Basics of Mental Health and Clinical Psychiatry
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Lecture 38
Mood Stabilizer

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Hello everyone, let us start lecture number 38 that is Mood Stabilizers. So in the previous mood stabilizer that we will be discussing are lithium, valproate, lamotrigine, carbamazepine and topiramate.

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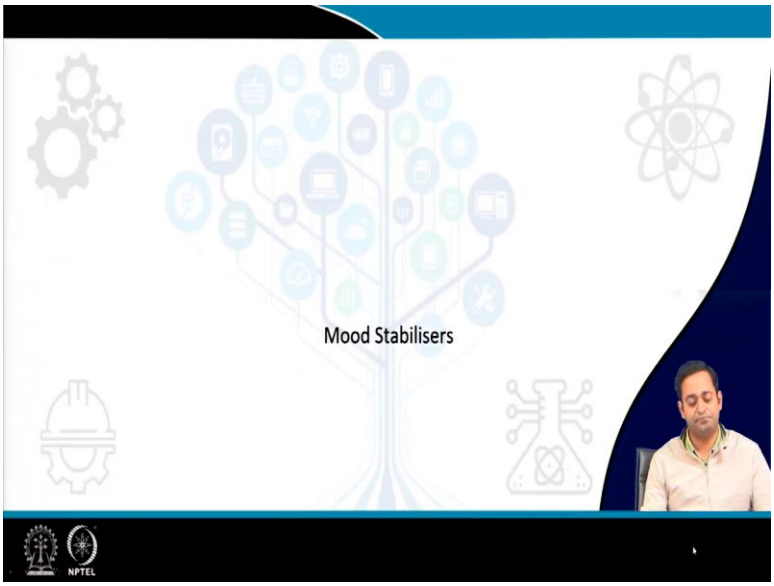

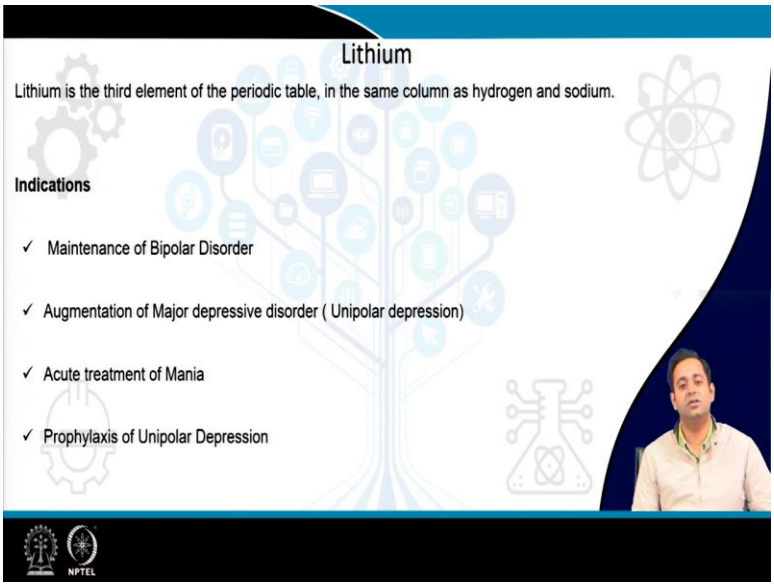

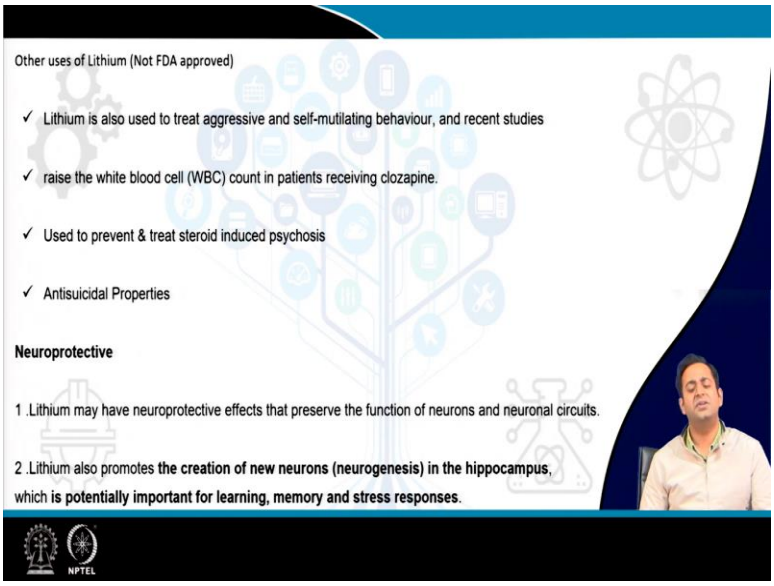

So mood stabilizers are basically the ones which are most commonly indicated for the treatment of bipolar disorders in psychiatry, bipolar disorders, major depressive episodes of depression, or certain behavioral issues, agitations, and yes, most primarily indicated for seizures that is a epilepsy.

So let us start with lithium first, lithium is actually the classic mood stabilizer which is used in psychiatric illnesses. This is a third element of the periodic table which is placed aside hydrogen. What are the indications? Most commonly it is indicated for bipolar disorder, maintenance of bipolar disorder, augmentation of major depressive illnesses that is unipolar depression, acute treatment of mania, and prophylaxis of unipolar depression.

