

Basics of Mental Health and Clinical Psychiatry
Dr Sumit Kumar
Department of Psychiatry
Tata Main Hospital, Jamshedpur
Lecture 26
Substance -I

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The slide features a blue header with two circular logos. Below the header, a blue banner reads "NPTEL ONLINE CERTIFICATION COURSES". The main content area is white and contains the following text:

Course Name Basics of Mental Health & Clinical Psychiatry
Faculty Name Dr Sumit Kumar
Department Name Psychiatry
TATA MAIN HOSPITAL

Lecture 26 : SUBSTANCE -I

Hello everyone, let us start with substance use disorders.

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The slide has a blue header with the title "CONCEPTS COVERED" in yellow. The main content area is white and contains a list of topics:

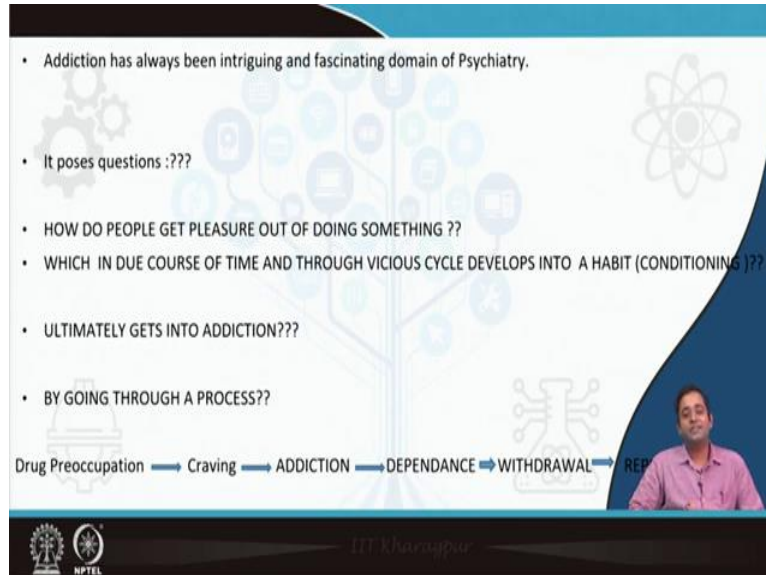
- Concept of Addiction .
- Criteria for Dependence according to ICD
- Concepts of Opioids dependence and its treatment.
- Concepts of Alcohol Dependence and its treatment
- Concepts of Benzodiazepine dependence and its treatment

A small video inset in the bottom right corner shows Dr. Sumit Kumar. The footer includes the NPTEL logo and the text "IIT Kharagpur".

What are the topics that will be discussing? Substance concept of addiction, criteria for dependence that is how the substance use disorders are diagnosed, the criteria according to International classification of diseases, concept of opioid dependence its

treatment, concept of alcohol dependence its treatment, concept of benzodiazepines dependence and its treatment.

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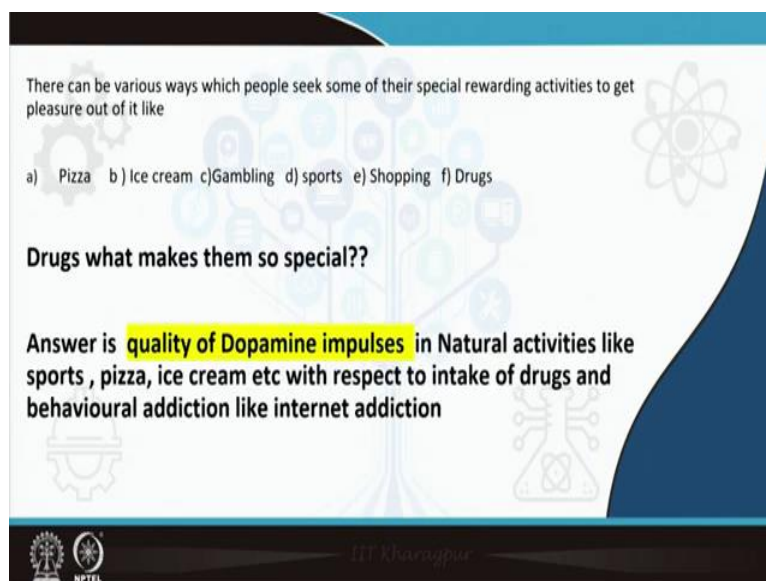
This slide introduces the concept of addiction as a fascinating domain of psychiatry. It lists several key questions: 'It poses questions :???', 'HOW DO PEOPLE GET PLEASURE OUT OF DOING SOMETHING ??', 'WHICH IN DUE COURSE OF TIME AND THROUGH VICIOUS CYCLE DEVELOPS INTO A HABIT (CONDITIONING)??', 'ULTIMATELY GETS INTO ADDICTION??', and 'BY GOING THROUGH A PROCESS??'. A flowchart at the bottom illustrates the process: Drug Preoccupation → Craving → ADDICTION → DEPENDANCE → WITHDRAWAL → REP. The slide features a background with a stylized tree of icons and a presenter in the bottom right corner.

- Addiction has always been intriguing and fascinating domain of Psychiatry.
- It poses questions :???
- HOW DO PEOPLE GET PLEASURE OUT OF DOING SOMETHING ??
- WHICH IN DUE COURSE OF TIME AND THROUGH VICIOUS CYCLE DEVELOPS INTO A HABIT (CONDITIONING)??
- ULTIMATELY GETS INTO ADDICTION??
- BY GOING THROUGH A PROCESS??

Drug Preoccupation → Craving → ADDICTION → DEPENDANCE → WITHDRAWAL → REP.

So, addiction is an important fascinating domain of psychiatry. And it gives rise to a number of questions that how people do get addicted out of doing something which in due course of time through a vicious cycle develops into a habit, it develops into a conditioning and people get addicted to any sort of substances or a kind of behaviour which goes through a process of drug preoccupation, craving, addiction, dependence and ultimately withdrawal and leading to relapse.

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This slide discusses the role of dopamine in addiction. It starts with the statement: 'There can be various ways which people seek some of their special rewarding activities to get pleasure out of it like'. It then lists examples: 'a) Pizza b) Ice cream c) Gambling d) sports e) Shopping f) Drugs'. The question 'Drugs what makes them so special??' is posed, followed by the answer: 'Answer is quality of Dopamine impulses in Natural activities like sports, pizza, ice cream etc with respect to intake of drugs and behavioural addiction like internet addiction'. The slide features a background with a stylized tree of icons and a presenter in the bottom right corner.

