Here some (keys) we are goanna use in this sheet :-
* SSRI (Serotonin-specific reuptake inhibitor) .
* MAOI (mono amine oxidase inhibitor) .
* schizo (Schizophrenia) .
* NT (neurotransmitter) .
* 5HT (Serotonin) .
* NE (nor- epinephrine) .
* BP (blood pressure) .
* HR (heart rate) .
* Tx (treatment) .
* cus' (because) .
* y? (why ?) .

* **Auto receptors** : they're mostly presynaptic . The fast releasing of NT is regulated by negative feedback through these auto receptors .
- But the problem here if there's continuously overdose of 5-HT , that'll desensitize the autoreceptors , then more release of 5-HT and more what so called neurogeneration (i.e no more feedback inhibition to these autoreceptors) .

serotonin syndrome

It happens at high doses or combined with other drugs an exaggerated response can occur .
• This is due to increased amounts of serotonin .
• Alters cognitive function, autonomic function and neuromuscular function .
• Potentially fatal .
In this syndrome the patient badly will face : **seizures** , **arrhythmia**, **hypotension** and **hypothermia** .
NEVER combine two drugs increasing 5-HT level because it may precipitate the patient with serotonin syndrome .

Depressed patient : We start using SSRI , If there was no response or partial response , we start increasing the dose of SSRI's or we change the strategy .
One way of changing the strategy by using SNRI .

Serotonin/Nor-epinephrine reuptake inhibitors (SNRIs)

* Slightly greater efficacy than SSRIs (Some patients respond better to them as we're dealing with increasing two NTs rather than ONLY serotonin) .
* Slightly fewer adverse effects than SSRIs .
- **Examples** : Venlafaxine and Duloxetine .

* but unfortunately it has some **side effects** :-
1. **Can cause a 10-15 mmHg dose dependent increase in diastolic BP** (Increasing NE will increase BP and HR) .
2**. May cause significant nausea**, (it's very nauseatic , more than SSRI because increasing both NE & 5-HT its effect will be directly on brain to cause nausea) .
3. **Can cause a bad discontinuation syndrome, and tapering recommended after 2 weeks of administration** (also because we have to withdrawn our patient with high NE & 5-HT) .

* After all , SSRI is the first line therapy for every single depressant patient except those atypical type of patients .
*So they're considered as 2nd line therapy .

atypical depression

Here you don't feel his depression , so after giving him a joke he'll laugh but deeply in his soul he isn't that much interested in life and feel the desire of suicide from time to time .
But how to figure his symptoms and reveal his depression : he'll gain more weight , keep sleeping (hypersomnia) .

So for these atypical patient we give them the oldest antidepressant , which is the Monoamine oxidase inhibitors (**MAOI**) .
(MAOI's) are bad drugs but here we have to use it with those atypical depressant patient and it's activity will be superior (we don't know why).

(MAOI) are two main types :-
(**type A**); mostly for metabolizing NE & 5-HT .
(**type B**) mostly for metabolizing Dopamine .

*** Now here is the non-selective MAOI (Phenelzine) :-**
It's a bad drug because it inhibit both the A & B types (Non-selective) .
Note : what I need is just type A ; mainly 5-HT .

Some useful info about the non-selective MAOI (Phenelzine) :-
Inhibition of intra-neuronal degradation of serotonin and nor-epinephrine causes an increase in extracellular amine levels.

Side effects: Blood pressure problems , Dietary requirements , Weight gain , Insomnia , Edema.

Note : tyramine present in cheese and alcohol .
So any patient taking this medication must be under dietary restriction and shouldn't eat cheese or drink alcohol y?
cus' tyramine won't be metabolize this will lead to increase NE level .

So tyramine without metabolization equals increase in the NE .

Because of badness of the non-selective MAOI they improved a new drug :
Selective MAO-A Inhibitors (Moclobemide) No dietary restrictions, except in high-dosage treatment, where in they lose their selectivity in A rather than B .

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Summary

(1) We started taking about (Tricycle antidepressant (Amitriptyline)) which work by inhibiting transporters ; also they inhibit H1 , alpha1 and muscirinc receptors so they have many side effects .
(2) SSRI with less side effects , but u should keep an eye on nausea , sexual ability and serotonin syndrome .
(3) SNRI they increase both NE & 5-HT so there will be increase in BP ; it will produce more nausea and vomiting with problems in discontinuation .
(4) Atypical patients we use (Phenelzine)& (Moclobemide) ; Dietary restriction regarding cheese and alcoholic drinks are important in Phenelzine and in high doses of Moclobemide .

clinical Pharmacology

How to give the antidepressant course to the patient ?

