	++	+	++	±	±

*Dose-related.

Key: ±=none-to-minimal; +=mild; ++=moderate; +++=marked; ?=no data, compared to placebo rates.

EPS=extrapyramidal symptoms; TD=tardive dyskinesia; DM=diabetes mellitus; QTc=corrected Q-T interval; BP=blood pressure.

Glick ID, He X, Davis JM. *Primary Psychiatry.* Vol 13, No 12. 2006.

Table 2
Relative Adverse Effect Incidence of Antipsychotics

	Sedation	EPS	Anticholinergic	Orthostasis	Seizures	Prolactin Elevation	Weight Gain
Typical Low Potency							
Chlorpromazine	High	Moderate	Moderate	High	Moderate	Moderate	Low
Thioridazine	High	Low	High	High	Low	Very high	Moderate
Typical High Potency							
Trifluoperazine	Low	High	Low	Low	Moderate	Moderate	Low
Fluphenazine	Low	Very high	Low	Low	Low	Moderate	Low
Thiothixene	Low	High	Low	Low	Low	Moderate	Low
Haloperidol	Very low	Very high	Very low	Very low	Low	Moderate	Low
Loxapine	Moderate	High	Low	Moderate	Low	Moderate	Very low
Molindone	Very low	High	Low	Low	Low	Moderate	Very low
Atypicals							
Clozapine	High	Very low	High	High	High	0	High
Risperidone	Moderate	Very low*	Low	Moderate	Low	0 to moderate††	Low
Olanzapine	Moderate	Very low†	Moderate	Low	Low	Very low	Moderate
Quetiapine	Moderate	Very low	Low	Low	Low	0	Low
Ziprasidone	Low	Very low	Low	Low	Low	0	Very low
Aripiprazole	Low	Very low	Low	Low	Low	0	Very low

** Very low dosages (<8 mg/day); † With dosages <20 mg/day; †† Dose related. EPS: extrapyramidal symptoms.*

Classification of Antipsychotic drugs

First-generation Antipsychotic (low potency) *"Doses are higher"*	First-generation Antipsychotic (high potency) *"Doses are lower"*	Second generation Antipsychotics
Chlorpromazine	**Fluphenazine**	aripiprazole
prochlorperazine	**Haloperidol**	asenapine
thioridazine	pimozide	**Clozapine**
	thiothixene	iloperidone
		lurasidone
		Olanzapine
		Quetiapine
		Risperidone
		paliperidone
		Ziprasidone

Antipsychotics average Daily Doses in mg (not important)
Lower numbers indicate higher potency

Typical	Atypical
Haloperidol (5 – 15 mg)	Risperidone (4 – 8 mg)
Thioridazine (100 – 300 mg)	Olanzapine (10 – 20 mg)
Chlorpromazine (50 – 400 mg)	Quetiapine (600 – 1200 mg)
perphenazine (8 – 16 mg)	Clozapine (100 – 600 mg)

Depot antipsychotics

Giving to patients who cant take the drug everyday specifically psychotic patient with poor insight

- Injection every 2 to 4 weeks.
- Releases the medication slowly over this time.
- Both typical and atypical.

Indication:

- **Poor compliance.**
- **Patient preference.**

Pharmacological Treatment Algorithm Adapted from the Maudsley prescribing Guidelines (Taylor et al, 2005)

Either:
Agree choice of antipsychotics with patient
Or if impossible
start atypical antipsychotics

→ **Titrate** as necessary to minimum effective dose **Adjust dose** according to response and tolerability

→ Asses over 6-8 weeks

- if poor compliance is due to poor tolerability discuss with patient and change drug
- if poor compliance is related to other factors, consider a depot or compliance therapy
- change drug and repeat above process
- consider both typical and atypical antipsychotics

→ Clozapine

"if 2 drugs (multiple) do not work we use Clozapine. (Due to its side effects)"

Continue at established effective dose

Antipsychotics

Extrapyramidal Symptoms (EPS)