This particular model molecule was discovered by John F Kate of Australia. So this was actually encountered in the hot water springs where various other soils of lithium were found that is lithium carbonate, lithium citrate, lithium orotate, so various other soils are present. What are the other uses of lithium, which are not FDA approved? These are to treat that is aggressive episodes or nucleative behaviors.

It raises the white blood cell count on patients who are giving, who are on close up in. They are also used to prevent steroid induced psychosis and has a very important anti-suicidal property. Among neuroprotective role of lithium it is, because it preserves the various neurons in your

dendritic processes and in the neural circuits, it promotes the creation of neurogenesis in the hip procampus, which is potentially important for learning memory and stress responses.

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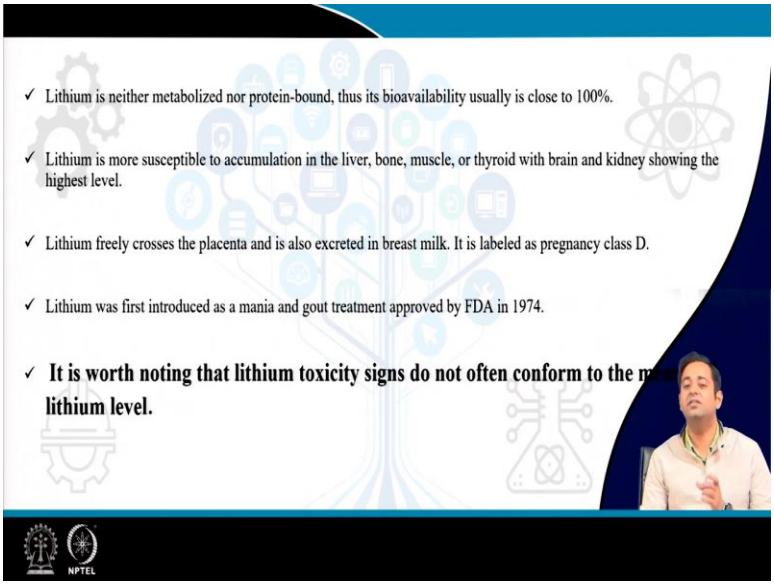

So it is neither metabolized or not protein bound, thus if having a bioavailability of 100 percent. It is more susceptible to accumulating liver, bone, muscle, thyroid, brain, kidney that is why we need to have repetitive investigations pertaining to thyroid levels or kidney function test or liver function tests.

So lithium, it crosses placenta very easily and is excluded in breast milk also and that is why is labeled as pregnancy class D. And the most peculiar feature of lithium is that, the signs and symptoms of lithium toxicity are visible even though the serum lithium levels of, serum lithium levels in the blood is within the control or in the maintenance level.

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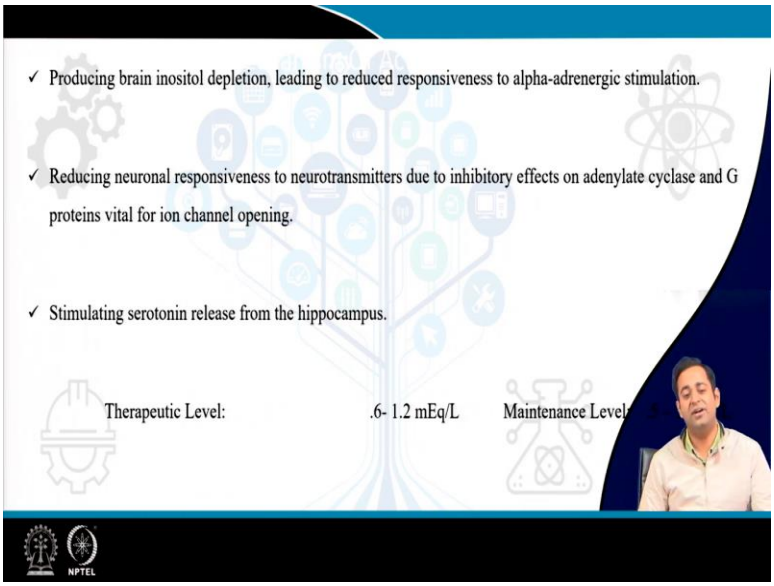

So that needs to be the ones the clinicians are should be very much should be very much aware of this particular fact and that the side effects are like it is most obviously expressed out even before the serum levels are beyond the range, therapeutic range. So lithium reduces neuronal responsiveness to neurotransmitters due to inhibitory effects of adenine cyclists, G proteins, vital for iron channel opening.

And it stimulates serotonin release from the hippocampus. It produces brain anastrozole depletion leading to reduce responsiveness to alpha adrenergic stimulation. The therapeutic level is 0.6 to 1.2 and the maintenance level is 0.5 to 1 milliequivalent per liter. The dosage for which it should be having 0.6 to 1.2 is 600, 600 to 800 milligrams and for 900 to 1200 milligrams it should be 0.8 to 1.2 milliequivalent per liter.

