

Depression

So, your patient is depressed... HOW depressed, you ask?

WHEN DOES SADNESS BECOME DEPRESSION??
Negative feelings become **persistent and pervasive**
= people are **unhappy most of the day, every day**
for **more than two weeks. (quoth the DSM-IV)**

HISTORY OF DEPRESSION

5 or more of the following 9, in the same 2 weeks:

DYSTHYMIA: 2 years of "depression lite", only 2 of the major depressive criteria; but long-lasting.

- **DEPRESSED MOOD:** can be **IRRITABILITY** in kids and teens
- **ANHEDONIA:** loss of interest in formerly pleasurable activities
 - **ASK: has some sort of life event caused this?**
MELANCHOLIC depression is not caused by any life events.
IT IS BIOLOGICAL: and features a **PSYCHOMOTOR DISTURBANCE**
ADJUSTMENT DISORDER or **BEREAVEMENT** have an identifiable stressful event as a cause
 - **Do the symptoms last all day, every day?** Melancholia = worse in the morning
 - **Are there times they feel UNUSUALLY ELEVATED?**
I.e. is there a **BIPOLARITY?** Ask mania questions.
- **Is there a SLEEP DISTURBANCE? Too much, too little?**
- **Weight loss? Weight gain? 5% either way is significant**
- **Psychomotor Agitation or Retardation:** melancholia has more of this
THIS MUST BE OBSERVABLE: not merely reported
This usually looks like either an irritability and restlessness, or a marked delay in answering your questions. The person may move slowly, uncoordinatedly, with what seems like a sort-of general uncaring about the consequences of the movement.
- **LOSS OF ENERGY** fatigue, de-motivation. Cannot start any tasks.
- **FEELINGS OF GUILT or WORTHLESSNESS**
These may be delusional, paranoid;
ask some psychosis questions, challenge the beliefs (can you reason with this person?)
- **LOSS OF CONCENTRATION or INDECISIVENESS-** either reported or observed
- **SUICIDAL IDEATION:** this is probably why they arrived to Emergency.
 - **ASK: have they tried that before? Have they made any plans?**
 - **What stopped them from doing it the last time they thought about it?**

risk factors for suicide:

SAD PERSONS mnemonic:
Sex (women = attempt, male = success)
Age (teenagers and elderly highest risk)
Depression (15% of depressed pts suicide at some stage)
Previous attempt (10% of attempt succeed)
ETOH abuse: (15% of alcoholics complete suicide)
Rational thinking loss: psychosis is risk factor
Social supports lacking
Organised plan
No spouse or partner
Sickness, i.e chronic illness

ASK ABOUT SUICIDE RISK FACTORS:

- **Living alone? Many friends? Got a partner? Been drinking?**

OTHER IMPORTANT HISTORY:

SOCIAL HISTORY:
support from friends? Or from family? Quality of relationships with these?

- **Drugs and Alcohol:** will almost certainly be using some substance or another
- **Previous admissions to some sort of psychiatric unit**
- **Previous history of psychotic illness or depressive episode**
- **Family history:** there is a genetic component; monozygotic twins develop depression with about 60-70% concordance (STILL NOT 100%, so environment plays a major role). The number is 19% for fraternal twins, which is still higher than the general population.

MENTAL STATE EXAMINATION:

Appearance: may show evidence of poor self-care
Behaviour: ... evidence of recent self-harm?
Speech: low volume, slow; may be agitated with rapid bursts
Mood: duh, depressed!
Affect restricted, unhappy face. Does not smile very much.
Thought Form may be distorted if there are psychotic features

Thought Content may be delusional, eg. "I'm already dead"
Perceptual Disturbance ?... hallucinations?.....
Insight do they realise they are clinically depressed?
Judgement may be impaired in severe depression
Cognitive Testing to gauge extent of psychomotor impairment, eg. can they concentrate, **can they copy a picture, what is their short-term memory like**

MAJOR FOCUS: PSYCHOTIC FEATURES and BIPOLAR FEATURES; you want to know whether they need antipsychotic drugs or mood stabilisers in their management cocktail.

DIFFERENTIALS: physiological causes of depression

Lets face it: If you admit this patient and treat them for depression, it would be very embarrassing to eventually discover after 2 years of ineffective electroconvulsive therapy that their depressive symptoms are the consequence of an underactive thyroid.

