# Parkinson's Disease

PD is Ch. Progressive Neurological disease associated c loss of Dopaminergic neurons in the Substantia Nigra.

- Dopamine is Chemical Messenger that transmits signals b/w 2 regions of the brain to coordinate activity
- If dopamine is deficient in striatum the Nerve cells in this region 'fire' out of control which leaves the individual unable to direct or control Movements
- As substantia nigra connects to corpus striatum to regulate Muscle activity.
- PD is a type Movement disorder when brain cell doesn't produce Enough dopamine.

Exposure to Chemicals in the Environment (Pesticides Insecticides) play Imp role in dopaminergic toxicity

Oxidative Stress also play a role

Etiology : Cause : Involves Genetic factor
Environmental factors like pesticides & herbicides
Traffic & Industrial pollution
Contribute
Other cause : Medication & antipsychotic drug.
Cerebrovascular disease.

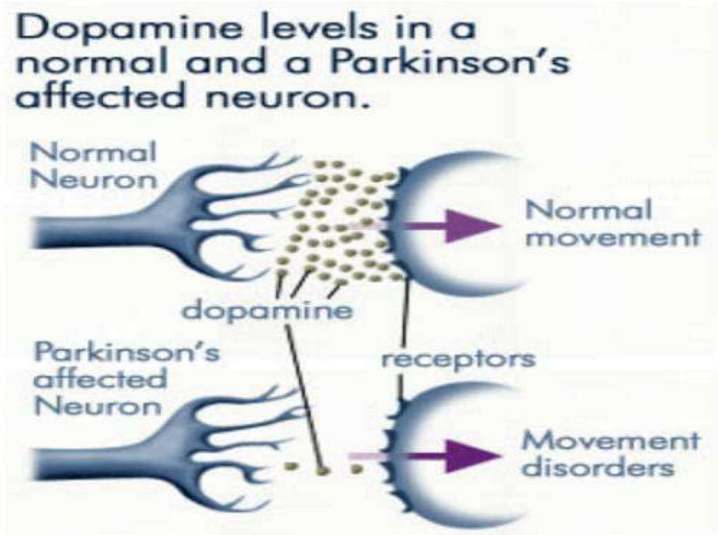
Epidemiology : PD 1-2 / 1000 population
Prevalence ↑ing & Age
PD affect 1% of population above 60 yrs.
Estimated that PD will rise from 4.1 to 4.6 Mill in 2005
- by 2 times 8.7 to 9.3
- million in yr 2030.

PD pat's in China, India, Indonesia, Pakistan
Bangladesh Japan → will rise
Expected to rise from 2.5 million 2005 to
6.1 million in 2030.

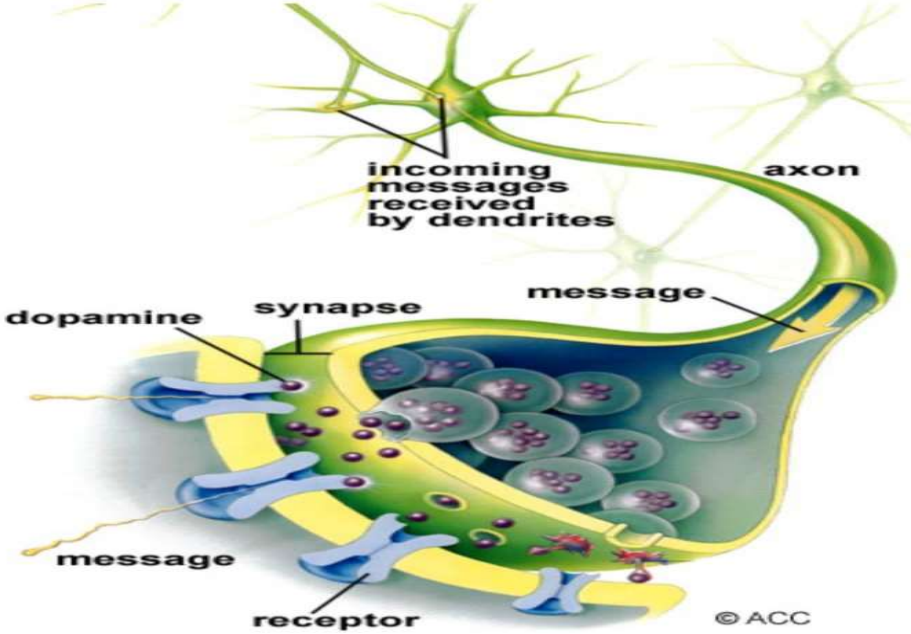
Symptoms Tremor of hands, legs Jaw & face
Slowness of Movement.
Rigidity
Stiffness of limbs & trunk.
Impaired balance.
Speech & writing changes

Non Motor Symptoms : Sleep disturbances
Depression
Cognitive deficit.

