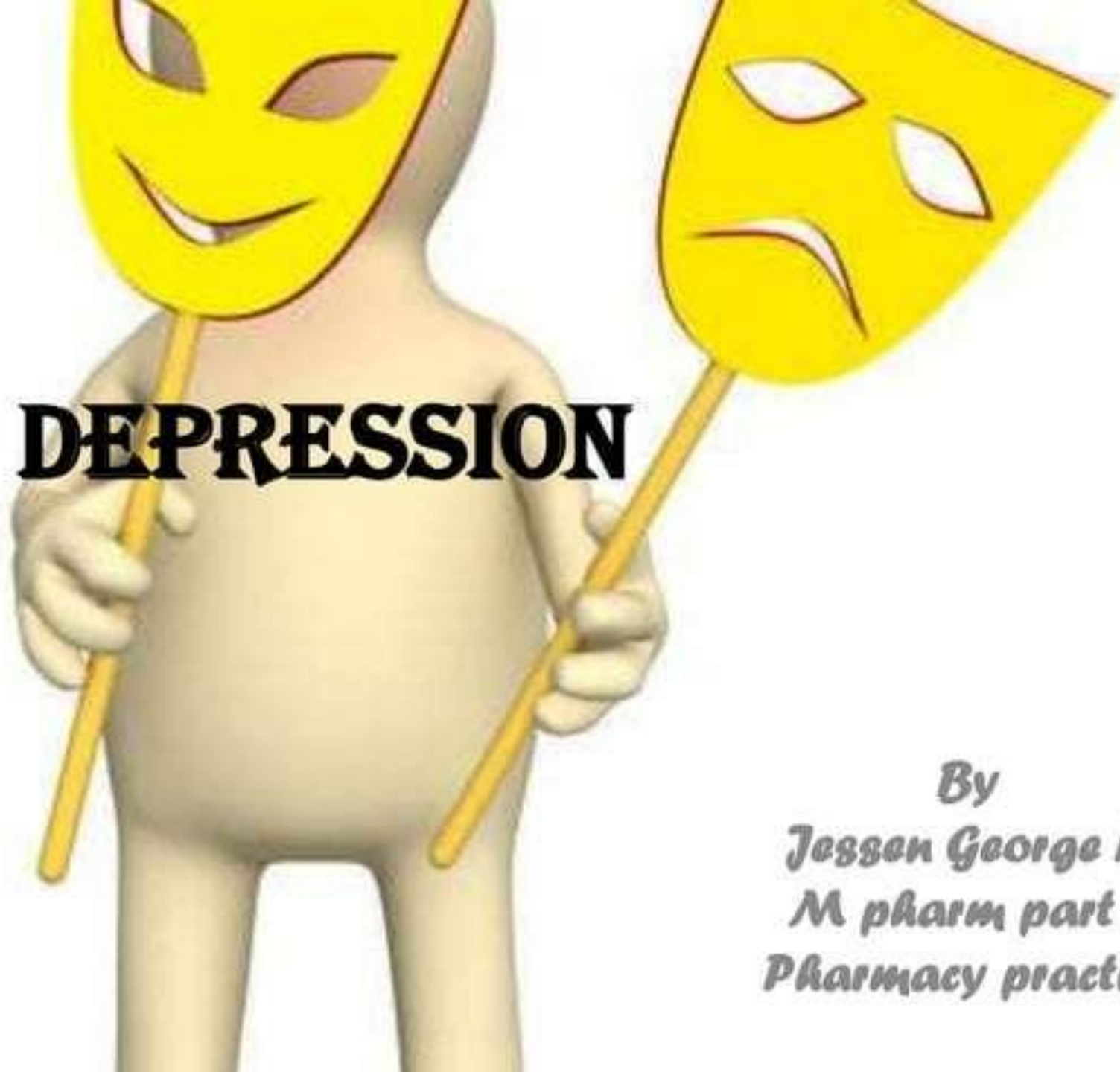

DEPRESSION

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INTRODUCTION

- Depression is a affective disorders.
- Affective disorders : mental illnesses characterized by pathological changes in mood.
- Depression : pathologically depressed mood

DEFINITION

- DEPRESSION (By WHO) : Common mental disorder that presents with depressed mood, loss of interest or pleasure, feelings of guilt or low self-worth, disturbed sleep or appetite, low energy, and poor concentration.