CNS conditions:

- Dementia
- Parkinson's
- Multiple Sclerosis
- Huntington's
- Stroke
- Epilepsy
- Neoplasm

Autoimmune:

- Lupus (SLE)

Hematological:

- Anaemia

Infectious:

- Syphilis
- HIV
- Influenza
- Viral Hepatitis

Endocrine:

- Hyperthyroidism
- Hypothyroidism
- Addison disease
- Cushing disease

Just about any drugs, and any heavy metal poisoning can be the cause of depression

DIFFERENTIALS: different flavours of depression

- **Major depressive episode:** vanilla depression; happens to many people, can be quite severe, and often results in suicide. Typical features. Mean duration is about 6 months.
- **Recurrent Major depressive episode** : if you ever had a major depressive episode, you're likely to get another one. There is often something approaching normal mood between such episodes. The gap between episodes narrows as you age.
 - o Alternatively, you can have major depressive episodes on the background of a simmering dysthymia
- **Dysthymic disorder** (only 2 of the major depressive criteria, for 2 years or more)- rarely presents in hospital except as the result of a co-morbidity (eg. chronic drinking) – NOT mild! Chronic and disabling.
- **Mood disorder due to a medical condition** – coping with a diagnosis or with chronic pain, etc...
- **Substance-induced mood disorder** – notoriously, chemotherapy of the cytotoxic kind (eg. vinca alkaloids), corticosteroids and retinoic acid derivatives eg. Roaccutane can all cause depression. Plus there is the depression related to alcohol abuse, amphetamine withdrawal, cannabis withdrawal, etc etc....
- **Anxiety coexisting with depression:** they normally coexist anyway, but the mixed presentation will have more symptoms from both.

Weird gourmet flavours of depression

- **Depression with Psychotic Features:** mood-congruent delusions and hallucinations; often of persecution, with accompanying guilt and the sense of deserving punishment (see Dostoyevski, *Notes from the Underground*)
- **Adjustment disorder** –this can come in an anxiety flavour or in a psychotic flavour
- **Schizoaffective disorder** is really just schizophrenia with a mood disturbance component
- **Bereavement** –is culturally inappropriate and excessive depression following a loss.

INVESTIGATIONS

- **FBC, EUC, TFT, LFT, serologies, CT or MRI of head, EEG.**

Trying to rule out the physiological differentials as well as determining the extent of comorbidities: eg. if you're depressed, it's less of a problem than the death of your liver from your depressive drinking.

MANAGEMENT

Immediate: focus is on RISK

- **SCHEDULE THEM** if at risk to self or others; OR if seriously disturbed

PSYCHOSIS? Depression with delusions and hallucinations?

Nobody wants a raving loon in their ED. These people belong in specialist units.

- **This requires acute management with an antipsychotic drug:**

HALOPERIDOL and MIDAZOLAM keep them calm until they can be assessed by the mental health team.

Push for a voluntary admission with non-psychotic patients.

To admit or not to admit?

Short Term: assessment and management of related problems

Address the consequences of mental disturbance: suture wrist cuts, administer overdose counter-agents....

PRACTICAL CLASSIFICATION OF DEPRESSION FOR MANAGEMENT

One must assign a name and rank to their enemy. This will guide one's long term treatment decisions.

DIMENSIONAL METHOD: by severity; mild, moderate, severe.

- On the basis of how many symptoms they have (eg. Sleep disturbance, appetite etc)
- Also, how great the disruption of function is.

CATEGORICAL METHOD: Melancholic, Non-melancholic, and Psychotic depression.

- **MELANCHOLIC depression** seems more "physiological" because
 - Genetic contribution to pathology is greater
 - Stronger evidence of abnormality in neurophysiology
 - Minimal placebo response to drugs
 - Relatively specific response to drugs and ECT

Characterised by the **PRESENCE OF CERTAIN FEATURES:**

- Non-reactive mood
- Anhedonia
- Early morning waking
- Mood worse in the morning
- Significant weight loss
- Psychomotor disturbance: which is either
 - **RETARDATION** i.e slower everything (speech, movement etc...)
 - **AGITATION** i.e inability to keep still, pacing, faster speech, picking at skin etc etc- and these anxiety features **DO NOT** settle during an interview!