## Progressive Loss of Dopamine




As less and less dopamine is produced by the neurons affected by Parkinson's disease, far less dopamine is available to bind to the dopamine receptors on the post-synaptic membrane. Source: anti-agingfirewalls.com.




**Neurons talk to each other in the following manner (Fig. 1):**

1. Incoming messages from the dendrites are passed to the end of the axon, where sacs containing neurotransmitters (dopamine) open into the synapse.
2. The dopamine molecules cross the synapse and fit into special receptors on the receiving cell.
3. That cell is stimulated to pass the message on.
4. After the message is passed on, the receptors release the dopamine molecules back into the synapse, where the excess dopamine is "taken up" or recycled within the releasing neuron.
5. Chemicals called MAO-B and COMT break down any remaining dopamine so that the synapse area is "clean" and ready for the next message.

**Figure 1. Neurons communicate with each other across a tiny gap called a synapse. Incoming messages from the dendrites are passed to the axon where the nerve cell is stimulated to release neurotransmitters into the synapse. The neighboring nerve cell receptors pick up these chemical messengers and effectively transmit the message onto the next nerve cell.**

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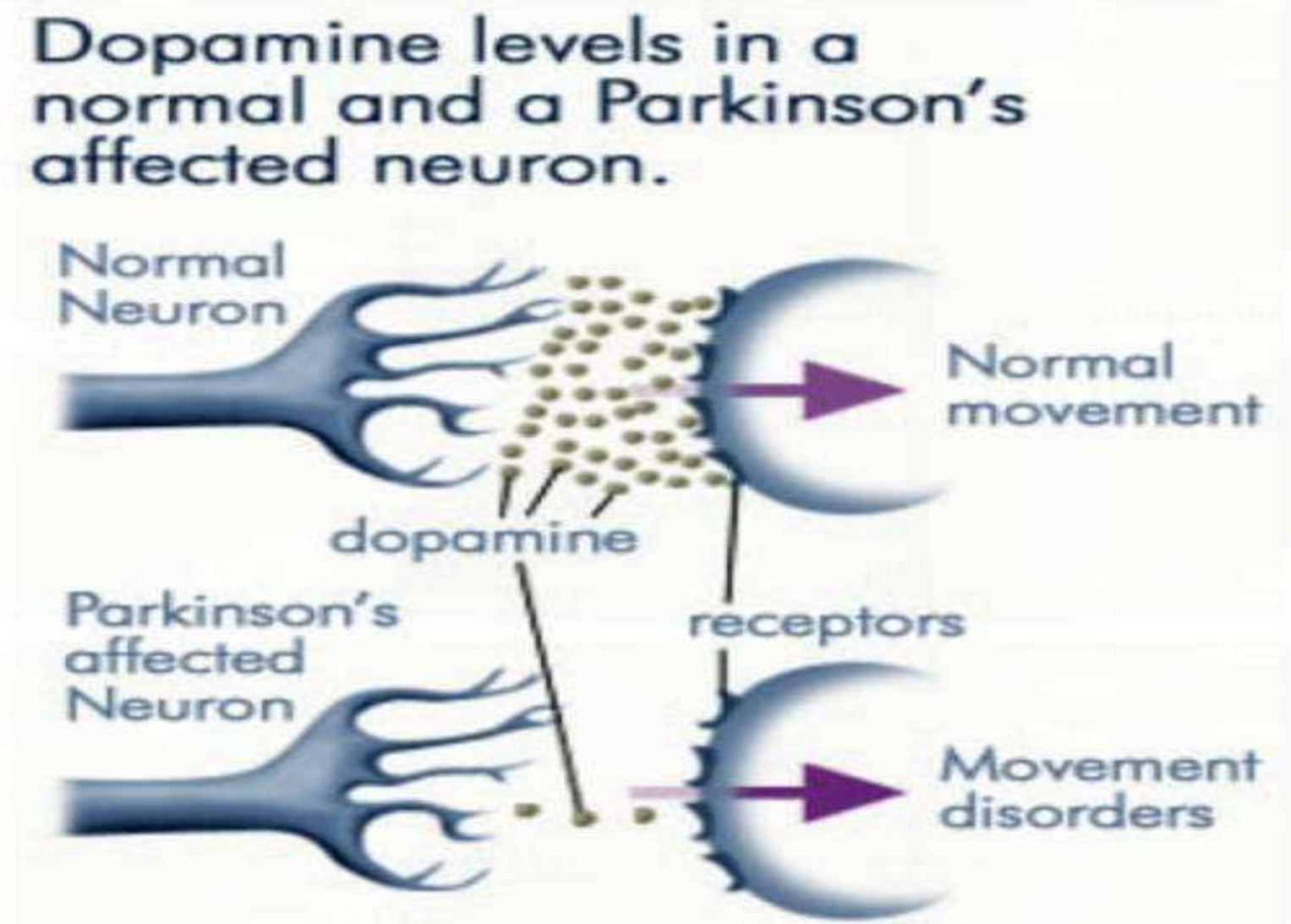