Very important for video cases/SAQ and MCQs

Acute Dystonia
(Hours)

Sometimes develop within 30 minutes

- **Involuntary spasms or stiffness.** *"especially in Neck / Jaw Muscles"*
- Can be terrifying to the patient.
- Risk is higher in males and at younger age (Blocky muscles).
- Is more likely to develop in patients treated with high-potency First generation antipsychotic with inherently low anticholinergic activity (e.g., **Haloperidol**, **Fluphenazine**).
- Laryngospasm and swelling of the tongue (can close the airway) (Rare).
- **Spasmodic torticollis (spasm of cervical muscles of the neck).**
- Trismus (spasms of the muscles of mastication).
- **Oculogyric crisis** (eyes rolled back in a locked position).

➔ **Treatment is by *adding an anticholinergic agent*:**
- **Benztropine mesylate** (Cogentin) 1–2 mg orally BID–TID or 1–2 mg intramuscularly on an as-needed basis.
- Other options: **Trihexyphenidyl**, **Procyclidine**, and **Diphenhydramine**.

Akathisia
(Days)

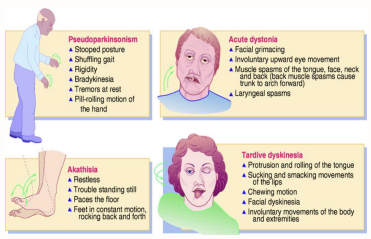
Can lead to suicide

- **Motor restlessness; inability to sit still due to inner tension.**
- Typically seen early in treatment or with dosage increases of antipsychotics (typical more than atypical).
- Is the most common **antipsychotic-induced movement disorder**.
- Symptoms increase in severity with increasing antipsychotic dose.
- Are a major cause of **poor compliance to antipsychotic medications.** *"It is very annoying to the patient"*

➔ **Treatment is by adding a beta-blocker** (effective for akathisia):
- **Propranolol** 20–40 mg bid
- Nadolol up to 80 mg/day
- Metoprolol up to 100 mg/day

Pseudoparkinsonism
(Weeks)

- Also referred to as **parkinsonism**.
- **Symptoms can be identical to those observed in Parkinson's disease:** (TRAP)
  - **Tremors** at rest.
  - **Rigidity** in arms and shoulders.
  - **Akinesia** ***(absence of movements)***
  - **Postural instability** ***(e.g., shuffling gait)***
  - **Bradykinesia** ***(slowness of movements)***
  - **Hypersalivation**
  - **Mask like facies**
  - **Cogwheel rigidity**



➔ **Treatment is by adding a dopaminergic agent:**
- **Amantadine** (a dopaminergic agent) 100 mg orally bid (effective for parkinsonism and dystonia)

"The treatment in this case is debatable, mostly we won't ask you about it"

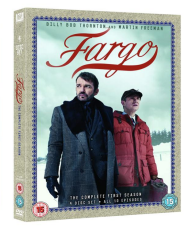
Tardive Dyskinesia
(Years)

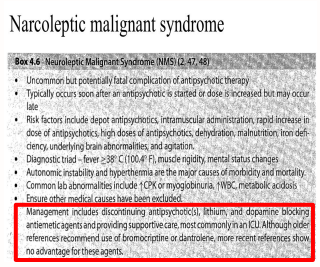
- Literally means **late-appearing (tardive) abnormal involuntary movements (dyskinesia).** *"Takes ~5 years to develop that's why it's very rare"*
- Is more likely to develop in **patients who have experienced EPS.**
- Presents with involuntary movements characterized by a mix of orofacial dyskinesia, tics, chorea (jerking movements), and athetosis (writhing movements):
- **Orofacial dyskinesia is the most common presentation** and includes rhythmic movements of the lips (e.g., puckering, **smacking**), tongue (e.g., undulations, rolling motions, protrusions, "fly catching" movements), jaw (e.g., chewing, side-to-side movements, biting), and face (e.g., involuntary **blinking**, grimacing).
- Tongue fasciculations and periorbital movements are common early signs, Involuntary movements of the extremities are less common, Involvement of the esophagus, pectoral muscles, and diaphragm is rare but can be fatal.