No reason why the two classification systems shouldn't overlap. Thus, one may suffer from a severe psychotic depression, a moderate psychotic depression,

- **PSYCHOTIC Depression:** also has specific features; eg **DELUSIONS + HALLUCINATIONS** (Duh)
 - Guilt and persecution delusions are the most common feature
 - Lack diurnal variation (no worse in the morning than in the evening)
 - May not be aware of depressed mood- more like a "flatness".
 - May present with somatic symptoms instead of mood disturbance
 - Very poor concentration and memory
- **Non-Melancholic Depression:** pretty much everything else left over; the **MOST COMMON** form
 - No positive defining features; they belong in this group if there is no features of melancholia or psychosis.

GUIDE TO MANAGEMENT OF DEPRESSION

The idea is to start psychotherapy no matter the type or severity, and then to titrate drugs according to the symptoms. Some people don't need drugs. Some people will not benefit from psychotherapy. Most will get something out of both.

General rules for Non-Melancholic Depression:

- When there is a definable trigger, use psychotherapy to **TEACH COPING SKILLS** to deal with future situations of that nature.
- If FAMILY problems are involved, use FAMILY GROUP THERAPY
- If the depression is not exactly "mild", or psychotherapy is inappropriate, use **ANTIDEPRESSANTS**.
- **start SSRI** and if that does not help, keep going down the **Melancholia drug guidelines**
 - 2/3rds of people will get something out of antidepressants.
 - Placebo and spontaneous remission rates are 30% to 50%
 - These drugs could take up to 4 weeks to work...
 - ...That said, if after 2 weeks there is absolutely NO RESPONSE, time to try another one.
- **FOR HOW LONG DO WE DRUG THEM? As long as needed.** Say, once the triggering factor (such as a destructive relationship) is gone, the drugs don't need to stay. If the drugs were ameliorating unhelpful yet permanent character traits eg. anxiety, they should keep taking the drugs.

General rules for Melancholic Depression:

Choice of antidepressant: the more severe the depression, the more side-effects you should accept

IS THE DOSE HIGH ENOUGH?
You can safely raise the dose a little every month until the desired effect is achieved

- **trial SSRI**; it probably won't work, but if it does, they will thank you (less side-effects)
- **Venlafaxine (Efexor)** is the preferred second line option.
- **Tricyclics** if efexor does not work
- **MAOIs** if tricyclics not working or contraindicated
- **Add mood stabiliser** if antidepressants aren't working
- **ECT** if drugs have failed
- **ECT with Drugs** if ECT alone has failed
- **Last resort: weirdness** like Thyroxine therapy (! One study said they were "surprised with how few side-effects" there were on "super-physiological thyroxine dose")

TRICYCLICS pose a SERIOUS OVERDOSE RISK
Think twice about them

FOR HOW LONG DO WE DRUG THEM?

- **DRUGS for 6 to 12 months following the first episode** is a good general rule;
- For 2 years if there are 2 episodes in 2 years
- For 5 years if 3 episodes in 3 years
- The more "melancholic" or "psychotic" the episode, the longer the maintenance.

General rules for Psychotic Depression:

- Antidepressants alone = effective in 25%;
- Antipsychotic alone = effective in 33%;
- **Antidepressant + antipsychotic = effective in 80%**
- **ECT = effective in 80%**
- **Psychotherapy still helps, use it**

Amoxapine: TCA with good effects in depression with psychotic features. Is metabolised into loxapine, an antipsychotic agent

General rules for SPECIFIC SYMPTOMS:

- **INSOMNIA: the following antidepressants are sedating**
 - **Fluvoxamine**
 - **Nefazadone**
 - **Mirtazapine**
 - **Amitriptyline**
 - **Trimipramine**
 - **Doxepin**
- **APPETITE LOSS: Mirtazapine** gives you the munchies

Fluoxetine and Protryptiline may actually CAUSE insomnia

General rules for ECT:

- **BAD side effects:** anterograde or retrograde amnesia, headache, confusion, etc...
- **ONLY AFTER FIRST AND SECOND LINE DRUGS HAVE FAILED**
- One course is 12 or so treatments, so 6 to 4 weeks with 2 or 3 times a week
- **IMPROVEMENT IS DRAMATIC AND SUDDEN:** thus, ECT is great for patients who are acutely suicidal, severely psychotic, malnourished, or otherwise in extremis

General rules for PREFRONTAL LOBOTOMY:

In the field, one may have to crudely sever the white matter tracts that connect the frontal lobe to the rest of the brain. (its very 1936)

When time is permitting, one may target the hippocampus and its connections to the mammillary body, anterior thalamus and cingulate cortex.