There can be various ways which people seek some of their special rewarding activities to get pleasure out of it like

a) Pizza b) Ice cream c) Gambling d) sports e) Shopping f) Drugs

Drugs what makes them so special??

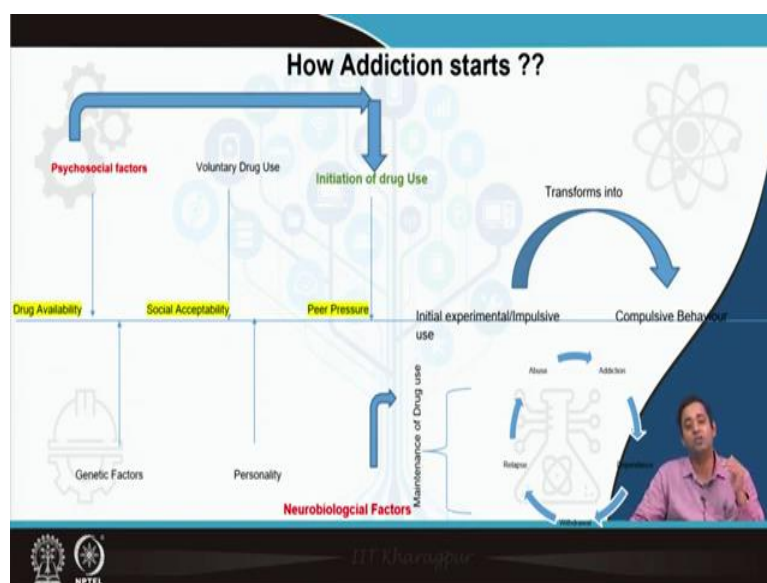
Answer is quality of Dopamine impulses in Natural activities like sports, pizza, ice cream etc with respect to intake of drugs and behavioural addiction like internet addiction

Now, there can be various ways people seek some of their special rewarding activities like people can get pleasure out of doing anything, if they are eating lots of pizzas, ice cream, they are doing gambling, sports activities, shopping, drugs these all kind of activities can give rise to an elevated kind of, an feeling of well-being and these all substances, these all ways of doing, this all behaviours they ultimately go and increase the level of dopamine which is giving the effect of well-being a good.

So, what is the hedonistic centre of the brain? It is the nucleus accumbens where all these impulses go and hit and that creates a feeling of high. Then what is this drugs the substances like smoking, alcohol, your cannabis, marijuana, cocaine all this it makes what them, what actually makes them so special apart from all other activities?

Now, answer is the quality of dopamine impulses which is secreted when the person is under the effect of substances, it is the burst of neural impulses which actually causes the drugs making them so special rather than the other sort of addiction or behavioural addiction like sports, is eating pizzas, ice creams, sports, like that.

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So, how it starts? How addiction starts? There is drug availability in younger years, there is social acceptability like in the society people are actually accepting this drug procurement getting high, getting involved in these substances, getting addicted to it, getting dependent and whenever they are not doing this kind of behaviour when you are not under the influence of the substances they undergo physiological withdrawals leading to relapse.

There are some genetic factors like if a person who is maturing from children to an adult if his forefathers or his parents, they used to do any kind of addiction like alcohol, smoke so their children they are being predisposed, they actually have those genes, so whenever there is those environment which actually makes them which facilitates them to go and procure the drugs so those are the genetic factors which plays an important role.

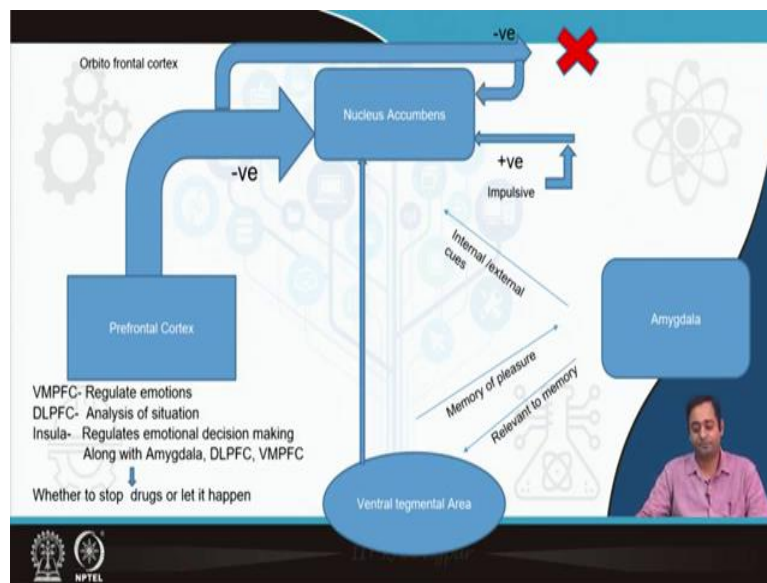
Then there is a personality, there are some persons who are impulsive who actually go and procure drugs whenever they are irritable they are agitated in order to counteract their mood their feelings of in health. So, in order to self-medicate their problems, in order to ignore their problems, in order to escape from their problems they actually try to go and procure the substances so those are the impulsive personality which actually goes on to procure these drugs.

Then there are some psychosocial factors, psychosocial factors means childhood development in the early ages where the parents are very punitive, they are punishing, you have poverty, you do not, your parents are not looking after the child or the life events which actually gives rise to this substance procurement behaviour or the person actually who has, who was actually not taking those substances in the early part of his years starts to take or pressurized by their peers by friends that you should take this in order to come out of the, of your helpless situations.

So, there is voluntary experimental use of the drug which gives rise to initiation so this is how your addiction, your substance taking behaviour it starts. So, initial experimental use which is voluntary in nature you are not being pressurized but you yourself takes the substances, it converts and transforms into a compulsive behaviour through a vicious cycle by abuse initially in a small amount later you get addicted, you get dependent then withdrawal occurs when you are not taking this kind of substances and ultimately leading to a relapse where you again go back to procure these substances.

Now, what happens your initiation of the drugs the substances they are due to psychosocial factors but the maintenance of the, your addiction that from last five years, ten years you are still going on and you are under the effect of your substances like smoking, alcohol, cocaine, cannabis whatever it is it is due to the neurobiological factors, your brain is addicted to that, because of that you need to undergo that substance procurement act.