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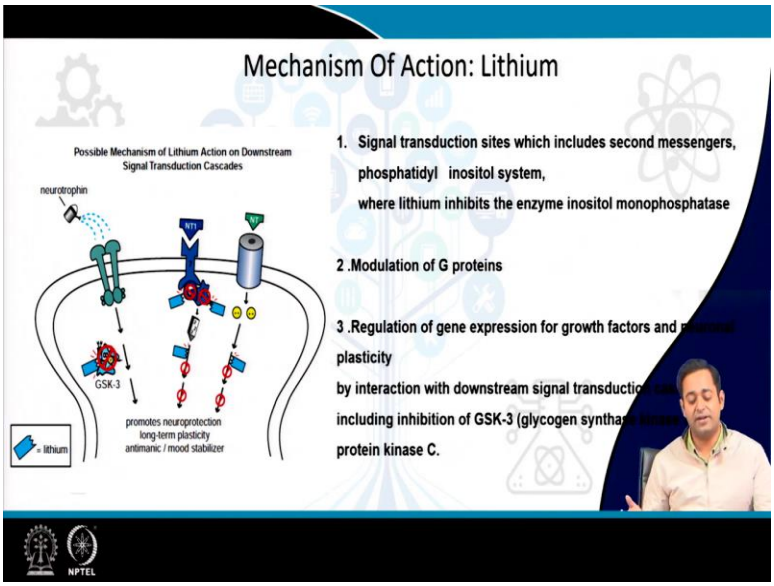

What are the mechanism of action? First is signal transaction various cascading effects, second is by modulation on the G proteins, and third is by the neutral neurotopins, those growth factors which mediate neural plasticity.

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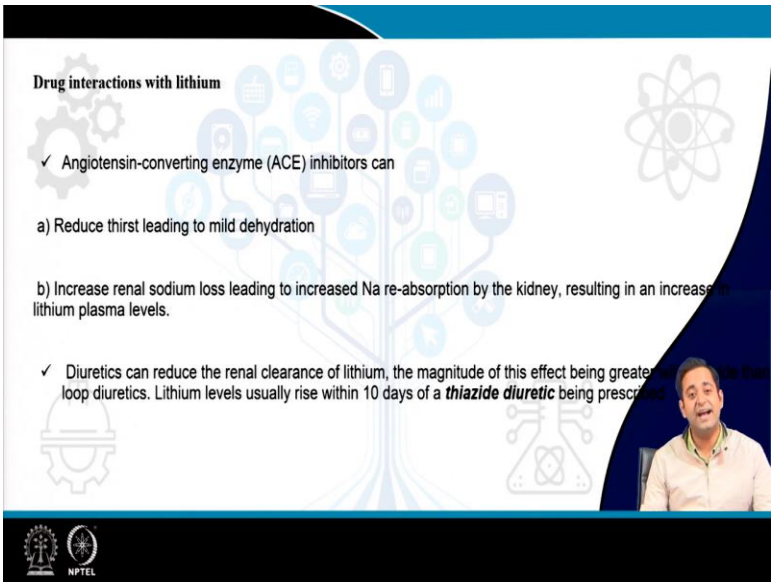

So how does it interact with other molecules. So AC inhibitors are the ones, it has a very important role. It reduces thirst leading to mild dehydration. It will increases the renal sodium loss leading to increased sodium reabsorption by the kidney, resulting in an increase in lithium

plasma levels. Diuretics can reduce the renal clearance of lithium, that is thiazide diuretics have a prominent role in this.

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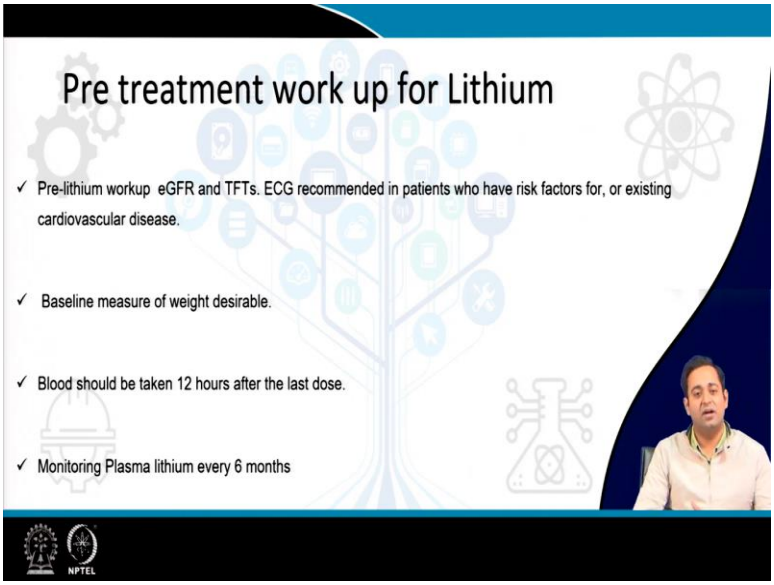

There has to be a pre-treatment workup of lithium before the lithium is started for a patients that is globular filtration rates the thyroid function tests and ECGs are recommended primarily before starting the lithium molecule and there should be a, the test should be repeated within six months.

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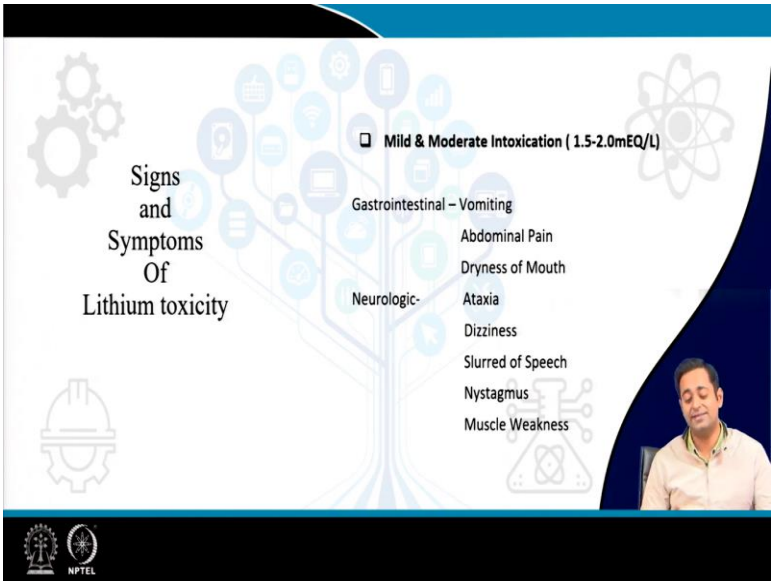