TYPES OF DEPRESSION

- Major depressive disorder : recurrence of long episodes of low moods, or one extended episode that seems to be 'never-ending.
  - Atypical depression
  - Post partum depression
  - Catatonic depression
  - Seasonal affective disorder
  - Melancholic depression

- Manic depression (bipolar disorder)

  Four ‘Episodes’ of Bipolar Disorder

  - depressive episode
  - manic episodes
  - hypomanic episode
  - mixed-mood states

- Dysthymic depression
  - lasts a long time but involves less severe symptoms.
  - lead a normal life, but we may not be functioning well or feeling good
- Situational depression
- Psychotic depression
- Endogenous depression

EPIDEMIOLOGY

- Globally more than 350 million people of all ages suffer from depression. (WHO)
- For the age group 15-44 major depression is the leading cause of disability in the U.S.
- Women are nearly twice as likely to suffer from a major depressive disorder than men are.
- With age the symptoms of depression become even more severe.
- About thirty percent of people with depressive illnesses attempt suicide.

ETIOLOGY

- Genetic cause
- Environmental factors
- Biochemical factors : Biochemical theory of depression postulates a deficiency of neurotransmitters in certain areas of the brain (noradrenaline, serotonin, and dopamine).
- Dopaminergic activity : reduced in case of depression, over activity in mania.
- Endocrine factors

  - hypothyroidism, cushing's syndrome etc

- Abuse of Drugs or Alcohol
- Hormone Level Changes
- Physical illness and side effects of medications

DRUGS

- Analgesics
- Antidepressants
- Antihypertensives
- Anticonvulsants
- Benzodiazipine withdrawal
- Antipsychotics

PHYSICAL ILLNESS

- Viral illness
- Carcinoma
- Neurological disorders
- Thyroid disease
- Multiple sclerosis
- Pernicious anaemia
- Diabetes
- Systemic lupus erythematosus
- Addison's disease

PATHOPHYSIOLOGY

- The Biogenic Amine Hypothesis
- The Receptor Sensitivity Hypothesis
- The Serotonin-only Hypothesis
- The Permissive Hypothesis
- The Electrolyte Membrane Hypothesis
- The Neuroendocrine Hypothesis

- The Biogenic Amine Hypothesis

  - caused by a deficiency of monoamines, particularly noradrenaline and serotonin.

  - cannot explain the delay in time of onset of clinical relief of depression of up to 6-8 weeks.

- The Receptor Sensitivity Hypothesis

  - depression is the result of a pathological alteration (supersensitivity and up-regulation) in receptor sites.

  - TCAs or MAOIs causes desensitization (the uncoupling of receptor sites) and possibly down-regulation (a decrease in the number of receptor sites).

- The Serotonin-only Hypothesis
  - emphasizes the role of serotonin in depression and downplays noradrenaline.
  - But the serotonin-only theory has shortcomings:
    - it does not explain why there is a delay in onset of clinical relief
    - it does not explain the role of NA in depression.

- The Permissive Hypothesis

  - the control of emotional behavior results from a balance between noradrenaline and serotonin.

  - If serotonin and noradrenaline falls to abnormally low levels, the patient becomes depressed.

  - If the level of serotonin falls and the level of noradrenaline becomes abnormally high, the patient becomes manic.

- The Electrolyte Membrane Hypothesis

  - hypocalcemia may be associated with mania.