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Now, as I told you nucleus accumbens happens to be the agonistic centre of the brain where the dopamine gets where the dopamine is actually hitting it. So, from the ventral tegmental area these impulses are going towards the nucleus accumbens whenever there is a impulse and that the substance should be procured and the amygdala as you know it is the emotional centre of the brain it has some internal as well as external cues.

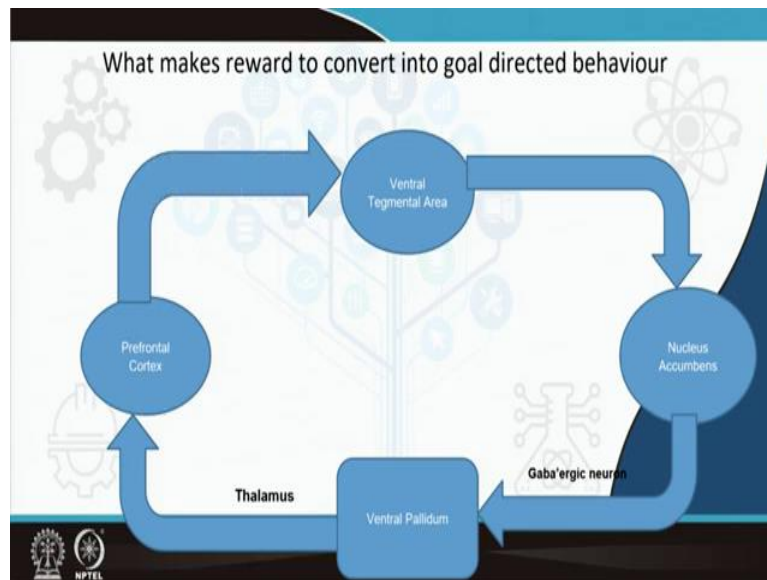
Internal cues is when in the past you have already taken the substance it can be anything cannabis, smoke or alcohol or anything else cocaine, so there are memories formed so that actually instigates you to go and procure the substance whereas the external factors where you are actually being persuaded by your friends, your sometimes colleagues that we should go and do this and this so there the memory which was stored it gets re-stimulated.

So, ventral tegmental area it also so gives this kind of memories that okay there was some incidents in the past that party was very good that Saturday night, some last weekend, some fortnight, two weeks back we had a very good time by doing some kind of, some peculiar kind of stuff where we have taken the special substance like cocaine, MDMA anything else.

So, that actually gives rise to another kind of stimulation which instigates or actually persuades the people to go on to procure the drug. There can be yes, the personality factor of impulsiveness where the patient, where the person actually go and procures the drug. And how there is this reward functioning and when the patient actually wants to stop this drug procurement behaviour, how does it happen, how can you stop yourself, how can you inhibit yourself?

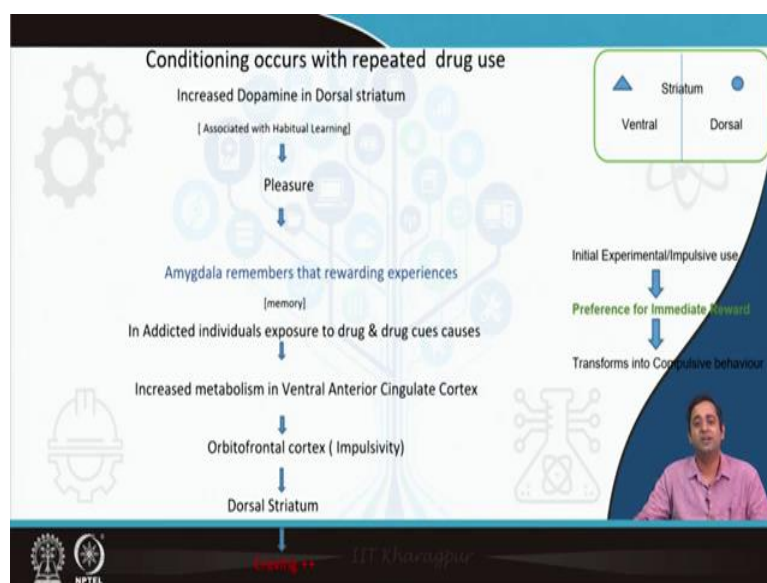
Now, this happens with the prefrontal cortex, especially the orbital frontal part of the prefrontal cortex which actually makes you control your kind of emotions, your impulses. And if that occurs you are feeling, your impulse to procure the drug it is stopped.

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Now, what makes that reward convert into a goal directed behaviour where the impulsive acts of yours gets converted transformed into a compulsive act? It is with the help of this ventral tegmental area, it gives rise to the impulses towards nucleus accumbens, ventral pallidum through gaba'ergic neurons further going towards prefrontal cortex via Thalamus and ultimately going back to ventral tegmental area.

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Now, conditioning occurs with repeated drug use, there is increased dopamine in the dorsal striatum and you have two parts of striatum, one is ventral striatum, one is dorsal striatum. Ventral striatum is basically the nucleus accumbens and the dorsal striatum is where the drugs actually act.

So, the natural rewarding activities like eating disorders like when you are addicted to pizza or ice cream or you are studying or into sports there your ventral part of the striatum is most commonly stimulated but in case of drugs there are so, that is why they makes, it makes them so special is that the drug use it stimulates the dorsal striatum which converts the impulsive acts into a compulsive drug taking procurement act.

So, in addicted individuals exposure to drug and drug cues causes increased metabolism in ventral anterior cingulate cortex, orbital frontal cortex which is given as to impulsivity ultimately eating the dorsal striatum and that is how craving is manifested.

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Later on there are phases where the person actually becomes, they actually lose control of this drug procuring behaviour. Now, at times there has been instances in the family where the son or the brother or the father they are under the substances from last, under the effect of these substances from last 10 years, 15 years and the family members they have been trying to ask to stop this drug but they helplessly tell their family members that I am trying my best to stop this but I am not under the control of myself because I am losing my control, I am not able to stop myself.

Now, this actually happens by dopamine reactive reward pathway and goal directed behaviour which is occurring due to dysfunction in the glutamatergic projections from prefrontal cortex to ventral tegmental area and nucleus accumbens.