So there are three stages for lithium toxicity which should be assessed very properly. So that the patient can be saved from lithium toxicity, these are mild, moderate, and severe toxic. In case of mild, toxicity of lithium that is gastrointestinal and logical manifestations among gastrointestinal manifestations the patient might be suffering from vomiting, abdominal pain, dry mouth. And neurological manifestations are ataxia, and dizziness, slurred of speech, nystagmus, muscle wasting.

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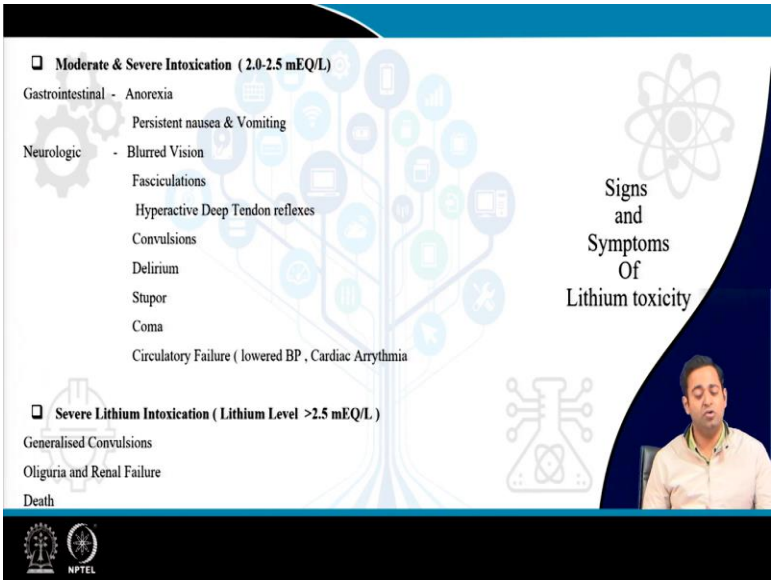

In case of moderate or severe intoxication, you have anorexic. Patient can become anorexia, persistent nausea, or vomiting, can be blurred vision, convulsions, deep tendon reflexes are hyperactive, super delirium. And in case of severe serum lithium levels, where it is more than 2.5 the patient can have convulsions, oliguria and renal failure leading to death.

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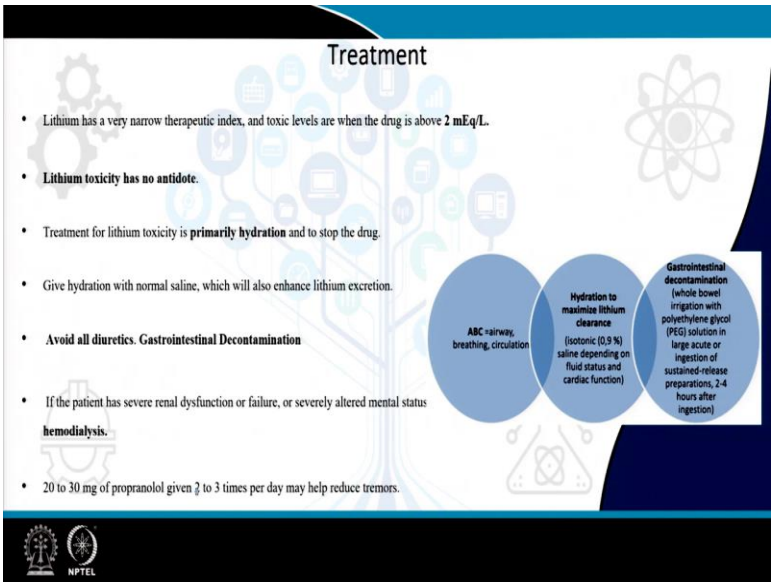

So how can we treat this problem since lithium does not have any antidote primarily we should go for supportive therapy and the primary hydration of the patient. So avoid all, diuretics gastrointestinal decontamination should be done and if the left serum levels of lithium has gone beyond four mille equivalence per liter then the hemodialysis should be done for the patient.

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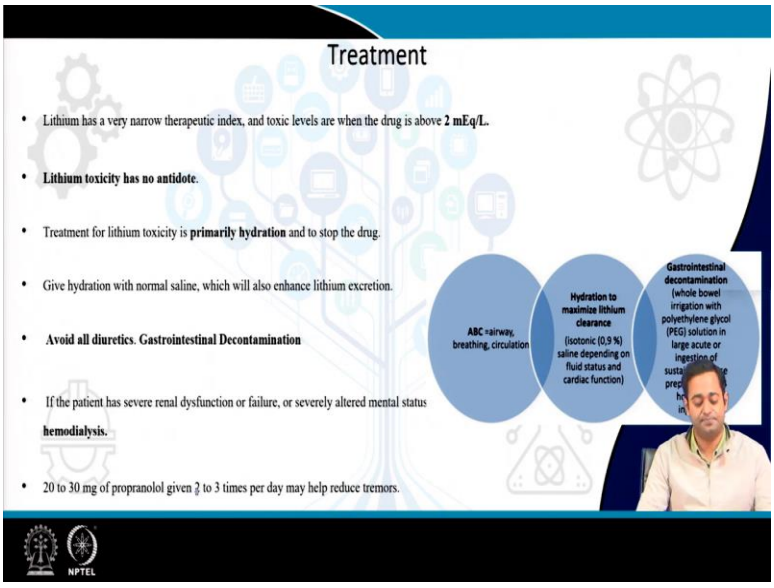