➔ **Treatment is by prevention.** *"if started we can't treat it"*

★Neuroleptic Malignant Syndrome (NMS)

- Fatal, can happen in any time of the drug course, especially for patients receiving Antipsychotics for the first time OR when we have to increase the dose.
- Can conceptually be characterized as "**severe EPS** (i.e., **extreme Rigidity**) with **fever**".
- Possibly secondary to **dopaminergic receptor blockade** in the **Substantia Nigra** producing rigidity and fever.
- Can develop with **any Antipsychotic medication.**
- Presents with symptoms easily recalled with the acronym **(F + ARGO):**
  - **F** **Fever**
  - **A** **Autonomic dysregulation** (e.g., hypertension, tachycardia, urinary incontinence, diaphoresis)
  - **R** **Rigidity** ("lead-pipe")
  - **G** **Granulocytosis** (as well as increased lactic dehydrogenase, liver function tests, **↑↑↑↑ Creatine Phosphokinase [CPK]** "high in trauma patients", and myoglobinuria)
  - **O** Orientation changes (**confusion**, coma)
- Can additionally present with **acute renal failure** (due to myoglobinuria), proteinuria, deep vein thrombosis, respiratory distress, and dehydration.
- **Management: stop the drug then supportive.**
- **Any patient on Antipsychotics and presents with Fever,Rigidity and Confusion→ NMS.**