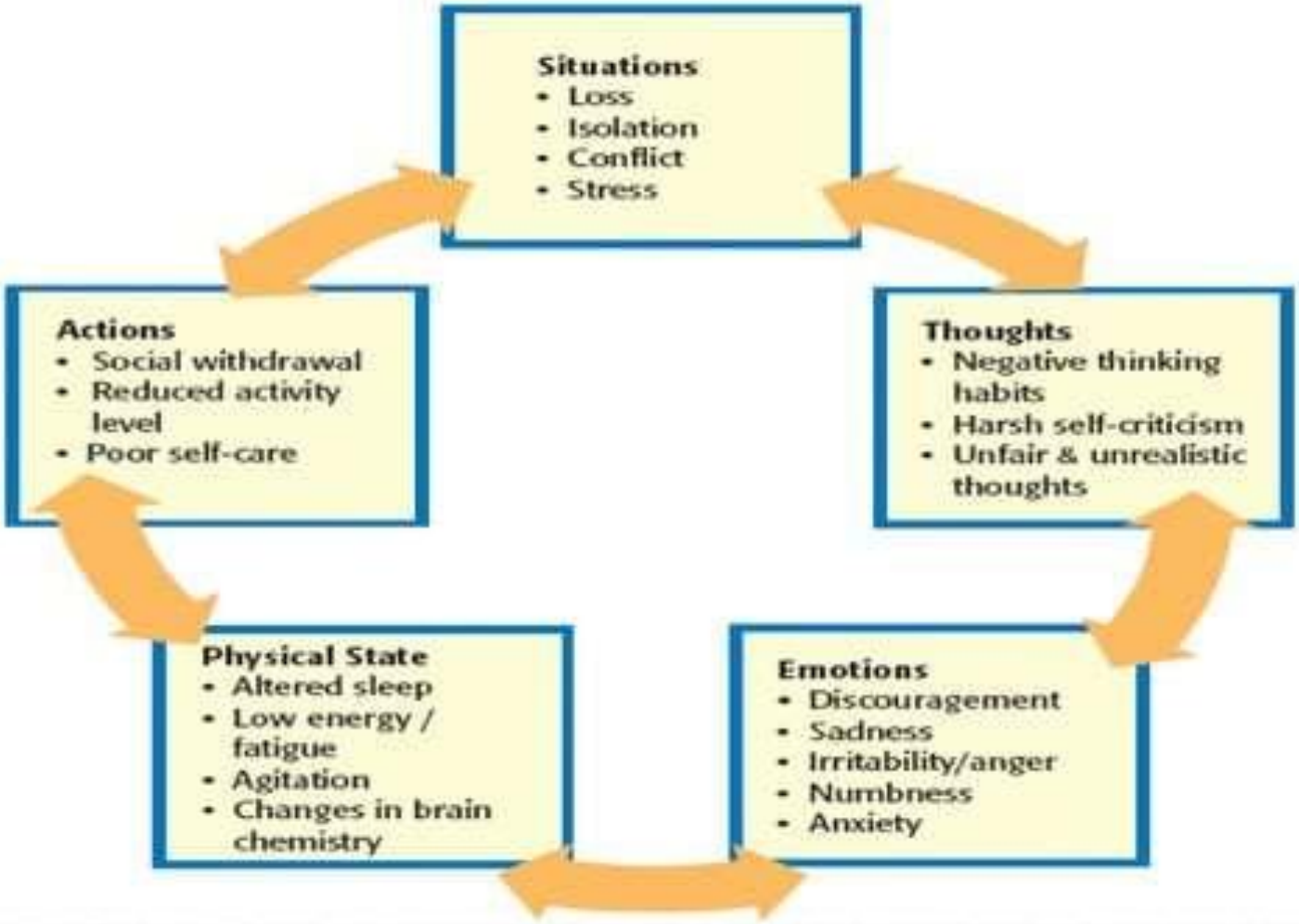
  - hypercalcemia is associated with depression.

- The Neuroendocrine Hypothesis

  - pathological mood states are explained or contributed to by altered endocrine function.

CLINICAL MANIFESTATIONS

- DEPRESSIONS
  - Thinking is pessimistic and in some cases suicidal.
  - In severe cases psychotic symptoms such as hallucinations or delusions may be present.
  - Insomnia or hypersomnia, libido, weight loss, loss of appetite.
  - Intellectual or cognitive symptoms include a decreased ability to concentrate, slowed thinking, & a poor memory for recent events.