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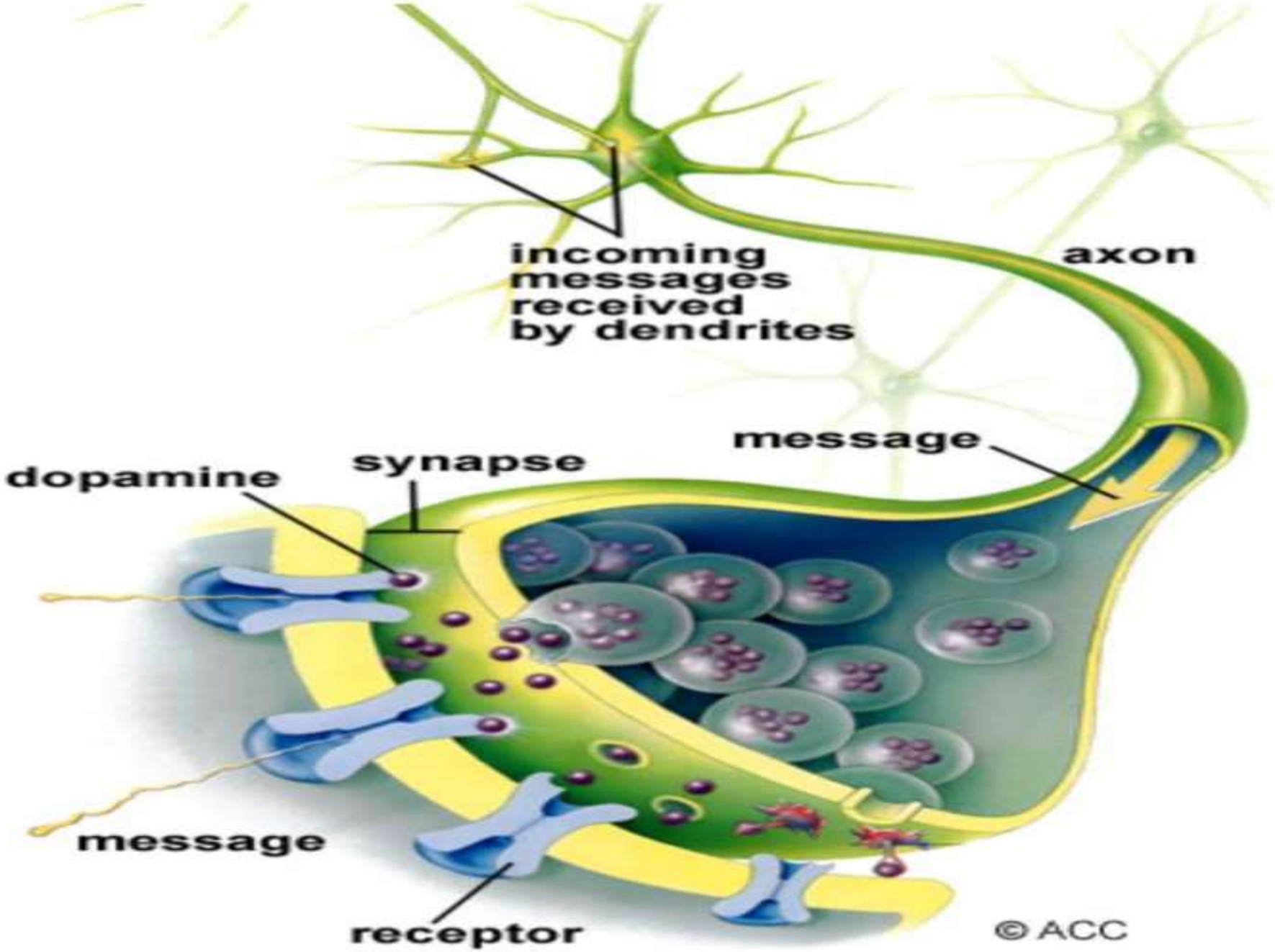