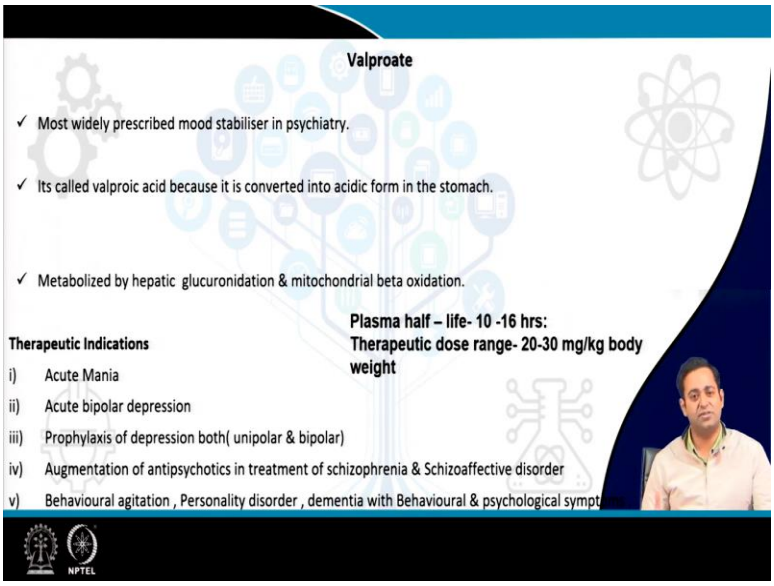

It is come to sodium valproate, it is most commonly mood stabilizer which is used in psychiatry and it is metabolized by hepatic, glucuronidation and mitochondrial beta oxidation. Plasma half-life is from 10 to 16 hours and the therapeutic dose ring for the molecule is desired by 20 to 30 milligram per kg body weight.

The indication is with acute mania bipolar depression, prophylaxis of the bipolar disorder, augmentation of any antipsychotic given for a psychiatric illness, a behavioral agitation personality disorders dementia with behavioural and psychological symptoms.

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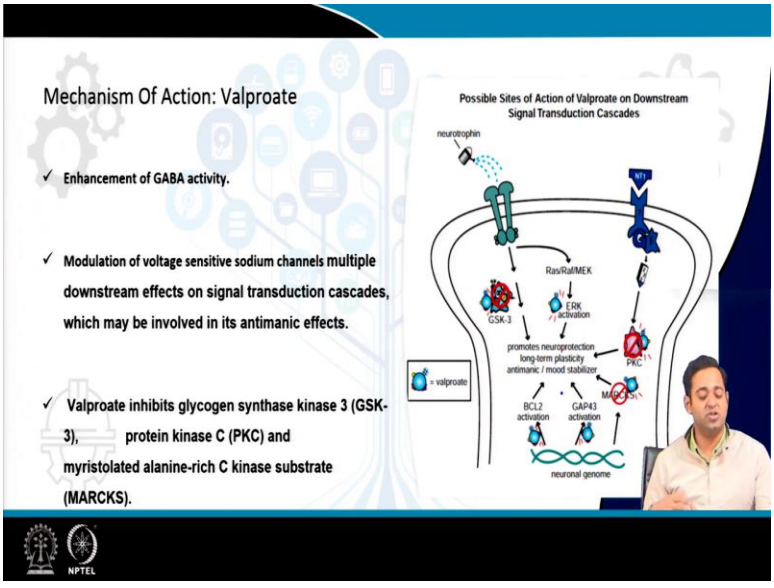

Mechanism of action of valproate is by enhancement of GABA activity. Second is by modulation of voltage sensitive sodium channels by various downstream effects on signal transduction cascades. And thirdly is by those glycogen synthesis inhibition of glycogen synthase, 3 inhibitors and protein kinase 3 inhibitors.

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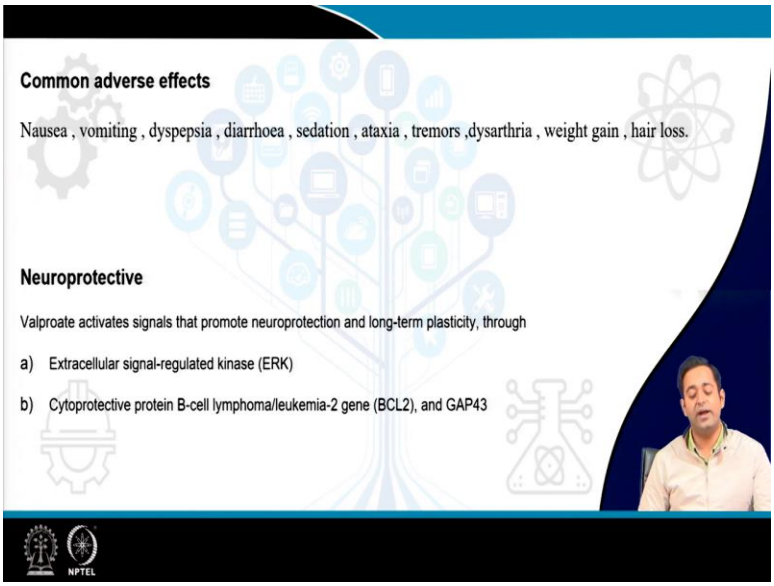

The common side effects are in the form of nausea, vomiting, hair loss, weight gain, ataxia, tremors. The neuroprotective role is basically due to extracellular signal transaction cascades and cytoproductive protein B lymphoma that is BCL2 and glycogen AP43 proteins.