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The slide is titled "Dependence" and is part of a presentation by IIT Kharagpur, NPTEL. It lists the ICD criteria for substance dependence, which require at least 3 out of 6 items to be satisfied in the last 12 months. The criteria are: 1. strong desire or compulsion to take the substance, 2. Difficulty in controlling the onset, termination or levels of use, 3. Experiencing withdrawal symptoms if substance not taken, 4. Use of substance to relieve from withdrawal symptoms, 5. Tolerance as evidenced by the need to escalate dose over time to achieve same effect, and 6. Salience – neglecting alternate forms of leisure or pleasure in life. A note at the bottom states: "* The narrowing personal repertoire of substance use." The slide features a blue background with a white atom-like graphic and a small inset video of a man in a pink shirt.

Dependence

According to ICD

Dependence requires at least 3 out of following list satisfied in last 12 months:

1. strong desire or compulsion to take the substance
2. Difficulty in controlling the onset, termination or levels of use.
3. Experiencing withdrawal symptoms if substance not taken
4. Use of substance to relieve from withdrawal symptoms
5. Tolerance as evidenced by the need to escalate dose over time to achieve same effect
6. Salience – neglecting alternate forms of leisure or pleasure in life

* The narrowing personal repertoire of substance use.

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Now, let us look at the diagnostic criteria as given by ICD for a drug dependent, substance dependence, there are six. First is strong desire the compulsive urge to take the substance, difficulty, second is difficulty in controlling the substance taking behaviour that is onset termination, experiencing withdrawal symptoms the physiological withdrawal when you are not under the effect of that substance.

Use of substance to relieve those withdrawal symptoms when you are not taking it you are having tremors, you are having irritability, agitation, you are having sleeplessness those kind of problems if they occur so to stop that and terminate that counteract that you actually go back and take those substance again.

Tolerance as evidenced by the need to escalate the dose, how, what, now what is tolerance? Tolerance is when initially you are taking some four pegs or six pegs of alcohol or some three cigarettes or four cigarettes to attain a normal high where you actually had a good feel of good well-being, now in from months from use of like six to ten months, one year, two years after that if you are using, if you are taking six cigarettes if your taking four pegs of alcohol you are not getting that much high which you used to be in those last years, so now you have to take more number of alcohol, more like more quantity of alcohol more quantity, more in number of cigarettes more frequency, the frequency also increases so that is how this is called

tolerance that your drug taking ability to taking the attainment of that high has been the threshold has become increased.

And salience is neglecting other forms of leisure or pleasurable forms of like when you have your birthday parties, your marriage anniversaries you tend to forget that but at the same time you go and invest your time in procurement of the substances. And the last is narrowing of personal repertoire when you are not actually aware of those problems in your life and you go on to search and procure those substances.

Now, how is that very relatable like very commonly you can see and like Independence Days or in October 2 Gandhi Jayanti where you have dry days for alcoholics they actually go on to procure the alcohol two days in advance of those declament of those dry days so that is how you there is narrowing of the repertoire, you forget you tend to forget your personal life, you tend to forget your official your social life your friends families but you are always under the your strict act of those under the influence of those substances which makes your life miserable.

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Important Terms related to Substance use Disorders

- Misuse- Applies to drugs prescribed by physicians that are not used properly.
- Abuse- Use of any drug , but usually by self administration, in a manner that deviates from approved social or medical patterns(for Non medical purposes).
- Addiction- A behavioural pattern of drug abuse charaterized by overwhelming involvement with the use of drug (Compulsive use), securing of its supplies and a high tendency to relapse after discontinuation.

Behavioural Dependence	Physiological Dependence	Psychological dependence
Consequences Of Behaviour	Withdrawal	Habituatation

Dr. Khuram

NPTEL

What are the important terms related to substance use disorder? These are misuse, abuse, addiction, behavioural dependence, psychological dependence and physiological dependence. Now misuse is when your drugs being prescribed by physicians that are not used properly and abuse is it is for non-medical purposes when you go on to self-made self administer your drugs in a deviated kind of socially approved manner.

Addiction is a behavioural pattern of drug abuse characterized by overwhelming involvement with the use of compulsive drug use, securing of its supplies and a high tendency to relapse after discontinuation so the moment you stop you tend to have physiological withdrawal all those kind of symptoms under when you were not having the effect of those substances.

Now, what is behavioural dependence? It is the consequences of your behaviour like you go and procure the substance like you go and smoke, you go and take alcohol, you go and smoke cannabis. So, the act which the consequences of your act which gives you a high, you feel good it gives you, you the act is being positively reinforced every time you go on and repeat those behaviours.

Now, what is physiological dependence? The withdrawal when you are not taking the substances, when you are not smoking, when you are not taking alcohol, when you are not taking those cannabis, when you are not taking cocaine so that feeling of flow that crash it actually provokes to go and to take and procure the substances.

Now, what is psychological dependence, it is the habituation that okay I have to go to escape from the problem suppose if I am having any issues at home if I am having any issues at office, at school, college, so in order to escape from the problem we actually develop this habit to go and get dependent on those substances, so that is how it is called psychological dependence.

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Opioids

- Obtained from Papaver Somniferum.
- Opiates are natural
- Opioids are synthetic, examples include meperidine, methadone, pentazocine propoxyphene, morphine, heroin
- M: F = 3:1
- Method of administration
Smoking, Snorting, orally, Intravenous, Intramuscular, Subcutaneous.

Effects of Opioids are due to opioid receptors, namely 3

1. Mu	2. Kappa	3. Delta
Analgesia, constipation, respiratory depression, sedation	Analgesia, diuresis, sedation	Analgesia

- 3 Classes of endogenous opioids within the brain: Endorphins, Dynorphins, Enkephalins

Rewarding properties of various drugs like Alcohol, cannabis and opioids are mediated through endogenous opioids.

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Let us start with opioids. Opioids is actually obtained from papaver somniferum, the plant. Opioids are natural as well as synthetic, synthetic examples include meperidine, methadone,

pentazocine, propoxyphene, the substance taking behaviour in case of genders you have male they are more commonly implicated, they go on to develop this kind of dependence more often.

Method of administration for opioids is they can be taken by smoke orally, they can be snorted intramuscular as well as subcutaneous use. Now, the effects of opioids is basically due to three receptors mu, kappa and delta. Mu receptors they have the effect on analgesia, constipation, respiratory depression, sedation. Kappa you have analgesia, sedation and diuresis and for Delta it is analgesia itself.