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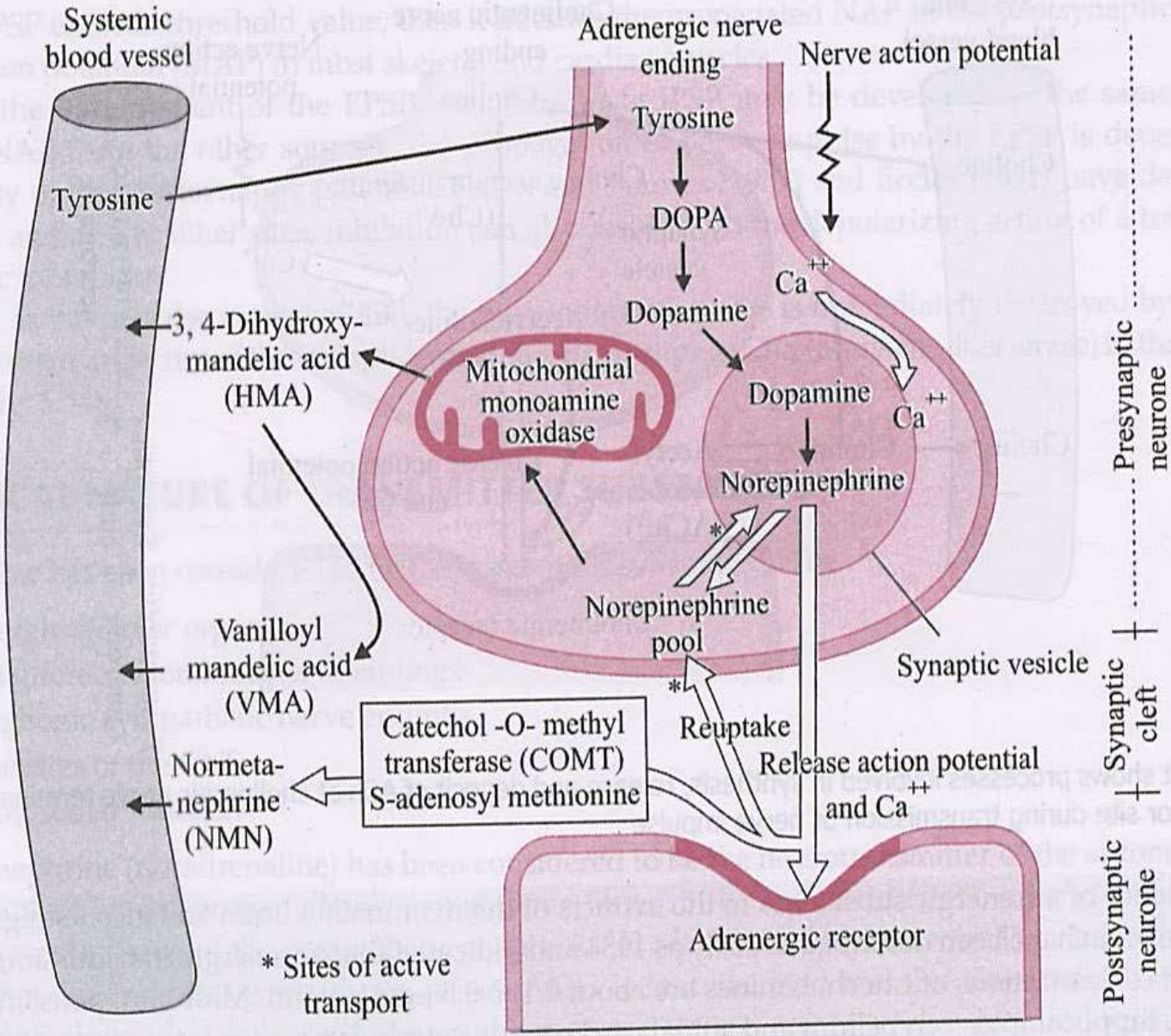
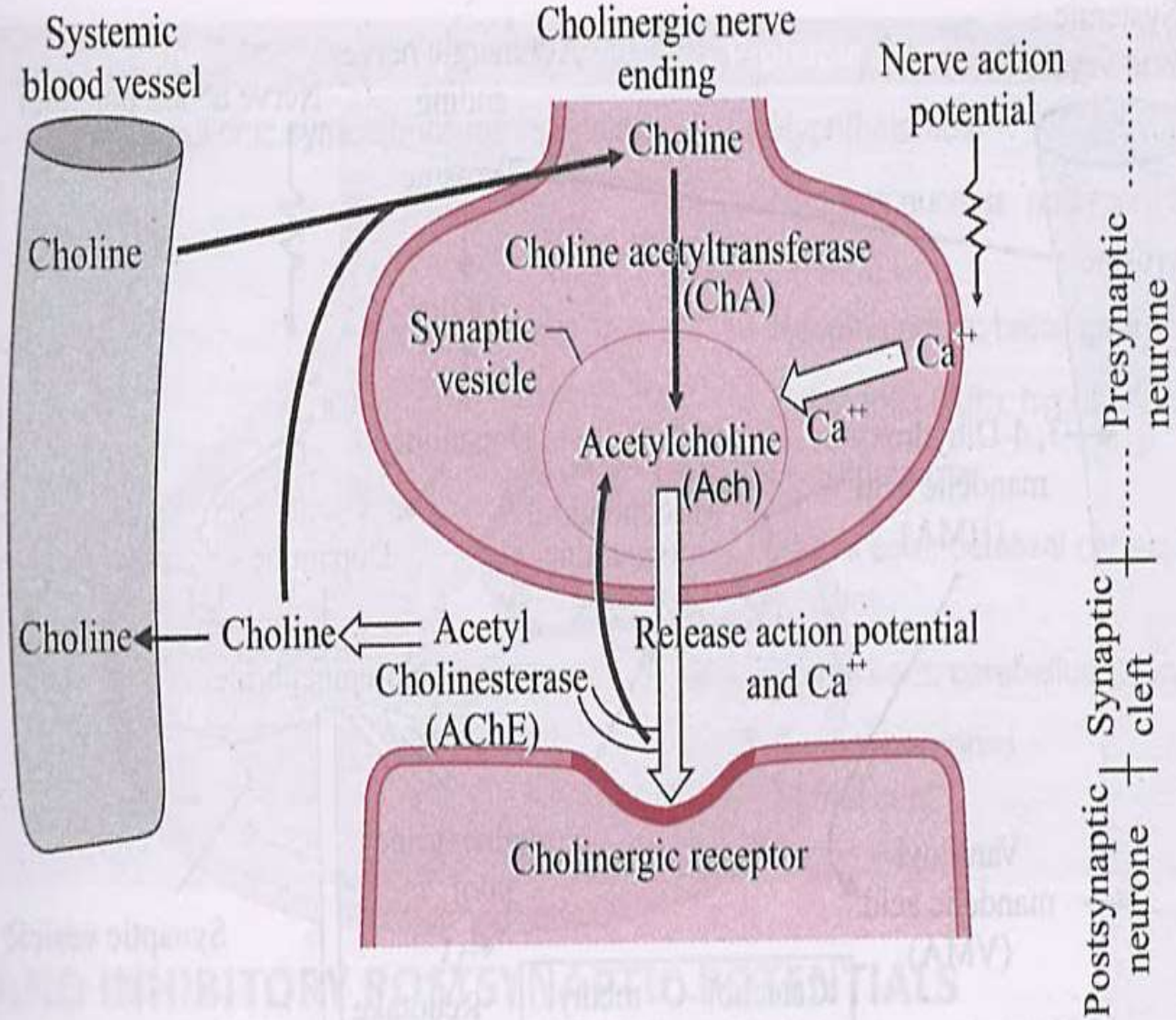