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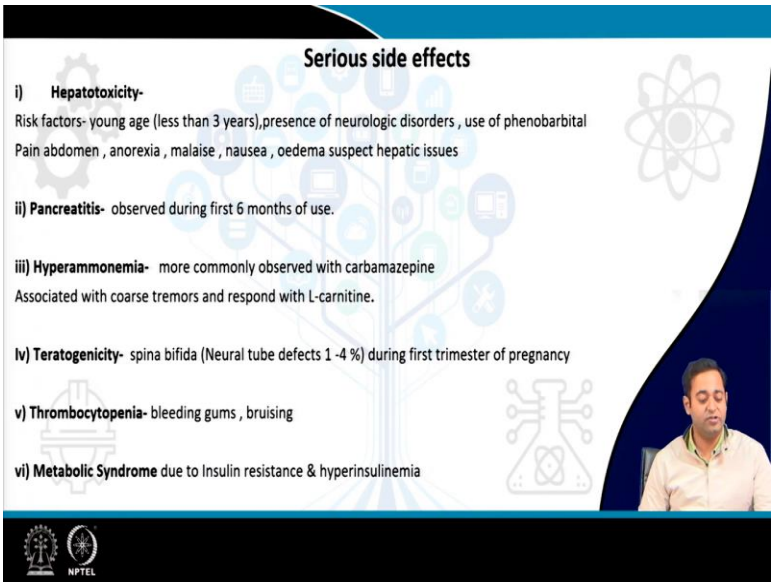

Serious side effects are in the form of hyperatoxicity, pancreatitis, hypeammonia, teratogenicity that is (())(8:34) defects, thrombocytopenia leads to bleeding disorders, and metabolic syndrome due to his insulin resistance and hyperinsulinemia.

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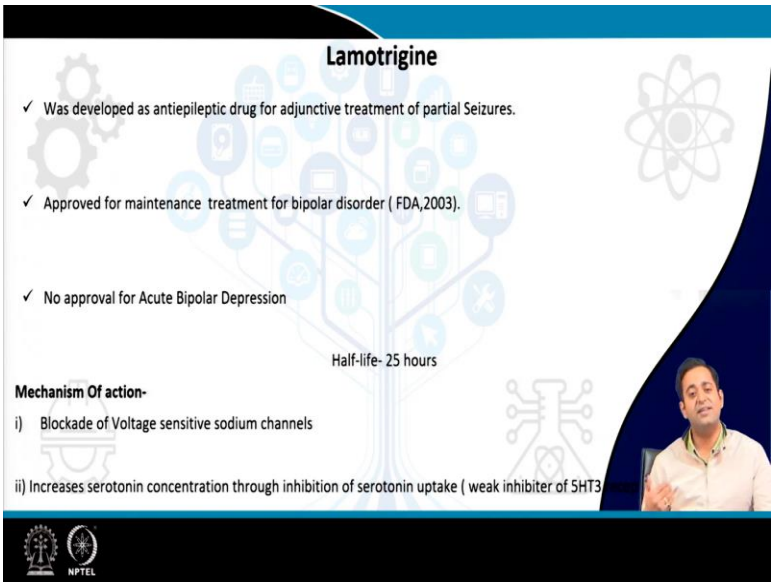

Let us come to lamotrigine. So lamotrigine was antiepileptic drug for adjunctment treatment of partial seizures, it was developed due to this. Approved from maintenance of treatment of bipolar disorder that is FDA approved in the year 2003 and there is no approval as such for acute bipolar

depression although there are evidences for which lamotrigine is utilized and indicated in psychiatric (())(9:09) practice.

So half-life for the drug is 24 hours and the mechanism of action is block out of voltage sensitive sodium channels. And the second is increases serum constant serotonin concentrations through inhibition of serotonin reuptake.

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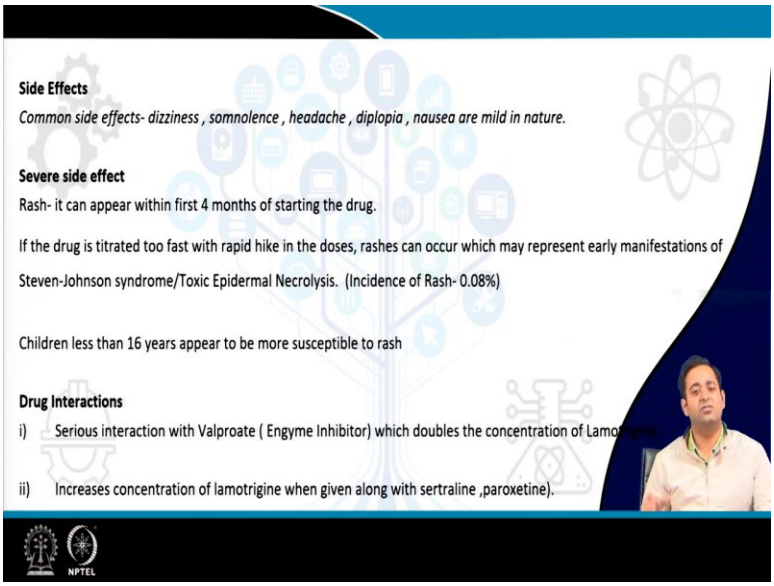

Side effects are in the form of dizziness, somnolence, headache, diplopia, at times nausea. The serious most serious side effect seen or associated with lamotrigine is the rash. So rash it appears within the first four months of starting the drug. And the drug is titrated too fast if you are hacking the drug too fast, it leads to rashes or more progressed severest form that is Steven Johnson's syndrome.