Now, there are three classes of endogenous opioids in the brain. Endorphins, dynorphins and enkaphalins where the properties of the drug is being manifested through these endogenous opioids. Rewarding properties of various drugs like alcohol, cannabis and opioids are mediated through this endogenous opioids.

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Clinical features

- Feeling of warmth, dry mouth itchy face (nose), facial flushing.
- Initial euphoria is followed by sedation.
- For 1st timers nausea, vomiting, dysphoria

Physical effects

- Respiratory depression, pupillary constriction, smooth muscle contraction, constipation, changes in BP and heart rate.

Intoxication

- Unresponsiveness
- Coma Hypothermia
- Hypotension
- Slow respiration
- Coma, Pinpoint pupils, respiratory depression triad---
-- Opioid over dose

Withdrawal

- Yawning
- Pupillary dilatation
- Lacrimation, rhinorrhoea
- Dysphoric mood
- Muscle aches Diarrhoea
- Insomnia Hypothermia

What are the clinical features? Feeling of warmth, dry mouth, itchy nose, flushed face there is initial euphoria you tend to get high followed by a sedation you get sleepy so initially you are very very much high and then you go to a stage of sedation. First timers for those who are taking the drug for the first time opioids they undergo nauseating kind of feeling, vomiting and a dysphoria and generalized feeling of uneasiness.

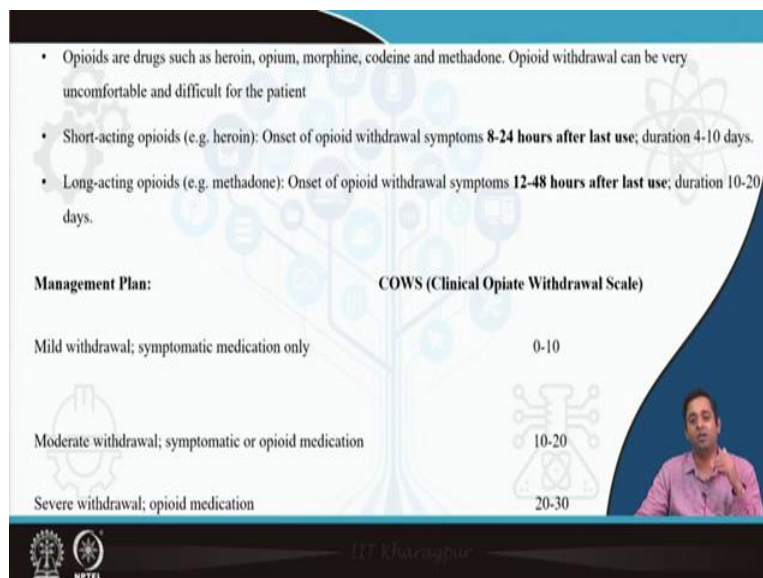
What are the physical effects in the human body? Those are respiratory depression, pupillary constriction, smooth muscle contraction, constipation and there is autonomic changes that is

changes in the BP and blood pressure. Now, what happens when opioid intoxication occurs and what happens when there is opioid withdrawal?

Now, opioid intoxication is associated with unresponsiveness, coma, hypothermia, slow respiration, there is hypotension your blood pressure falls, coma pinpoint pupils and respiratory depression those are basically the triad of opioid overdose we need to get, we should be very careful regarding this opioid overdose where we actually come across we encountered this in the emergency casualty areas where the patient can come up with opioid overdose with coma, comatose (18:37) pinpoint pupils and respiratory depression.

In terms of withdrawal the symptoms are actually reverse, these are yawning, pupillary dilatation, dysphoric mood, lacrimation so there is parasympathomimetic excess in this opioid withdrawal.

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The slide contains the following text:

- Opioids are drugs such as heroin, opium, morphine, codeine and methadone. Opioid withdrawal can be very uncomfortable and difficult for the patient
- Short-acting opioids (e.g. heroin): Onset of opioid withdrawal symptoms **8-24 hours after last use**; duration 4-10 days.
- Long-acting opioids (e.g. methadone): Onset of opioid withdrawal symptoms **12-48 hours after last use**; duration 10-20 days.

Management Plan:

Withdrawal Severity	Management	COWS Score
Mild withdrawal; symptomatic medication only		0-10
Moderate withdrawal; symptomatic or opioid medication		10-20
Severe withdrawal; opioid medication		20-30

COWS (Clinical Opiate Withdrawal Scale)

The slide also features a background graphic of a tree with icons and a small video inset of a speaker in the bottom right corner.

Opioids are drugs such as heroin, opium, morphine, codeine and methadone. Short acting opioids they have withdrawal symptoms from 8 to 24 hours, long acting they have from 12 to 48 hours. Now, how do we manage this? We actually have a scale called clinical opioid withdrawal scale with the help of this we assess what is the nature of the severity of the withdrawal which the patient is undergoing.

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Mild Cases

Patients should drink at least 2-3 litres of water per day during withdrawal to replace fluids lost through perspiration and diarrhoea. Also provide vitamin B and vitamin C supplements.

Symptomatic treatment for insomnia, abdominal cramps, diarrhoea, muscle cramps and supportive care are usually sufficient for management of mild opioid withdrawal.

Moderate Cases

As for management of mild withdrawal, but with the addition of clonidine or opioid medications such as buprenorphine, methadone.

For Severe cases

Clonidine	Buprenorphine
Alpha-2 adrenergic agonist. Relief to physical symptoms of opioid withdrawal including sweating, diarrhoea, vomiting, abdominal cramps, chills, anxiety, insomnia, and tremor. It can also cause drowsiness, dizziness and low blood pressure.	It alleviates withdrawal symptoms and reduces cravings . Its pharmacological action (partial opiate agonist). Buprenorphine should only be given after the patient begins to experience withdrawal symptoms (i.e. at least eight hours after last taking heroin).

Dr. Kharasch

So, for mild cases there is supportive therapy along with vitamins and replenish of the nutrients with fluids. For moderate cases mild the management given for mild and there is addition of clonidine and opioid medications such as buprenorphine or methadone. For severe cases we have we need to rely heavily on the medication as clonidine and buprenorphine.

Now, what is clonidine, clonidine is basically alpha to adrenergic agonists they give relief of physical symptoms of opioid withdrawal which includes sweating, diarrhoea, all those parasympathomimetic supply which increases due to withdrawal of the opioids which it actually basically counteracts those symptoms, like vomiting, abdominal cramps, chills, anxiety, insomnia, tremors.