Situations
• Loss
• Isolation
• Conflict
• Stress
Thoughts
• Negative thinking habits
• Harsh self-criticism
• Unfair & unrealistic thoughts
Emotions
• Discouragement
• Sadness
• Irritability/anger
• Numbness
• Anxiety
Physical State
• Altered sleep
• Low energy / fatigue
• Agitation
• Changes in brain chemistry
Actions
• Social withdrawal
• Reduced activity level
• Poor self-care

DIAGNOSIS

- ICD 10 Diagnostic criteria for a depressive episode {who}

USUAL SYMPTOMS

- Depressed mood.
- Loss of interest and enjoyment.
- Reduced energy leading to increased fatiguability and diminished activity.

COMMON SYMPTOMS

- Reduced concentration and attention.
- Reduced self esteem and self confidence.
- Ideas of guilt and unworthiness.
- Bleak and pessimistic views of future .
- Ideas or acts of self harm or suicide.
- Disturbed sleep.
- Diminished appetite.

MILD DEPRESSIVE EPISODE

- For at least 2 weeks, at least two of the usual symptoms of a depressive episode plus at least two common symptoms.

MODERATE DEPRESSIVE EPISODE

- For at least 2 weeks, at least two or three of the usual symptoms of a depressive episode plus at least three of the common symtoms.

SEVERE DEPRESSIVE EPISODE

- For at least 2 weeks all three of the usual symptoms of a depressive episode plus at least 4 of the common symptoms some of which should be of severe intensity.

INVESTIGATIONS

- RATING SCALES
  - Beck depression inventory
  - Hamilton depression rating scale
- DEXAMETHASONE SUPPRESSION TEST

TREATMENT

ANTIDEPRESSANTS

1. MAO inhibitors:

- Irreversible: Isocarboxazid, Iproniazid, Phenelzine and Tranylcypromine.
- Reversible: Moclobemide and Clorgyline.

2. Tricyclic antidepressants (TCAs)

- NA and 5 HT reuptake inhibitors : Imipramine, Amitryptiline, Doxepin, Dothiepin and Clomipramine.
- NA reuptake inhibitors : Desimipramine, Nortryptyline, Amoxapine.

3. Selective Serotonin reuptake inhibitors:

- Fluoxetine, Fluvoxamine, Sertraline and Citalopram

4. Atypical antidepressants:

- Trazodone, Mianserin, Mirtazapine, Venlafaxine, Duloxetine, Bupropion and Tianeptine

MAO Inhibitors

- Drugs act by increasing the local availability of NA or 5 HT.
- MAO is a Mitochondrial Enzyme involved in Oxidative deamination of these amines.
  - MAO-A: Peripheral nerve endings, Intestine and Placenta (5-HT and NA).
  - MAO-B: Brain and in Platelets (Dopamine).
  - Selective MAO-A inhibitors (RIMA) have antidepressant property (eg:Moclobemide).

- Side effects : postural hypotension, weight gain, atropine like effects and CNS stimulation.
- Severe hypertensive response to tyramine containing foods-cheese reaction
- Drug interaction : Ephedrine, Reserpine.
- Moclobemide (Rimarex) : 150 mg BDS-TDS

  Max : 600 mg/day
- Less ADR as compared to irreversible MAOI

TCAs

- NA, 5 HT and Dopamine are present in Nerve endings
- Normally, there are reuptake mechanism and termination of action.
- TCAs inhibit reuptake and make more monoamines available for action.
- In most TCA, other receptors (incl. those outside the CNS) are also affected: blockade of H1-receptor, Alpha-receptors, M-receptors.