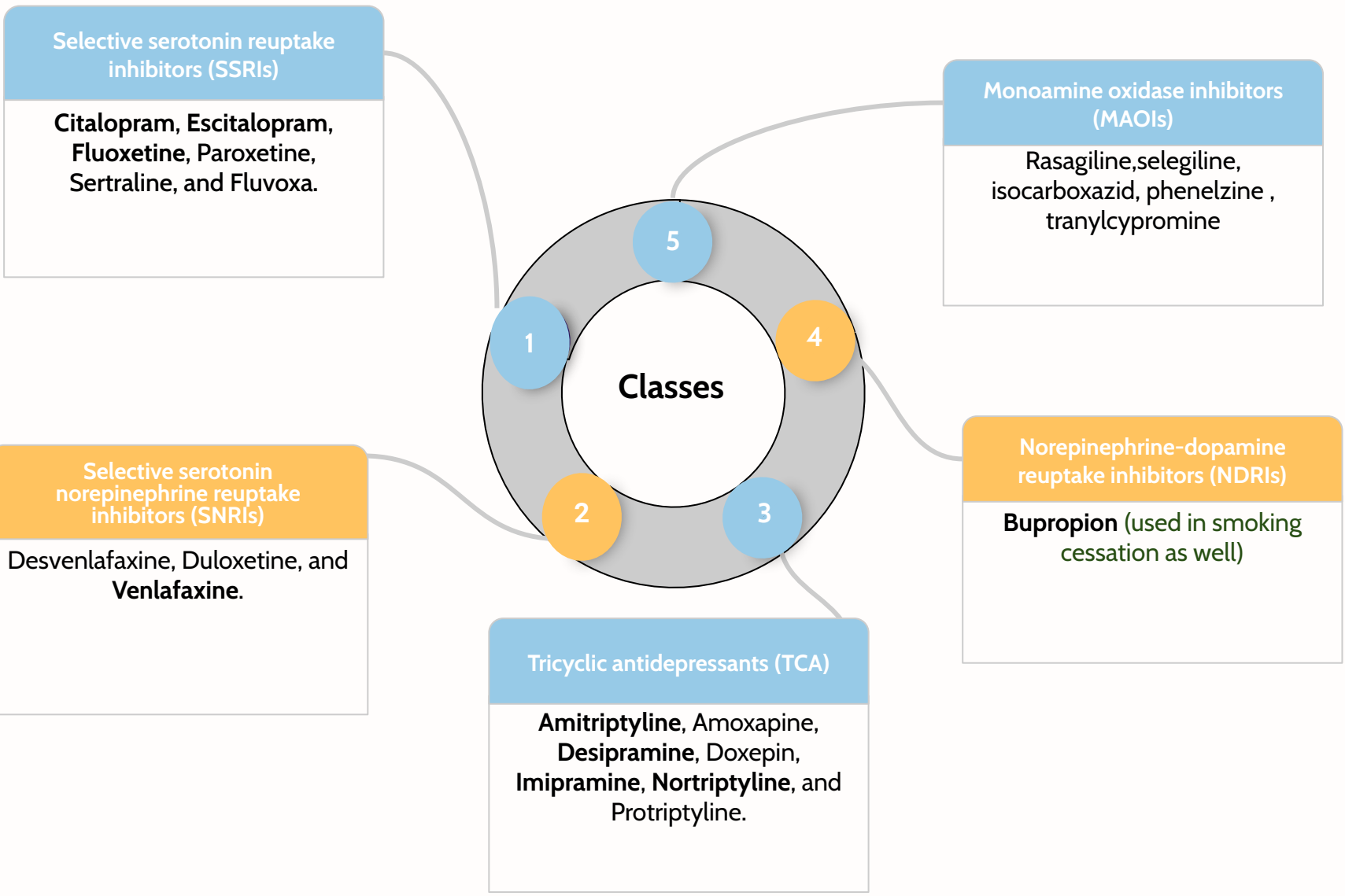

Narcoleptic malignant syndrome

Box 4.6 Neuroleptic Malignant Syndrome (NMS) [2, 47, 48]

- Uncommon but potentially fatal complication of antipsychotic therapy
- Typically occurs soon after an antipsychotic is started or dose is increased but may occur late
- Risk factors include depot antipsychotics, intramuscular administration, rapid increase in dose of antipsychotics, high doses of antipsychotics, dehydration, malnutrition, iron deficiency, underlying brain abnormalities, and agitation.
- Diagnostic triad – fever ≥38°C (100.4°F), muscle rigidity, mental status changes
- Autonomic instability and hyperthermia are the major causes of morbidity and mortality.
- Common lab abnormalities include ↑CPK or myoglobinuria, ↑WBC, metabolic acidosis
- Ensure other medical causes have been excluded

Management includes discontinuing antipsychotic(s), lithium, and dopamine blocking antiemetic agents and providing supportive care, most commonly in an ICU. Although older references recommend use of bromocriptine or dantrolene, more recent references show no advantage for these agents.

Antidepressants



Serotonin's pharmacological function across multiple domains

- Depression
- Obsessions
- Migraines
- Anxiety
- ADRs :
- Intestines
- Nausea
- Sexual

Indications

- **Depression**
- Organic mood disorders
- **OCD**
- **Anxiety disorders**: including panic, social phobia, and PTSD
- Premenstrual dysphoric disorder and impulsivity associated with personality disorders

Full clinical response

- 4 - 6 weeks in major depression
- Up to 6 - 12 weeks in obsessive compulsive disorder