What does buprenorphine do? Buprenorphine actually elevates the withdrawal symptoms and it reduces the craving of the person. The pharmacological action it is a partial opiate agonist and should be given only after the patient begins to experience withdrawal symptoms that is at 8 hours after the last take, when you have last taken the opioid after the 8 hours.

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CNS depressants- Alcohol , Barbiturates, Benzodiazepines , Inhalants

CNS Stimulants- Cocaine, Amphetamines,

Now, there are broadly classified as CNS depressants and CNS stimulant. Now CNS stimulants are cocaine, amphetamines, nicotine. CNS depressants are alcohol, benzodiazepines, barbiturates and inhalant substances, we will be dealing in detail.

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Alcohol withdrawal

Simple withdrawal

Tremulousness develops	6-8 hrs
Psychotic and perceptual disturbances	8-12 hrs
Seizures	12-24 hr
Delirium Tremens	any time within 1 st week

Black outs:


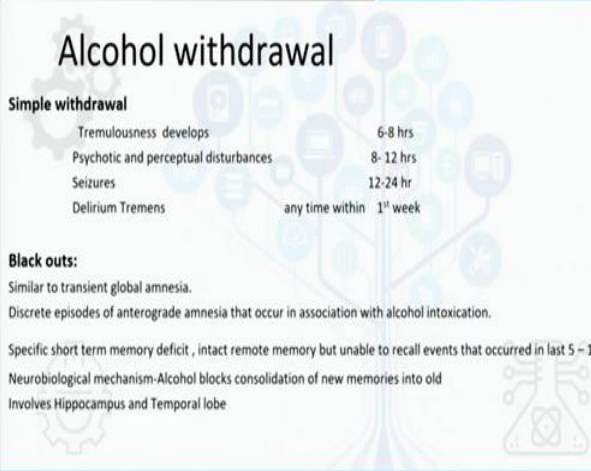

Similar to transient global amnesia.

Discrete episodes of anterograde amnesia that occur in association with alcohol intoxication.

Specific short term memory deficit , intact remote memory but unable to recall events that occurred in last 5 – 10 mins.

Neurobiological mechanism Alcohol blocks consolidation of new memories into old

Involves Hippocampus and Temporal lobe



IIT Kharagpur

Let us come to alcohol, how do alcohol withdrawal patients they present with? Now, initial part of the alcohol withdrawal starts with tremulousness with 6 to 8 hours of last alcohol intake it is a sequential process where the next 8 to 12 hours is with psychotic and perceptual disturbances where you have all sorts of delusion or hallucination commonly visual hallucinations, auditory hallucinations, tactile hallucinations.

You can have seizures in 12 to 24 hours and further delirium prevalence it is a acute emergency kind of condition and it can happen within first week of last alcohol intake. What is blackouts? Now, it is similar to a transient global amnesia discrete episodes of anti-grade amnesia that occur in association with alcohol intoxication.

So, whenever there is acute amount of alcohol which is taken in a dose which is very lesser as compared to a normal alcoholic this gives a short term memory deficit with intact remote memory but unable to recall those events which was happening in that very specific moment when the patient undergo blackout.

Now what are the neurobiological mechanisms associated with that? Alcohol actually blocks the consolidation of new memories into old and the structures which is commonly implicated is hippocampus and temporal lobe.

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Delirium tremens

- Delirium is characterized by a rapid onset and fluctuating course with disturbances in the level of consciousness, cognition, psychomotor activity, and sleep-wake cycle.
- **Thomas Sutton 1813 coined the term "Delirium Tremens"**
- Inattention, disorientation, motor agitation, alteration of sleep wake cycle and disturbance in short term memory as common presentations of DT. Severe form of alcohol withdrawal
- DT is a short lasting condition with a usual duration of 3–4 days (but might last for even 8 days) and it classically ends with a prolonged sleep.

Characteristic Features

Prevalence of < 1 % in general population
nearly 2 % in Alcohol Dependence.

Coarse tremors of hands
Insomnia Nausea Vomiting Psychomotor agitation Anxiety Transient Visual
Tactile or Auditory Hallucinations , along with increase in sweating, body temperature, heart rate, respiratory rate and blood pressure

Treatment Benzodiazepines Antipsychotics Thiamine & Vitamins

NPTEL

Let us come to delirium tremens. It is characterized by rapid onset and fluctuating course with disturbances in the level of consciousness, cognition, psychomotor activity and sleep cycling. It was coined by Thomas Sutton. What are the characteristic features which actually happens in delirium tremens?

Now, there is inattention, disorientation, hallucinatory experiences, agitation, altered sleep wake cycle and short-term memory disturbances, it is a severe form of alcohol withdrawal, it is short lasting condition which usually has a duration of three to four days and it classically ends with a prolonged sleep.

What are the characteristic features? Coarse tremors of the hand, insomnia, nausea, vomiting, psychomotor agitation, anxiety, initial transient anxiety, tactile or auditory hallucinations with there is increase which is associated with sweating, autonomic symptoms where you have decrease in blood pressure and increase in heart rate that is tachycardia and respiratory rate is also increased.

How can we treat this? With the help of benzodiazepines and thiamine in order to counteract the side effect of alcohol that is giving rise to thymine deficiency. Antipsychotics are given in order to counteract the hallucinatory experiences along with vitamins.

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Wernicke's encephalopathy **Short term complications of alcohol**

Triad – Gait Ataxia, horizontal Nystagmus and Lateral Gaze Palsy.
It includes Sluggish eye reaction to light, Anisocoria
May progress into Korsakoff's Syndrome or spontaneously clear in a few days.
Treatment
100 mg Thiamine 2-3 times daily for 1-2 weeks. Thiamine should be given before any i.v. glucose. As glucose infusion exacerbates thiamine deficiency biochemically.
Ophthalmoplegia responds within hours of treatment

Korsakoff Syndrome
Impaired mental syndrome (recent memory) + anterograde amnesia
With or Without confabulation.
Treatment
100 mg 2- 3 times daily for 2-3 months

Rum Fits
Stereotyped
Generalised
Toni-clonic
Associated with alcohol withdrawal
Rx Benzodiazepines

NPTEL

Now, what are the short term complications of alcohol? These are Wernicke's encephalopathy, long term is Korsakoff syndrome and Marchiafava-Bignami syndrome. Let us look at the Wernicke's encephalopathy. Now, what is the triad? It has a diagnostic triad of Gait Ataxia, horizontal Nystagmus and Lateral Gaze Palsy. A patient is not able to work properly, there is nystagmus and there is lateral gaze Palsy where the lateral rectus muscles they are not able to coordinate the action of the eyeballs.