Specific procedures include limbic leucotomy, subcaudate tractotomy (this one best for depression), anterior cingulotomy and anterior capsulotomy.

Outcome is good! ...60-80% response rates. However double-blind trials have never been performed. This treatment is reserved for cases when no other therapy is effective, and everything else has been tried.

PSYCHOLOGICAL THERAPY in detail:

Cognitive behaviour therapy:

Patients are taught to **systematically identify, evaluate and challenge the thoughts and beliefs that are believed to maintain their depression.**

- i. identify unhelpful thoughts; eg "I suck because I have no girlfriend/boyfriend"
- ii. how valid is that thought? Are there dysfunctional assumptions? Eg. "I'm ugly"
- iii. Test the dysfunctional assumptions, prove that they are false; eg. get professional photograph taken
- iv. Replace unrealistic unhelpful thinking with realistic thinking eg "I'm not THAT fat, and I'm getting better"
- v. Set schedules, eg. for pleasant activities (counters loss of motivation) eg. "today: min. 3hrs of Buffy"
- vi. Set goals and solve problems to help set up a structure for coping with life problems.

Interpersonal therapy:

Works on the principle that most depression is related to interpersonal relationships.

Emphasis on improving social skills, improving social life, and developing relationships.

Problem solving therapy:

Emphasis on improving family and social relationships. Problems not caused by the patient; problems are a response to environmental pressures. Change the response to a better response and the problems will go away. Hence goal-setting and problem-solving.

The idea being that if you're in control of your life, you won't feel depressed anymore.

Brief supportive counselling:

short term, 1-5 sessions; using any number of approaches, but aiming to reduce reliance on counsellors. Good for first-time crisis events

Psychotherapy relies upon four major theoretical models of depression:

Seligman's learned helplessness theory;

CBT aims to help people with depressive disorders **understand the link between their thoughts, behaviour and emotions**
= **at least as effective as first-line pharmacological treatments** for major depression (eg. Elkins, Gibbons, Shea & Shaw, 1996; Scot, 1996).
= **of equivalent efficacy in the treatment of severely depressed outpatients** (DeRubeis et al., 1999).
= **more strongly indicated in cases of mild to moderately severe depression or as an adjunct to medication.**

Also indicated if there was prior positive response to CBT **if the patient has a preference for psychotherapy, if medication is contraindicated, if a competent trained clinician with expertise in CBT is available.**

when dogs and rats receive uncontrollable shocks they eventually become very helpless and give up trying to avoid the shocks.

Seligman found that humans react in much the same way, but only after making the attribution (or causal explanation) **that they have no control over the negative events** in their lives.

people's attributions for past events shape their expectations about future events.

When bad things happen to people with optimistic styles they attribute the negative outcome to causes that are

- specific (confined to a particular event),
- unstable (not likely to occur regularly)
- external (not their fault alone)

when bad things happen to those with a depressive style,

the negative outcome is attributed to causes that are

- stable (occur regularly),
- global (occur across many situations)
- internal (are their fault alone).

Abrahamson's attributional model,

highlighted the role of a sense of hopelessness critical in the development of depressive disorder.

When a person with a depressive or pessimistic style experiences a negative event they will see these events as being uncontrollable, feel

helpless, and become hopeless about regaining control. This hopelessness leads to depressive disorder.

Lewinsohn's learning-based model,

posits that **negative life events bring about a change in the degree to which a person's interaction with their environment is rewarding.**

Less rewards → decrease in reward-driven activities → even less opportunity for rewards → even less activity

Therapeutic strategies based on this learning based model require that **individuals with depression actively increase rewarding behaviours in their lives.**

!! Beck's cognitive model. !!

Beck's cognitive model of depression has been the most influential, widely researched and clinically applied model of major depression.

CORE OF THE MODEL: "COGNITIVE TRIAD"

1. **Seeing themselves as worthless**
2. **Seeing the world as hostile**
3. **Seeing the future as bleak**

PLUS: characteristic "THINKING ERRORS":

- black-and-white thinking
- overgeneralisation
- catastrophising

ALL THIS ARISES FROM EARLY LEARNING EXPERIENCES...?