Pharmacological Action	Adverse Effect
Muscarinic receptor Blockage/ Anticholinergic	•Dry mouth, tachycardia, blurred vision, glaucoma •Constipation, Urinary retention, Sexual dysfunction •Cognitive impairement
ά1 Adrenoceptor blockade	•Drowsiness, Postural Hypotension, Sexual dysfunction(loss of libido, impaired erection) •Cognitive Impairement
Histamine H1 receptor Blockade	Drowsiness, Weight Gain
Membrane stabilizing properties	Cardiac conduction defects, Cardiac arrythmia, Seizures
Others	Rash, Oedema, Leukopenia, Elevated liver enzymes

- Imipramine (depsonil) : 50- 200 mg/day

  - antidepressant action starts after few weeks, whereas blockade starts immediately

- Amitryptyline (tryptomer) : 50- 200 mg/day

SSRIs

- First line drug in depression.
- Relatively safe and better patient acceptability.
- Some patients not responding to TCAs may respond with SSRIs.
- SSRIs inhibit the reuptake mechanism and make more 5 HT available for action.

- Relative advantages:
  - No sedation, so no cognitive or psychomotor function interference
  - No anicholinergic effects
  - No alpha-blocking action, so no postural hypotension and suits for elderly
  - No seizure induction
  - No arrhythmia

- Drawbacks:
  - Nausea is common
  - Interfere with ejaculation
  - Insomnia, dyskinesia, headache and diarrhoea
  - Impairment of platelet function – epistaxis

SSRIs – Pharmacokinetic comparison

	Dose mg/day	Drug interaction	Half life	Steady state (Days)
Fluoxetine	5-20	high	2-4 days	30-60
Sertraline	50	low	26 Hrs	7-14
Paroxetime	20	high	20 Hrs	10-14
Citalopram	20-40	low	35 Hrs	7

Atypical antidepressants

1. Trazodone:
- Weak 5-HT uptake block, α – block, 5-HT2 antagonist
- No arrhythmia
- No seizure
- ADRs: Postural Hypotension

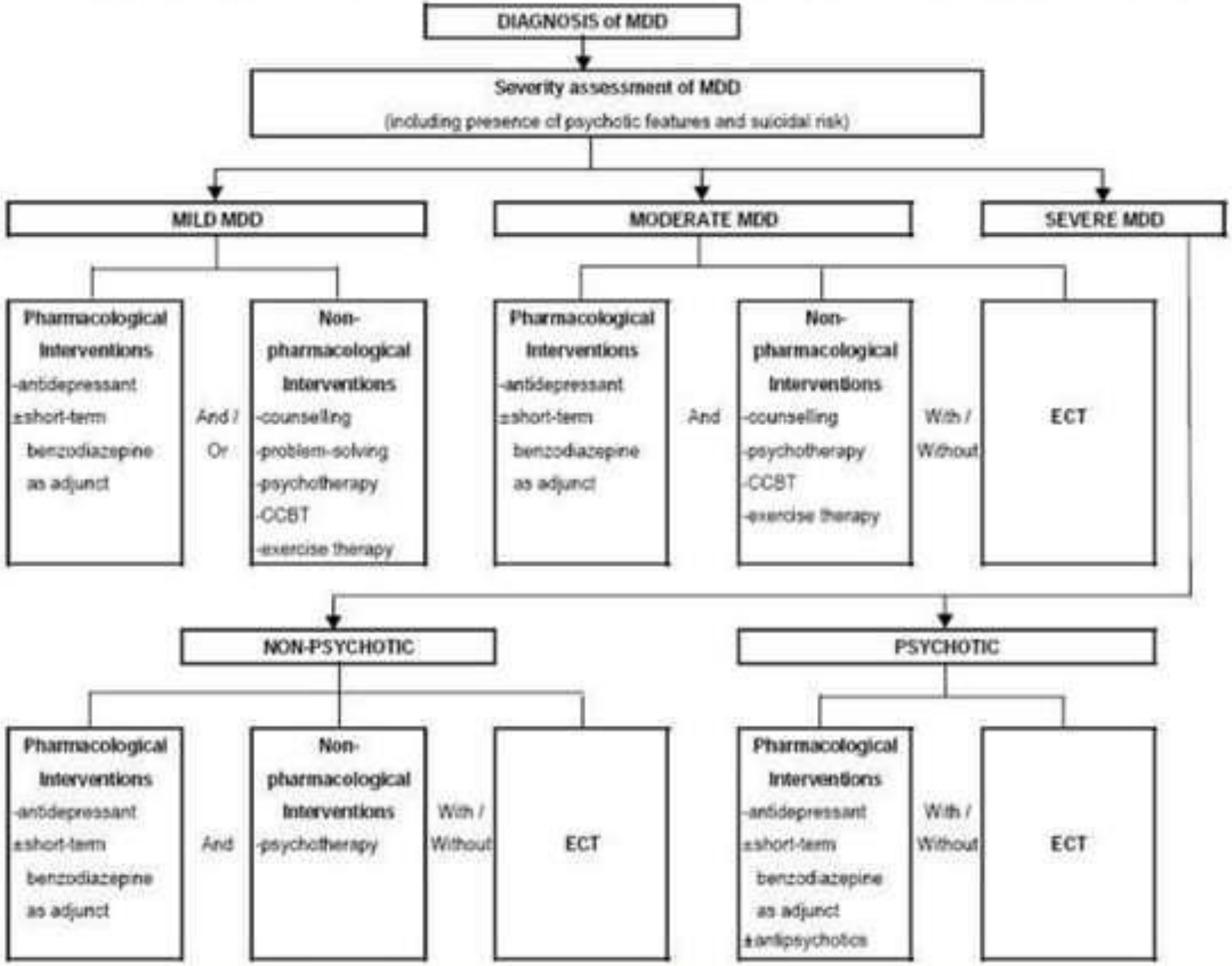
2. Venlafaxine:
- SNRI (Serotonin and NA uptake inhibitor)
- Fast in action
- No cholinergic, adrenergic and histaminic interference
- Raising of BP