It progresses into a Korsakoff syndrome in a few days when it is not being intervened properly the dose which is given is 100 milligrams of thiamine, two to three times daily and it should be given before IV glucose as glucose infusion exacerbates thymine deficiency biochemically. What is the effect, ophthalmoplegia actually responds within the hours of treatment of thymine.

So, next is Korsakoff syndrome. Korsakoff syndrome is there is also a condition where associated with Korsakoff syndrome it is the impaired mental syndrome where the recent memory deficits is associated with anterograde amnesia and this can be, this can occur with and without the confabulation, confabulation is when the person actually creates a kind of story in order to give responses to a, to the question which is being asked.

Treatment is again thymine with 100 milligrams two to three times daily for two to three months. The duration for Wernickes is less but the duration of thymine given in Korsakoff is more. What is Rum fit? Rum fit is a stereotype, generalized, tonic clonic seizures associated with alcohol withdrawal, it is treated generally with the benzodiazepines.

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The slide is titled "Long term complications" and features a background with various icons like gears, a tree, and a brain. The text on the slide is as follows:

Marchiafava Bignaminis.

- a) Generalised pyramidal tract lesion
- b) focal cerebellar tract lesions.

Carducci first described it in 1898 in Italian red wine drinkers.

Demyelination of Corpus Callosum and adjacent sub cortical white matter.

Dementia, dysarthria, spasticity, gait changes

At the bottom of the slide, there is a logo for NPTEL and the text "IIT Kharagpur". A small video inset in the bottom right corner shows a man in a pink shirt.

The long term complication of alcohol withdrawal is Marchiafava Bignaminis syndrome it is basically due to demyelination of corpus callosum and adjacent subcortical white matter areas. What are the malfunctioning which the patient presents with? There is generalized pyramidal tract lesion and focal cerebellar track lesion present.

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Treatment

- Intervention
- Detoxification & Deaddiction
- Rehabilitation

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Now, how can you treat this, basically done by intervention, detoxification, deaddiction and rehabilitation.

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Intervention

Confrontation by breakthrough feelings of denial and help the patient recognize adverse consequences.

Process aimed at maximizing the motivation for treatment and continued abstinence

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Now, how can we intervene? Confrontation by breakthrough feelings of denial and help the patient recognize adverse consequences, these processes are aimed at maximizing the motivation for treatment and continued abstinence.

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Detoxification

- If the patient is in good health and have adequate nourishment with good social support the withdrawal is managed mildly and with ease.
- Lasts 1 week to 10 days
- Include thorough physical examination
- Vitamins (thiamine), proper rest and sleep

The slide features a background with faint icons of a gear, a tree, and a molecular structure. A small video of a male presenter in a pink shirt is in the bottom right corner. The NPTEL logo and 'IIT Kharagpur' are at the bottom.

Detoxification if the patient is in good health and have adequate nourishment with good social support with withdrawal is managed mildly and with ease, it lasts for one to ten days and it includes thorough physical examination. Vitamins, thiamine, proper rest and sleep is given for detoxification.

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Naltrexone

Blocks opioid receptor **resulting in reduced craving and reduced reward.**

Nausea, vomiting, abdominal pain, constipation, dizziness, headache, anxiety

Serious hepatotoxicity

Contraindicated in acute withdrawal of Opioid

Acamprosate

Acamprosate is a derivative of the amino acid taurine, and reduces excitatory glutamate neurotransmission and enhances inhibitory GABA neurotransmission.

It blocks mGlu receptors and also NMDA receptors.

When alcohol is used chronically and then withdrawn, the adaptive changes causes glutamate hyperactivity—even excitotoxicity—and GABA deficiency.

By blocking glutamate receptors, acamprosate may mitigate glutamate hyperexcitability during alcohol withdrawal and is therefore sometimes called “artificial alcohol.”

Used for patients who have attained abstinence

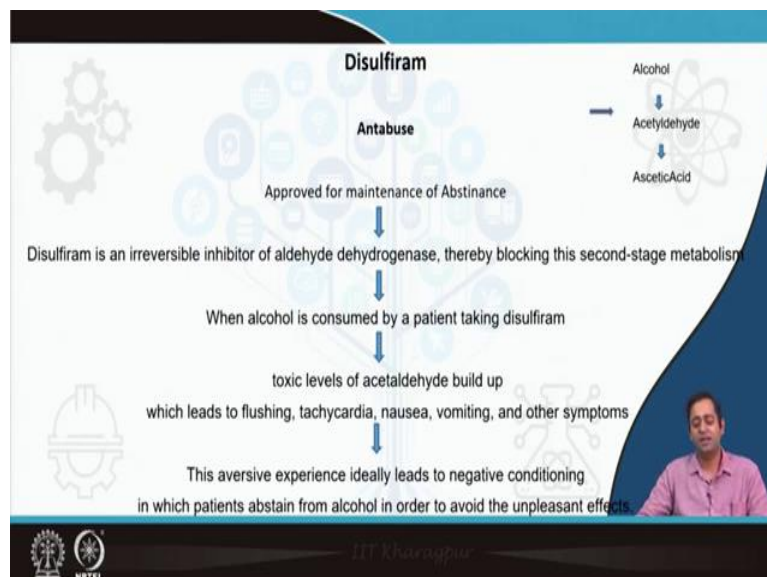
The slide features a background with faint icons of a gear, a tree, and a molecular structure. A small video of a male presenter in a pink shirt is in the bottom right corner. The NPTEL logo and 'IIT Kharagpur' are at the bottom.

How is deaddiction done? Deaddiction is done basically with the help of drugs these are naltrexone, acamprosate, naltrexone actually blocks the opioid receptors resulting in reduced craving of the substance procurement and decreased rewarding properties. The side effects being nausea, vomiting, abdominal pain, constipation, dizziness, headache, anxiety,

sometimes serious hepatotoxicity when the drug has been taken for a period of more than six months or one year.