Antidepressants side effect

Selective serotonin reuptake inhibitors (SSRIs)	• **Nausea** (Most common S/E associated with SSRIs) • **Diarrhea** • **Dry mouth** • Anxiety, agitation, insomnia • Drowsiness, fatigue • Effects on sleep (during REM) • **Headache** • **Sexual dysfunction** (e.g., anorgasmia, ↓ libido and late ejection) • **Weight gain**
Selective serotonin norepinephrine reuptake inhibitors (SNRIs)	• Side effects are similar to SSRIs • **Venlafaxine and Desvenlafaxine increase BP in high doses**
Tricyclic antidepressants (TCA)	• **Anticholinergic:** - Cardiovascular: tachycardia, arrhythmia. - Dry mouth - Urinary retention - Constipation - Blurred vision - CNS: Drowsiness, somnolence, myoclonic twitches, tremors and paresthesia. • **Endocrine**: weight gain due to H1 blockade tendency to increase blood sugars. • **Orthostatic hypotension**: - α-1 adrenergic blockade, transient (may not be dose dependent) • Cardiac: *"some patients try commiting suicide by overdosing (its toxic), so its not used very often nowadays"* - Sinus tachycardia (common): Quinidine-like type 1A antiarrhythmic effect. **Prolongation of PR, QT, wide QRS complex**
Monoamine oxidase inhibitors (MAOIs) *"Nobody uses them anymore"*	**Common side effects:** • weight gain • Orthostatic hypotension • Sexual dysfunction **Other side effects:** • Insomnia with daytime sedation "Nardil Nod" • Myoclonus, tremor and akathisia • Paresthesia – vitamin B6 deficiency-like • Mania – up to 35% in depressed bipolar and 4% in unipolar patients **Uncommon and serious side effects:** • **Hypertensive crisis** with ingestion of foods containing tyramine "Cheese reaction / Tyramine reaction" • Spontaneous hypertension (Parnate) • Hepatotoxicity – especially hydrazine group • Teratogenicity – increased incidence of malformations if taken in first trimester

Complications of Antidepressants

MAOIs Hypertensive crisis "Cheese Reaction"

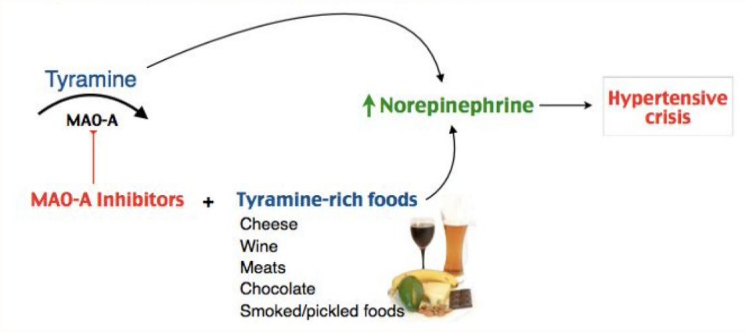
- Acute cardiovascular effect with **severe hypertension**
- Result from potentiation of **indirect sympathomimetic agents (tyramine)**
- Interact with **tyramine-containing food**
- Related to inhibition of tyramine metabolism
- Tyramine is normally deaminated in GI mucosa by MAO enzyme
- Tyramine is absorbed and taken up by **noradrenergic neurons**
- Displaces the stored norepinephrine from the synaptic vesicles
- Norepinephrine is released and free to exert its vasopressive effect
- Before starting new serotonergic drugs or ceasing dietary restrictions (e.g., foods containing tyramine), MAOI therapy has to be stopped for at least 2 weeks.

OTC drugs:

- Cold & cough remedies
- Decongestants
- Stimulants
- Appetite suppressants
- Dietary supplements

Indirect acting sympathomimetic amines:

- Amphetamine
- Ephedrine
- Cocaine
- Pseudoephedrine



Serotonin Syndrome

- Caused by an **excessive enhancement of serotonin neurotransmission when two different serotonergic agents are combined**
- Overstimulation of 5-HT1A & 5-HT2A
- **Consists of a triad of:**
  - **Mental status changes:** Confusion, delirium, hallucinosis
  - **Physical findings**: tremor, Myoclonus, hypertonicity, hyperreflexia
  - **Autonomic instability**: Fever, Diaphoresis, BP instability
- Onset range from hours to days: 50% within 2 hrs, 25% after 24 hrs
- Most cases involve only minor symptoms & resolve quickly
- **Serious complications**: seizures, DIC, respiratory failure, hyperthermia and death

"Myoclonus in SS, Rigidity in NMS"

Drugs that increase serotonin:

- **SSRIs**, TCA and MAOIs
- Buspar, Tryptophan, **Lithium**
- **Narcotic analgesics**: meperidine, **tramadol**, methadone and pentazocine...etc (morphine analogues are deemed relatively safe)
- Ecstasy and marijuana
- **Sumatriptan** and zolmitriptan (5HT1D agonist)

Increased risk with:

- **Concurrent use of two or more serotonergic drugs**
- **Switching from one serotonergic drug to another without tapering** (For Switching between SSRI / TCAs and MAOI, it is recommended to follow switching guidelines to avoid serotonin syndrome)

Antidepressant discontinuation syndrome (SSRI)

Description:

- Symptoms caused by abrupt withdrawal or dose reduction of antidepressants taken for ≥ 4 weeks.
- Most frequently cited with paroxetine (also SNRI: venlafaxine) (short half life drugs)
- Term not to be confused with withdrawal as seen with addiction

Clinical features:

- Flu-like symptoms, vertigo, dizziness and nausea jolt-like bursts several times throughout the day

Timing:

- Occur within 1 to 3 days after **abrupt discontinuation** of the SSRI.
- Subsiding within two to several days after the last dose

Treatment: Taper the SSRI very slowly or start another SSRI with long half life "like Fluoxetine"

Antidepressants & Cytochrome P450 System: (Reference) "not imp"

- Antidepressants and mood stabilizers may be inhibitors, inducers or substrates of one or more cytochrome P450 isoenzymes
- Knowledge of their P450 profile is useful in predicting drug-drug interactions
- P450 Subfamily: (CYP1A2, CYP 2C9, CYP 2D6 and CYP 3A4) are especially important to antidepressant metabolism and drug-drug interactions

Mood stabilizers

Mood stabilizers	
General information	- **Lithium, Valproic acid,Carbamazepine,** Lamotrigine, Gabapentin, Topiramate (what we are afraid the most about lamotrigine is Steven Johnson syndrome) - Used in the treatment of **Bipolar disorder** and similar conditions associated with impulsivity - Drug level measurements are available for many of them - Mechanism of action is **not clearly understood**
Lithium **(MCQ from Dr)** **Lady came to you and you want to start valproic acid what test should you do?** **pregnancy test** **Same applies for carbamazepine**	- **Common side effects:** benign: **nausea, diarrhea and lethargy , weight gain Hand tremor:** mild and fine, worse with high dose, caffeine and neuroleptic , **Hypothyroidism**– up to 5% of patients (usually mild) , **Polyuria** (urine volume > 3 L/day) and **polydipsia** - up to 40% of patients on Li+ therapy, **Nephrogenic diabetes insipidus** (5 - 6 L/day) is uncommon - Side effects Usually mild, **well tolerated and dose dependent** - Before and during the course of the treatment **we have to monitor 3 things**: - (**thyroid function test** for hypothyroidism , urinalysis and **RFT** :polyuria and polydipsia for nephrogenic diabetic insipidus , **ECG** For cardiac diseases) - **Treatment of tremor**: ↓ dose , stop caffeine, add β-blocker or switch to slow-release Lithium - **Lithium Toxicity: (Cause dehydration)** *"lithium is a salt"* - Lethargy , Muscular weakness , Ataxia , Hyperreflexia, Coarse hand tremor Dysarthria , Myoclonus , Neurological signs and , seizures , Coma and death in high level - treatment: **First thing is to stop the drug,** based on the amount of lithium and - clinical manifestation and **dialysis at > 3.0 mEq** Lithium Toxicity (chronic Ingestion) Level / s[Li] mEq/L / Clinical Manifestations / Treatment Grade 1 / 1.5-2.5 / Nausea, Vomitting, Tremor, Hyperreflexia, Ataxia, Agitation, Muscular Weakness / Hydration (x 4-6h), Kayexalate Grade 2 / 2.5 -3.5 / Stupor, Rigidity, Hypertonia, Hypotension / Hydration, Kayexalate, +/- dialysis Grade 3 / > 3.5 / Coma, Seizures / Hemodialysis
Carbamazepine	Therapeutic Level is (4 - 12) mg/ml Common side effects: **Dizziness, sedation, ataxia, leukopenia and rash , weight gain** **Dangerous side effects: 1-Agranulocytosis, 2- teratogenicity (neural tube defect), 3-induction of hepatic metabolism**
Valproic Acid	- therapeutic level is (40 - 100) mg/m - **Common side effects**: **Nausea, diarrhea, ataxia, dysarthria, weight gain, slight elevation of hepatic transaminases** - teratogenic (neural tube defects) should be avoided in pregnancy women