**Fig. 5.56** It shows processes involved in synthesis, release and deposit of norepinephrine at the adrenergic nerve terminal and receptor site during transmission of nerve impulse.




5.55 It shows processes involved in synthesis, release and deposit of ACh at cholinergic nerve terminals and receptor site during transmission of nerve impulse.

Treatment :

- Medications : Anti Cholinergics : Atropine
  Benzoatropine

  Dopaminergics : Levo dopa

  Dopamine agonist : Bromocryptine.

  MAO inhibitors : Selegine.

- Surgical : Thalamotomy
  Pallidotomy

- Transplantation of fetal tissue

- Transplantation of genetically engineering cell lines

**Depression :** Is one of psychiatric disorder

* It's a Mental Health disorder.
* Characterized by persistantly low mood
  feeling of sadness
  Loss of Interest.
  - Average both length of depressive episode is 6-8 months.
* Depressive disorder affect 1 in 4 women & 1 in 10 men
  have serious episodes of depression during life time
* Depression is due to bad Event like death of a loved person / frustrations

**Types of Depression :**

1. Major depression → 1. Episode lasts for 2 or 3 wk,
   2. Trouble to sleep.
   3. Lose enterest in activities
   4. Difficulty in Concentrating
   5. feel worthless & hopeless.
   6. Preoccupied with Death or Suicide.
2. Dysthymic disorder ← 1. Begin slowly
   2. Not able to pinpoint when depression started.
   3. also have Major depression Episodes in life
3. Bipolar disorder
4. Postnatal depression (post partum)
5. Seasonal affective disorder.

**Bipolar :** Mental illness for a person b/w terrible lows & Manic highs.

called bipolar disorder is called Manic depression where the person is optimistic and has exaggerated feelings of well being

- Minds are overactive and needs very little sleep
- but have plenty of Energy
- they lack concentration

During Depressive phase → person feels despairing & (losing all hope)
- May contemplate suicide.

4. Postpartum Depression: Depression begins after delivery
Mild to Severe

Factors which contribute: 1. Hormonal disturbances in pregnancy & Birth & Lactation
2. physical Exhaustion from broken sleep
3. Loss of independence
4. financial pressures
5. Changed Relationship with partner family & friends

5. seasonal affective disorder: More common in winter season.
The light hitting the retina stimulates the brain to release Mood Enhancing chemicals.

Characteristics are: Eating More & gaining wt.
Excessive Sleeping
withdrawing from people.

③

**Epidemiology** :- 70% women more likely than men to experience depression during their life.

Age group 15 – 44 yrs

30% of people with Depressive illness attempt suicide.

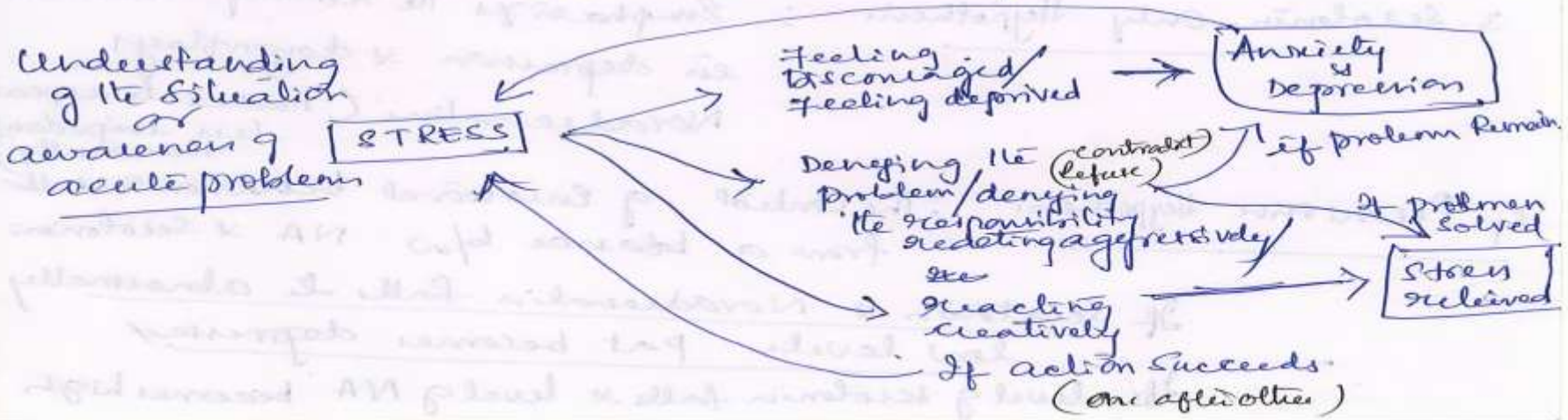
50–60% of individual in life time history of Major Depression have history of one or more anxiety disorder.