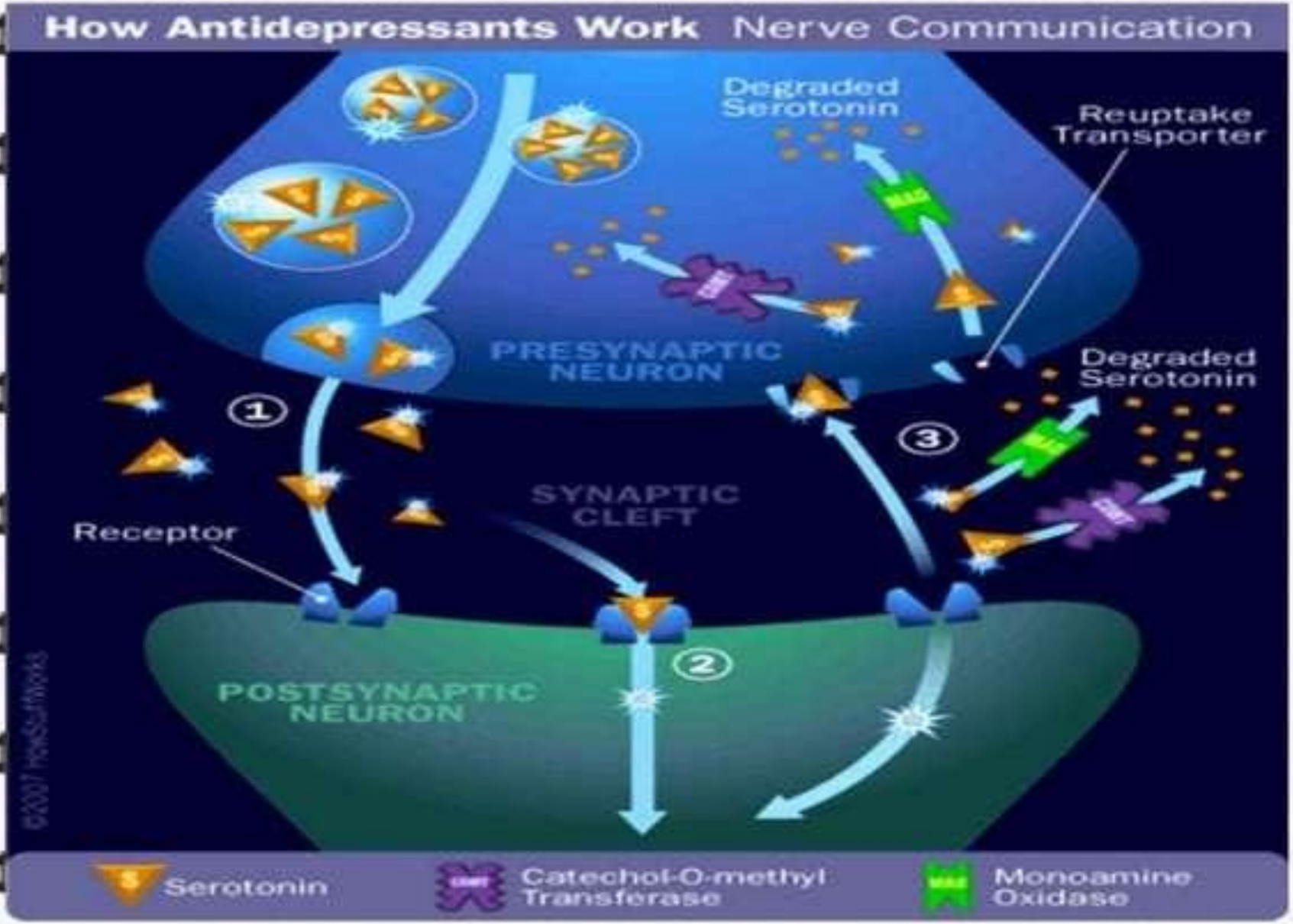
3. Mianserin

- Not inhibiting either NA or 5 HT uptake, but blocks presynaptic alpha-2 receptors- increase release of NA in brain.
- ADR : Blood dyscrasias, liver dysfunction.

4. Bupropion

- Inhibitor of DA and NA uptake (NDRI)
- Non-sedative but excitant property
- Used in depression and cessation of smoking
- Seizure may precipitated


DIAGNOSIS of MDD
Severity assessment of MDD
(including presence of psychotic features and suicidal risk)
MILD MDD
MODERATE MDD
SEVERE MDD
Pharmacological Interventions
-antidepressant
±short-term benzodiazepine as adjunct
And / Or
Non-pharmacological Interventions
-counselling
-problem-solving
-psychotherapy
-CCBT
-exercise therapy
Pharmacological Interventions
-antidepressant
±short-term benzodiazepine as adjunct
And
Non-pharmacological Interventions
-counselling
-psychotherapy
-CCBT
-exercise therapy
With / Without
ECT
NON-PSYCHOTIC
PSYCHOTIC
Pharmacological Interventions
-antidepressant
±short-term benzodiazepine as adjunct
And
Non-pharmacological Interventions
-psychotherapy
With / Without
ECT
Pharmacological Interventions
-antidepressant
±short-term benzodiazepine as adjunct
±antipsychotics
With / Without
ECT


How Antidepressants Work Nerve Communication
Degraded Serotonin
Reuptake Transporter
PRESYNAPTIC NEURON
Degraded Serotonin
1
3
SYNAPTIC CLEFT
Receptor
2
POSTSYNAPTIC NEURON
Serotonin
Catechol-O-methyl Transferase
Monoamine Oxidase

NON – PHARMACOLOGIC THERAPY

- LIFESTYLE CHANGES
  - Stress reduction
  - Social support
  - Sleep
- PSYCHOTHERAPY
  - Cognitive behavioral therapy
  - Interpersonal therapy
  - Psychodynamic therapy

- ELECTROCONVULSIVE THERAPY – ECT
  - Safe & effective disorder for all subtypes of major depressive disorder.
  - ADR : Cognitive dysfunction, cardiovascular dysfunction, prolonged apnoea etc.

CONCLUSION

- Affective disorders remain one of the most commonly occurring mental illnesses in adults.
- It is often undiagnosed and untreated.
- Both pharmacological and nonpharmacological interventions acts as cornerstone in the treatment of affective disorders.
- Pharmacist plays an important role in accomplishing these treatment goals.

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The datas were collected from various sources
Only for educational purpose


THANK YOU