Anxiolytics / sedatives

Anxiolytics / sedatives	
General definitions	➢ **Sedative**: Calm down and treat agitation ➢ **Hypnotic**: Induce sleep ➢ Go to sleep fast, feel refreshed tomorrow !!! ➢ **Anxiolytic**: Reduce anxiety ➢ (Physical, emotional, cognitive) Types: **Benzodiazepines** , Barbiturates (not used) , Antihistamines , Beta-blockers (relieve the physical symptoms of anxiety but the problem with it can cause thoughts block تنح ,Buspirone , Zolpidem
Benzodiazepines (BZD):	**Mechanism of Action:** - BDZ receptors **& it linked to GABA-A receptor complex (bound to Cl channels)** - BDZ enhance GABA effect *"just like alcohol"* ➢ GABA: an inhibitory neurotransmitter - **Effects**: Sedative, Hypnotic, Anticonvulsant, Muscle-Relaxant - **Used to treat insomnia, parasomnias and anxiety disorders** - Often used for CNS depressant withdrawal protocols (ETOH withdrawal) - Clinical Institute Withdrawal Assessment for Alcohol (CIWA) - **Side effects** : **Somnolence and Cognitive deficits , Amnesia and Disinhibition, Tolerance and Dependence (that's why we don't use it for more than 4 weeks)** Dr notes: In clonazepam we are afraid of seizures because ↓threshold Xanax (alprazolam) is the most dangerous type (short half life) lorazepam, clonazepam we are afraid of metabolic syndrome
Other Psychotropic classes:	• **Cholinesterase inhibitors:** ➢ Donepezil, Rivastigmine, Galantamine (used in dementia) • **Sympathomimetics:** ➢Methylphenidate, Dextroamphetamine (used in addiction) • **Anticholinergic agents:** ➢**Procyclidine, Benztropine**
Recall of the most important side effects Dr: very imp	• **Hypertensive crisis** : Associated with MAOIs • **Neuroleptic malignant syndrome** : Autonomic instability, severe EPS, delirium, ↑CK, ARF, myoglobinuria • **Serotonin syndrome** : Restlessness, myoclonus, ↑reflexes, tremors, confusion. Due to combination of serotonergic agents • **Agranulocytosis** : **(Clozapine, carbamazepine) Never combine them**

Drug	Usual daily dose range (mg)	Approximate equivalent dose (mg) to diazepam 5 mg	Elimination half-lives of drug and active metabolites (hours)
Alprazolam	0.5–4	0.5	10–20
Clonazepam	2–8	0.25	20–60
Diazepam	5–30	5	12–72, 30–200
Flunitrazepam	0.5–2	1	20, 24, 30
Lorazepam	2–4	1	8–24
Oxazepam	45–90	15	3–25
Buspirone	15–30	15	1–11

Summary and general principles in psychiatry	
Summary of Medications Role in Psychiatry:	• They are part of a comprehensive treatment plan • Basic knowledge of medications is important in daily clinical practice • Their prescription by the psychiatrist follows a systematic approach:
Prescribing a psychotropic agent after diagnostic assessment:	• Choose a medication based on FDA approval • Family or personal history of response • Adverse effects vs. key symptoms • Starting dose • Monitor side effects & clinical response • Adjust dose if needed
Failure of Response What to do?	• Check Compliance & bioavailability • Review the diagnosis • Is the dose appropriate? • Is the duration of treatment long enough? • Any ongoing substance abuse? • Other drugs/preparation causing drug-drug Interaction? • Individual Variations •
If no improvement:	1. After a trail of adequate length (at least 2 months) nd adequate dose 2. Switch to another antidepressant and wait for 2-4 weeks , if no improvement 3. Augment with another agent