Following the initiation of the antidepressant drug treatment there is generally a therapeutic lag lasting for 3-4 weeks .
Here we see that all antipsychotic and antidepressant drugs are trail drugs :-

- 8 weeks trial, then you allow to switch to another antidepressant (give it a time) .
- When you find Partial response then add one another drug from different class , but keep an eye on serotonin syndrome .
- If the initial treatment was successful then 6- 12 months maintenance periods.
  (i.e. if the patient show successful response within 6 weeks then you have to keep it up for one year) .
- If the patient has experience two episodes of major depression, then it is advisable to give an anti depressant lifelong .
- All antidepressants now carry a “black box” warning that they may lead to suicidal thoughts/behavior.

True medicine is not just being memorizing machine for the sake of marks , tmw ur gonna deal with real patients to apply Skillfully all what u learned in basic phase, so please always study for the sake of science and to serve ur self and the others .

 # AYHAM DGHAIM #

Schizophrenia

First of all its absolutely opposite to depression cus' patient here show positive thoughts and ideas with hallucination and delusion .
So (**schizo & psychosis patient**) he's messed up a lot , while he's speaking such as (we went to Makka , and visit the moon while we're getting back , we release the AQSA ...etc) or when you give him the Holly Qur'an he just Shred it (cus' he's not aware what he doing) all these called positive thoughts and elusion .
but in (**depression**) u see him setting in the corner thinking all the time about suicide , all what he has is negative thoughts , cus' he feel that he's useless and he just hate his life .

Features of **schizo** :-

- Pathogenesis is unknown (so it's based on theories) .
- Onset of schizophrenia is in the late teens - early ‘20s more commonly in men ; late 20's more commonly in women ; but overall more commonly in men (1.5:1) .
- Genetic predisposition -- Familial incidence .
  Genetic factors plus the environmental factors so schizo is a disease has both genetic and environmental factors , but the main player is the environmental factor .

Note : considering the causes of suicide and homosexuality as genetic predisposition is absolutely wrong .

- Multiple genes are involved .
- Affects 1% of the population worldwide .
- A thought disorder (thinking problem) .

You should know that schizo patient think in opposite and circular direction instead of straight direction , he also has interruption in his ideas .

Schizo symptoms

Positive Symptoms .
Hallucinations , delusions , paranoia , ideas of reference (which is ideas that he use to believe , like releasing AQSA , being pilot , or being astronaut) .

Negative Symptoms (similar to depression patients)
Apathy , social withdrawal , anhedonia , emotional blunting , cognitive deficits , lack of motivation to interact with the environment .

These negative symptoms are progressive and non-responsive to medication .

Note : not all patient seem to have schizo , but 2 lovely minutes setting with that patient more enough for figure out that he is .
Note : but there's some are not clear schizo patients --> no clear hallucination , but they have delusion or confusion , show they're having schizo monster .
Note : All schizo patients have both positive and negative symptoms ; keeping in mind that positive symptoms are more typical .

Treatment of schizo

one of the most sophisticated things in the psychiatric carrier is to convince the patient sticking with his medication as they have thoughts disorders .

These drugs are not a cure .

Schizophrenics must be treated with medications indefinitely, as the disease is lifelong and it is preferable to prevent the psychotic episodes than to treat them .
SCHIZOPHRENIA IS FOR LIFE i.e. most of schizo hit the early 20's cus' they face failure in their life or having that much of stress , and badly schizo stick to them for whole life .

Remember : there is no remission .

Dopamine Theory of Schizophrenia

This theory clearly show that increasing the dopamine will cause schizo .
Many lines of evidence point to the aberrant increased activity of the dopaminergic system as being critical in the symptomatology of schizophrenia .
There is a greater occupancy of D2 receptors by dopamine => greater dopaminergic stimulation .
So who has (+ve thoughts) then link with dopamine .
But who has (-ve thoughts) don't link with dopamine (might have high level of 5-HT) .

Note: even though the theory said that high dopamine cause schizo but also u can find that 5HT also high .

How they found dopamine activity is linked with schizo ? They tried the anti-dopamine with schizo patient ; most of them who're having +ve thoughts respond (but not all -ve thoughts responded meaning we have other factors NOT only dopamine) .

Slide 23

The improvement of Tx schizo with time :-

- The best results can be in the first 3 weeks from the beginning of therapy .
- Week 3 (noticeable improvement but the best at week 1&2) .
- Week 4 (more improvement but not noticeable)
- Week 5 (more and more improvement) .
- Week 7 (more improvement) .

The bottom line here that the bad +ve thoughts will improve noticeably at the beginning (first weeks) and with time other problems will start diminishing slowly (needs a lot of time) .

Note : as you're using anti-dopamine with continuous treatment overexpression of dopamine receptors will occur (Resistance) .