- Which seem to program enduring core belief systems about the person's view of themselves or their environment. Something of the Attachment theory in this.

ANTIDEPRESSANTS in detail:

Selective Serotonin Re-uptake Inhibitors:

- = block the action of a pre-synaptic serotonin re-uptake pump. Thus, there is more serotonin in the synaptic space.
- = these are highly protein-bound drugs, with average half-lives of around 24 hrs for the parent compound.
- = SSRIs competitively inhibit CYP450 enzymes; so **AVOID DRINKING ALCOHOL** while taking them.

Fluoxetine (Prozak), particularly: long half life (2 to 4 days); plus the metabolite is also active and has a whopping half life of 7 to 10 days. So wash-out should be longer (i.e greater gap between the cessation of fluoxetine and the commencement of the next drug)

SIDE EFFECTS:

Sexual dysfunction is the most common. usually a loss of libido or inability to orgasm.
WE CAN IMPROVE THIS with, erm, more drugs!

Viagra, Mirtazapine, Nefazodone, Bupropion 1 hr before sex.

Insomnia especially with fluoxetine

Nausea usually for no longer than a few days; **Diarrhoea** also short lasting

Dry mouth, dizziness, anxiety, tremor, fatigue, etc...

Serotonin syndrome: consequence of misguided SSRI overdose, or interaction between several antidepressants
nausea, confusion, hyperthermia, autonomic instability, tremor, myoclonus, rigidity, seizures, coma and death.

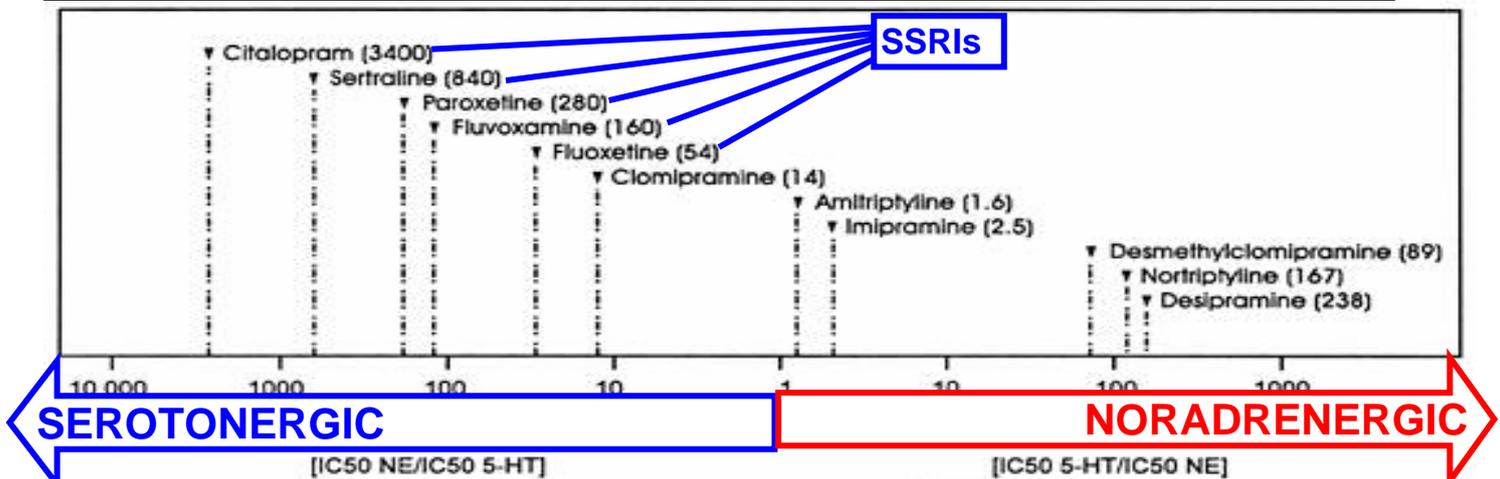
Rapid Cycling: is what happens to some bipolar patients on SSRIs. As the name suggests, this is a state of wildly fluctuating mood, switching to and fro as often as several times within a single day.