**Etiology** :- Lack of Noradrenergic Neuronal activity

Either due to Noradrenaline depletion or

lack of Noradrenalone receptors in the brain

Drugs which ↑ the availability of NA in the Brain cause sharp clinical improvement



Pathophysiology : 1) Biogenic amine Hypothesis :—

→ caused by deficiency of monoamines like Noradrenalin (Excitatory) & serotonin

Low levels of serotonin linked to depression as they regulate the mood & social behavior, sleep, memory appetite

2) Receptor sensitivity Hypothesis : Pathological alteration supersensitivity & upregulation in receptor sites.

TCA & MAOI's cause desensitization & decrease in Number of receptor sites.

3. Serotonin-only Hypothesis : Emphasizes the role of serotonin in depression & downplays Noradrenaline (Makes to appear less important than really)

4. Permissive Hypothesis : The control of emotional behavior results from a balance b/w NA & serotonin

If serotonin & Noradrenalin falls at abnormally low levels pat becomes depressed

If level of serotonin falls & level of NA becomes high

Pat becomes Maniac.

5. Electrolyte Membrane Hypothesis

Hypocalcemia May be associated ~ Mania
Hyper " is " ~ depression.

6. Neuro-endocrine Hypothesis : Pathological mood states are Explained or contributed by altered Endocrine function.

Symptoms.

Thinking is pessimistic (To see the worst aspect of things) x in some cases Suicidal
- Key psychotic symptoms such as hallucinations or delusions.
- Insomnia or Hypersomnia, wt loss x loss of appetite
- Intellectual or Cognitive (thinking x reasoning) symptoms - Used
  - ability to concentrate
  - Slowed thinking
  - Poor memory for recent events.

Diagnostic evaluation will include

Complete history of symptoms

i.e when they started
- How long they have lasted
- How severe they are
- Whether the patient have before and if so.
- If pat has thoughts about death / suicide

Mental status Examination to be done to determined → If ~~Speech / Thought pattern~~

Treatment: ECT Electro convulsive therapy : ∵ severe Depression / life threatening or who cannot take anti depressant drugs.

Done under anaesthesia provided Muscle relaxant.

→ Electrodes are placed at precise location on head to deliver Electrical impulses.

→ Stimulation causes brief seizures with in brain

(G) A Several sessions of ECT at rate of 3/wk are required.

Medication — Selective Serotonin reuptake inhibitors

TCA

MAOI

SSRI's affect Neurotransmitters like DA & NA

First line drug in depression.

They inhibit reuptake Mechanism and make More 5HT available for action

TCA : NA, 5HT & Dopamine are present in Nerve Endings. (as they are Neurotransmitters)

Normally there are reuptake Mechanism & Termination of action.

(Receptors uptake) TCA's inhibit reuptake & Make More Monoamine available for action

MAO Inhibitors : Act by ↑ing the local availability of NA or 5HT (Serotonin)

(Enzymes)

(8)

Prognosis : Depressive disorders do not have cure

Recover the pat upto 80% 90% { Medicines, cognitive & behavioural therapies, Civic relaxation techniques can help.

without treatment symptoms can last for weeks months or years.