Children less than 16 years, they are more susceptible to this development of rashes. The drug interactions that should be most cautious for is valproate with which it doubles the concentration of lamotrigine, because valproate being an enzyme inhibitor and the ones are the accessorized paroxetine sertraline, they also increases the concentration of lamotrigine.

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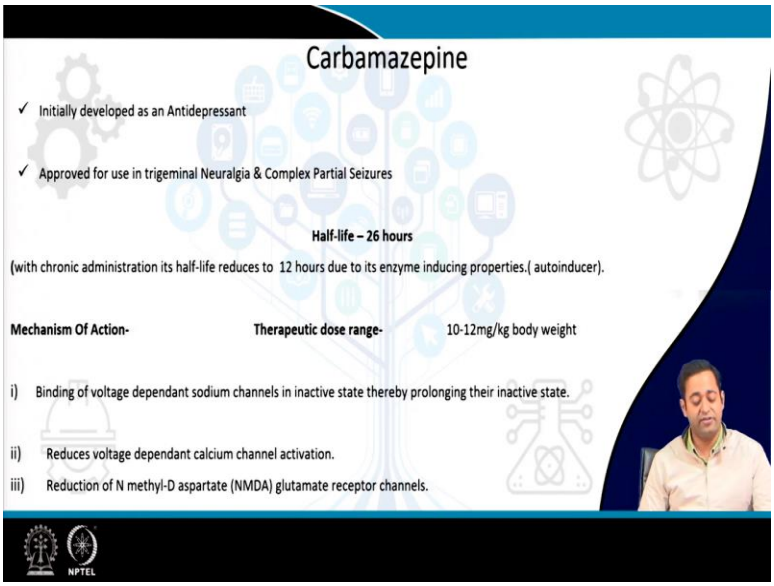

Next is carbamazepine, the carbamazepine was initially developed as an antidepressant and later on it there was approval by FDA where it is being used for trigeminal neuralgia and complex partial seizures. So half-life for the drug is 26 hours but this half-life is decreased because of the continuous or chronic administration of the drug, reason being auto induction of the enzymes, enzyme inducer. Carbamazepine is a auto enzyme inducer.

What is the therapeutic dose range, that is it is calculated on the basis of 10 to 12 milligram per kg body weight. Mechanism of action is binding of voltage dependent sodium channels in inactive state thereby prolonging their inactive state. So it reduces the calcium channel activation and there is reduction of NMDA glutamate receptor channels.

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What are the indications for carbamazepine? Acute mania, prophylaxis of bipolar disorder 2, it helps to control acute alcohol withdrawal, and it controls agitation, and impulsive aggressive behavior. That adverse effects are in the form of nausea, vomiting, gastric, distress, constipation, diarrhea, ataxia at times drowsiness. The serious side effect is pancytopenia, agranulocytosis, and aplastic anemia.

So the symptoms of if at all the patients with a little bit symptoms of sore throat, rash, bruising, easy bleeding they should be seeking the evaluation from a physician immediately in order to stop the drug, because these are most notorious to cause pancytopenia, agranulocytosis, and aplastic anemia.

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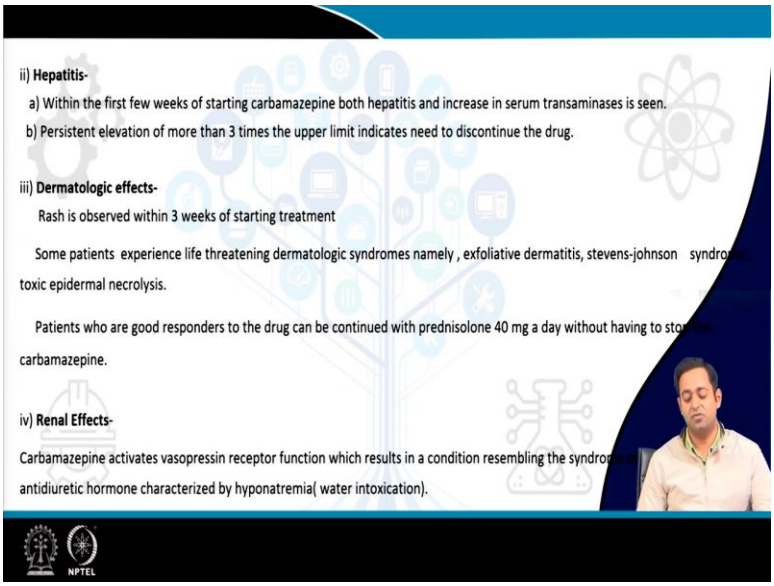

The next most serious side effect is hepatitis, it is it occurs within the first few weeks of starting the carbamazepine. So persistent elevation of more than three times the level of this leads to stoppage of the drug. Among dermatological effects, we have rashes which can be seen within the three weeks of starting the treatment.

And patients who are good responders to this drug can be continued with prednisolone 40 milligrams, if at all the patient does not respond to any other drug but carbamazepine. So they can be given with this, when the prednisolone that is corticosteroid is given along with the carbamazepine. Among renal effects you have a water intoxication where the patient results into syndrome of inappropriate antibiotic hormone.