Discontinuation Syndrome: what happens when you stop taking the SSRIs suddenly. Dizziness, lethargy, nausea, irritability, and headaches. Worst with short half-life drugs eg. Fluvoxamine, paroxetine.

UNNECESSARY DETAIL: which receptors are responsible for what

RECEPTOR ACTIVITY	CONSEQUENCES
Blockade of histamine (H-1 and H-2) receptors	Sedation, drowsiness; potentiation of central depressant drugs; weight gain
Blockade of muscarinic acetylcholine receptors	Dry mouth, blurred vision, sinus tachycardia, constipation, urinary retention, memory impairment
Blockade of noradrenaline uptake at nerve endings	Antidepressant efficacy (?); tremors, jitteriness; tachycardia; diaphoresis; blockade of the antihypertensive effects of guanethidine; augmentation of pressor effects of sympathomimetic amines; erectile and ejaculatory dysfunction
Blockade of serotonin uptake at nerve endings	Antidepressant efficacy (?); sexual dysfunction; nausea, vomiting, diarrhea; anorexia; increase or decrease in anxiety (dose-dependent); asthenia (tiredness); insomnia; extrapyramidal side effects; interactions with L-tryptophan, monoamine oxidase inhibitors, fenfluramine, and occasionally lithium
Blockade of serotonin-2 (5-HT ₂) receptors	Antidepressant efficacy (?), ejaculatory dysfunction, hypotension, alleviation of migraine headaches, decrease in anxiety (?), decrease motor restlessness (?)
Blockade of alpha 1 receptors	Postural hypotension, dizziness which predisposes to falls, potentiation of antihypertensive drugs
Blockade of alpha 2- receptors	Priapism; blockade of the antihypertensive effects of clonidine, a-methyl dopa, guanabenz, guanfacine
Blockade of fast Na ⁺ channels	reduce some arrhythmias at low concentrations, cause arrhythmias, seizures at high concentrations

Receptor selectivity profile for the TCAs and SSRIs:



Cyclic Antidepressants: Old-school sedating drugs with overdose potential

Dirty ugly drugs. Work on every receptor: mainly by blockade of reuptake mechanisms of serotonin, noradrenaline and dopamine. ALSO interact with alpha-adrenergic receptors, muscarinic acetylcholinergic receptors, and histamine receptors, hence the side-effects profile. These unwanted receptor interactions are also responsible for the overdose potential.

Side Effects:

- **SEDATION**
- **WEIGHT GAIN**
- **Dry mouth**
- **blurred vision**
- **sinus tachycardia**
- **constipation**
- **urinary retention**
- **memory impairment**
- **seizures**
- **mania in bipolar patients**
- **arrhythmias**
- **tremor and ataxia**
- **Delirium in the elderly (Ach!)**
- **Sexual Dysfunction**

Discontinuation Syndrome:

transient dizziness, nausea, headache, diaphoresis, insomnia, and malaise. These effects are mostly related to cholinergic and serotonergic rebound.

Secondary Amine Tricyclic Antidepressants:

DESIPRAMINE- least sedating, least anticholinergic; **first-line in the elderly**

NORTRYPTILINE- least likely to cause orthostatic hypotension; thus **also good for the elderly**

PROTRYPTILINE- THE least sedating TCA; **may actually cause insomnia.**

Tertiary Amine Tricyclic Antidepressants:

AMYTRYPTILINE- very sedating, excellent for **CHRONIC PAIN** and **MIGRAINE**

CLOMIPRAMINE- good for **OBESSIONS** of all kinds. Most likely to cause seizures. Very sedating and anticholinergic

DOXEPIN –Extremely sedating and antihistaminic! Excellent for relentless itching, i.e **ANTIPRURITIC**

IMIPRAMINE – Wonderful for **PANIC DISORDER** and **ENURESIS** in children

TRIMIPRAMINE – the dud of TCAs. No advantages over any other TCA. Basically a waste.

Tetracyclic Antidepressants:

AMOXAPINE- heavily dopaminergic (its metabolite is the antipsychotic loxapine); may cause extrapyramidal side-effects, lactation and menstrual weirdness. Greatest risk of seizure, cardiac toxicity and general fatality with this drug. Great for **PSYCHOTIC DEPRESSION**

MAPROTILINE- Dangerous drug for the frontier psychiatrist. Lots of seizures and arrhythmias. Long half life.