Table 4

Differentiating neuroleptic malignant syndrome and serotonin syndrome

Factor	Serotonin syndrome	Neuroleptic malignant syndrome
Causative medications	Serotonergic agents	Dopamine antagonists
Physical exam findings	Hyperreflexia, myoclonus, ocular clonus	Severe rigidity (lead pipe), hyporeflexia
Laboratory findings	More commonly no lab findings	More commonly increased creatine kinase, leukocytosis, low serum iron
Course of illness	Symptoms seen within 24 hours of starting/changing therapy and resolves within a few days of treatment	Slower in onset (1 to 2 weeks after starting/changing therapy) and resolves within 9 to 14 days of treatment

Source: Reference 17

Cases from Dr.Ali

Q1: A **young** (19 years old) patient presented to the **ER** and was **Agitated/Psychotic**, they gave him an injection (the name of the drug "haloperidol" may or may not be mentioned) to control his agitation. Afterwards he developed **spasms/contractions**.
What happened to him? Acute Dystonia.
How can we treat him? Benztropine (Or one of these drugs: Procyclidine, Diphenhydramine, Trihexyphenidyl).

Q2: An **in-patient** patient in the psychiatry **ward** (or Px in **clinic**), he **can't sit still** and has to move.
What is the side effect? Akathisia.
How to treat this? Propranolol.

Q3: A patient is taking an some medication for some time and presents with tremors, akinesia, rigidity and postural instabilities.
What is the side effect? Pseudoparkinsonism .
(the doctor didn't mention the case exactly, but only said that some Px presenting with parkinson's like features and you should recognize it)

Q4: A patient taking an **antipsychotic drug** presented with **Fever**, **Rigidity** and **Confusion**.
What is your diagnosis? Neuroleptic Malignant Syndrome (NMS).
What is the management of the Px in this case? Discontinue the drug.
How would you confirm your diagnosis? order CPK.

Q5: A bipolar/manic patient will be started on **Lithium** what are the investigations you would order before starting this drug?
1-Thyroid function test. 2-RFTs. 3- ECG.

Q6: A **female** patient will be started on **Carbamazepine**, what investigations would you order?
1- Pregnancy test. 2-LFTs. 3-CBC. 4-RFTs (Extra)

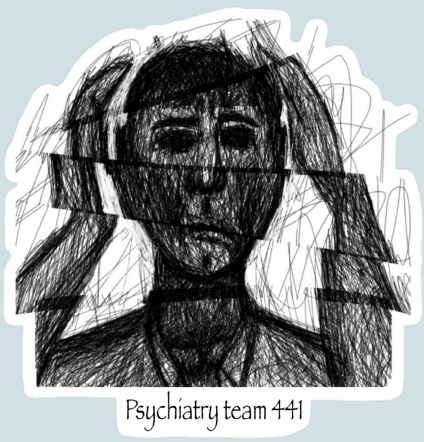
Q7: A patient taking a MAOI which drug would you avoid? Pseudoephedrine
What can they cause together? A hypertensive crisis.

Team leader

- **Saleh Aloraini**

Team members

- Abdulrahman Aljofan
- **Faisal Alhussaini**
- Alwaleed Bin shaya
- Faisal Bin moammar
- Mishari Alzoubi
- Abdulmajeed Namshah
- Abdulrahman bawazir
- Abdulmalik Alduraibi
- **Hamad Alothman**
- Sultan Alkassim
- **Faisal Alshuaibi**
- Abdullah Alyamani
- Talal Alanazy
- Yahya Alghamdi
- Osama Alsaaid



Good luck!!

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Special thanks to 439 & 438 psychiatry teams