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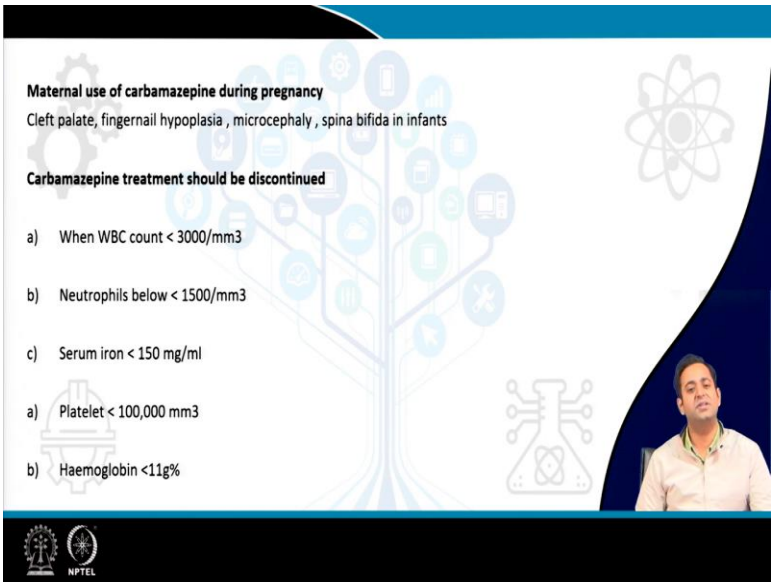

There are various other contraindications where the carbamazepine can present with, that is if the child if the, if there is maternal use of carbamazepine during the pregnancy and the child might develop cleft palate, fingernail hypoplasia, microcephaly, and spina bifida. So there are some chances at the patient that the child might develop.

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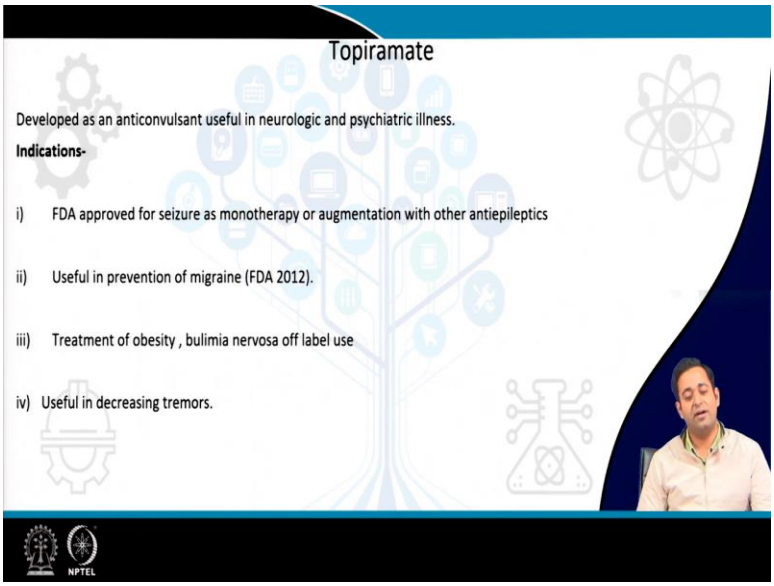

Next is topiramate, topiramate is developed as an anticonvulsant and useful in neurological and psychiatric illnesses. What are the indications? It has the FDA approval for seizures as

monotherapy and also for augmentation with other various other antiepileptic drugs, it is useful for prevention of migraine also, and it has off-label use of treatment in obesity and bulimia nervosa off.

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Mechanism of action is it blocks, it acts by blocking the voltage sensitive sodium channels. And it reduces the membrane depolarization by Kianate or AMPA receptors. And it enhances the GABA receptor activity. Most common adverse effects are the paresthesias, weight losses, somnolence, anorexia, dizziness, memory problems. And there leads to formation of renal stones.

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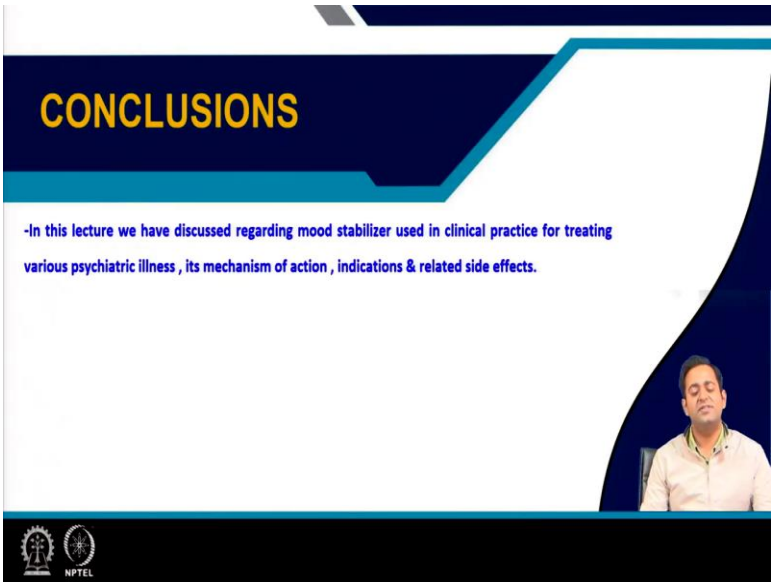

In this lecture we have discussed regarding the mood stabilizers that is lithium, valproate, lamotrigine, carbamazepine. Thank you.