MIRTAZAPINE –No adverse effects on sexual function! Sedating, but only in the first week. Lovely appetite-enhancing effect for **DEPRESSION with ANOREXIA**. Tiny chance of agranulocytosis)

Unicyclic Aminoketones:

BUPROPION- dopamine and noradrenaline reuptake inhibitor, short half-life. Fewer side-effects than TCAs and fewer sexual side-effects than SSRIs. Most common side effects are insomnia and hyperactivity (like amphetamines). + nausea, dry mouth, tremor.

Indicated for major depression, dysthymia, ADHD and bipolar disorder.

Assorted Atypical Antidepressants:

NEFAZODONE:- serotonin reuptake inhibitor, AND post-synaptic receptor blocker (only 5HT-2a).

Used for Postmenstrual Dysphoric Disorder, Post-Traumatic Stress Disorder...

Very short and unpredictable half life (2-18 hours). Normal pattern of serotonergic side-effects.

TRAZODONE: -similar to Nefazodone; somewhat less postsynaptic effect. good for **INSOMNIA and ANXIETY**.

VENLAFAXINE: –a phenylethylamine; inhibits reuptake of serotonin and noradrenaline. Causes insomnia, hypertension, anxiety, constipation, loss of appetite, sexual dysfunction etc... **BUT IT WORKS WELL FOR DEPRESSION**

REBOXETINE: Noradrenaline reuptake inhibitor. Tachycardia, dizziness, sweating, headache, urinary retention, and all for what?... its just another antidepressant. Consider it if **PSYCHOMOTOR SLOWING** is the primary problem.

Monoamine Oxidase Inhibitors: Irreversible

**The key to safe treatment:
STOP EATING EVERYTHING**

containing the amino acid tyramine

Food Taboos:

- Soy sauce
- sauerkraut
- liver
- aged cheese
- fava beans
- air-dried sausage
- pickled or cured meat or fish
- overripe fruit
- canned figs
- raisins
- avocados
- yogurt
- sour cream
- meat tenderizer
- yeast extracts
- caviar
- shrimp paste
- Beer and wine

Management of
Hypertensive Crisis:
1) Sublingual Nifedipine
Or: chlorpromazine
Watch the blood pressure:
don't let it too low

Must have tried everything else before resorting to MAOIs...

UNLESS: depression with atypical features, such as...

- mood reactivity
- increased appetite
- hypersomnia,
- sensitivity to interpersonal rejection.

Resort to MAOIs if SSRIs fail in this type of depression

ALSO: for phobia, social anxiety, agoraphobic panic disorder, and OCD

ACTION: irreversibly inhibit monoamine oxidase, located in

- the central nervous system
- the gastrointestinal tract
- the platelets

THUS: no degradation of monoamines.

THUS MORE SEROTONIN, ADRENALINE,

NORADRENALINE

You require about two weeks after discontinuing an MAOI to replenish the body with normal amounts of the monoamine oxidase enzyme.

HOWEVER:

Inhibition of MAOI at the gut results in increased absorption of **TYRAMINE** which acts as a false neurotransmitter, increasing blood pressure and maybe causing a **HYPERTENSIVE CRISIS**

OTHER SIDE EFFECTS:

Alpha-1 adrenergic blockade: thus **HYPOTENSION** (most common side effect)

Histaminic blockade: significant **WEIGHT GAIN**

Apart from that, the usual bouquet of nausea, headache, sexual dysfunction, agitation, constipation and seizures

PHENELZINE Phenelzine is associated with a **higher incidence** of weight gain, drowsiness, dry mouth, and sexual dysfunction than tranylcypromine.

TRANLYCYPROMINE: Tranylcypromine is more likely to cause insomnia than phenelzine.

Monoamine Oxidase Inhibitors: Reversible

MOCLOBEMIDE: Moclobemide is relatively selective for type A monoamine oxidase.

The inhibition is short lasting (approximately 24 hours). The metabolism of dopamine, noradrenaline and serotonin is decreased by this effect and this leads to increased extracellular concentrations of these neurotransmitters. **NON-SEDATING OR VIGILANCE-IMPAIRING** ... Sleep disturbances; dizziness; nausea; headache; dry mouth; constipation; diarrhoea; anxiety; restlessness;