Acamprosate is a derivative of amino acid taurine and it reduces excitatory glutamate neurotransmission and enhances inhibitory GABA neurotransmission, it blocks metabotropic glutamic receptors and also NMDA receptors. So, when alcohol is used chronically and then withdrawn what happens there are adaptive changes which occurs causing glutamate hyperactivity and GABA deficiency by blocking glutamate receptors acamprosate actually maintains the glutamate levels and increases the GABA level so that is why it is acting as artificial alcohol.

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How does the disulfiram act it basically inhibits the enzyme acetyl dehydrogenase which creates and accumulates the acetyldehyde levels, it increases acetyldehyde levels and thereby causing vomiting, flushing of the face, diarrhoea, autonomic symptoms. So, this toxic levels of acetyldehyde they build up leading to tachycardia, flushing and all those kind of symptoms, this is actually aversive kind of drug which is given to the patient who has a good motivation to quit drinking.

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Mild-Moderate Withdrawal

It occurs due to habituated depressant in the brain and its sudden stoppage or abrupt reduction of dosage.

Any Depressants Benzodiazepines, Barbiturates given in an tapering dosage (preferably Lorazepam if liver is compromised, or Chlordiazepoxide).

Dosage of the depressant to be tapered by 20 % reduction.

For Short acting drugs like lorazepam careful dose titration required as compared to long acting (diazepam/chlordiazepoxide).

Severe Withdrawal

Medical Problems needs to be ruled out

Adequate dosage for Benzodiazepines

Antipsychotics for Hallucinatory experiences (preferably Haloperidol)

Neurological Evaluation if patient does not respond with seizures.

Rehabilitation

Maintain high level of motivation for abstinence

Lifestyle modification , Relapse Prevention strategies , Cognitive behavioural therapy

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It is basically divided, the treatment is basically divided into moderate, mild and severe withdrawal phases. Now in mild to moderate phases the depressants like benzodiazepines, barbiturates is given in a tapering dosage, dosage of the depressant has to be tapered by 20 percent, for short acting drugs like Lorazepam careful dose titration is required, in case of severe withdrawal medical problems need to be ruled out, adequate dosage for benzodiazepines is given and antipsychotics is preferentially given for hallucinatory experiences like auditory or tactile visual and neurological evaluation is done if there is a focal and logical problems encountered along with seizures.

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Benzodiazepines

Short-acting benzodiazepines include oxazepam, alprazolam and temazepam.

Withdrawal typically **begins 1-2 days** after the last dose, and continues for 2-4 weeks or longer.

Long-acting benzodiazepines include diazepam and nitrazepam.

Withdrawal typically **begins 2-7 days** after the last dose, and continues for 2-8 weeks or longer

Symptoms include

- Anxiety
- Insomnia
- Restlessness
- Agitation and irritability
- Poor concentration and memory
- Muscle tension and aches.

The longer the interval between reductions, the more comfortable and safer the withdrawal.

Generally, there should be at least one week between dose reductions.

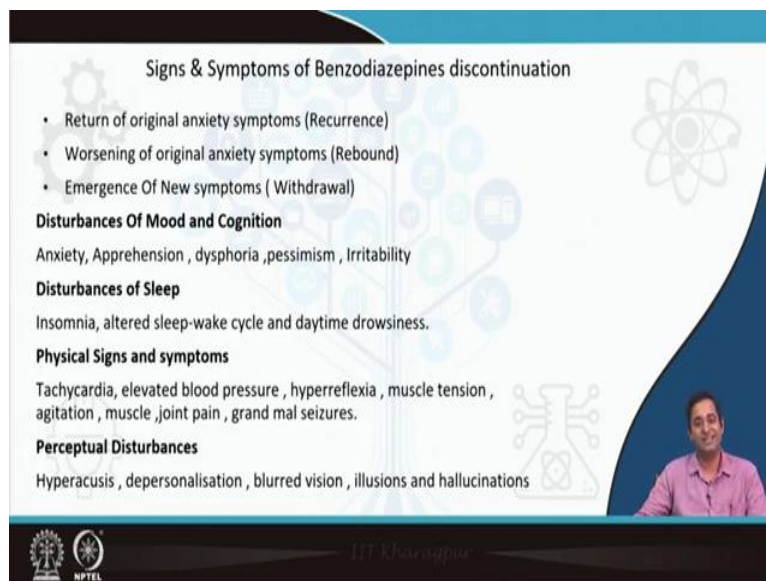
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Dr. Khanna

Let us come to benzodiazepines. Benzodiazepines are basically short acting or long acting, short acting ones are oxazepam, temazepam, alprazolam. The withdrawal typically begins between one to two days and for long acting like clonazepam, diazepam, nitrazepam their withdrawal begins with two to seven days.

Now, what is the trend for tapering this dosage for benzodiazepines? The longer the interval between reductions the more comfortable and safer the withdrawal is and generally there should be at least one week between the dosage of reductions when you are tapering the dose for benzodiazepines dependence patients.

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Signs & Symptoms of Benzodiazepines discontinuation

- Return of original anxiety symptoms (Recurrence)
- Worsening of original anxiety symptoms (Rebound)
- Emergence Of New symptoms (Withdrawal)

Disturbances Of Mood and Cognition
Anxiety, Apprehension , dysphoria ,pessimism , Irritability

Disturbances of Sleep
Insomnia, altered sleep-wake cycle and daytime drowsiness.

Physical Signs and symptoms
Tachycardia, elevated blood pressure , hyperreflexia , muscle tension , agitation , muscle ,joint pain , grand mal seizures.

Perceptual Disturbances
Hyperacusis , depersonalisation , blurred vision , illusions and hallucinations

The slide features a blue and white color scheme with a background of faint molecular and network diagrams. A small inset video of a male presenter is visible in the bottom right corner. Logos for IIT Kharagpur and NPTEL are at the bottom.

What are the signs and symptoms of benzodiazepines discontinuation? It basically affects four common domains these are mood, sleep wake cycle, physical signs and symptoms and perceptual disturbances.

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Signs of Benzodiazepines Intoxication

- Incoordination
- Dysarthria
- Nystagmus
- Impaired memory
- Gait disturbances.
- In severe cases stupor coma and death occurs

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The signs commonly encountered for benzodiazepines intoxication these are nystagmus, tremors, dysarthria, gait disturbances patient is not able to work properly, there is impaired memory not able to remember recent as well as remote and in severe cases there can be stupor coma resulting sometimes into death also.

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Guidelines for Benzodiazepines Withdrawal

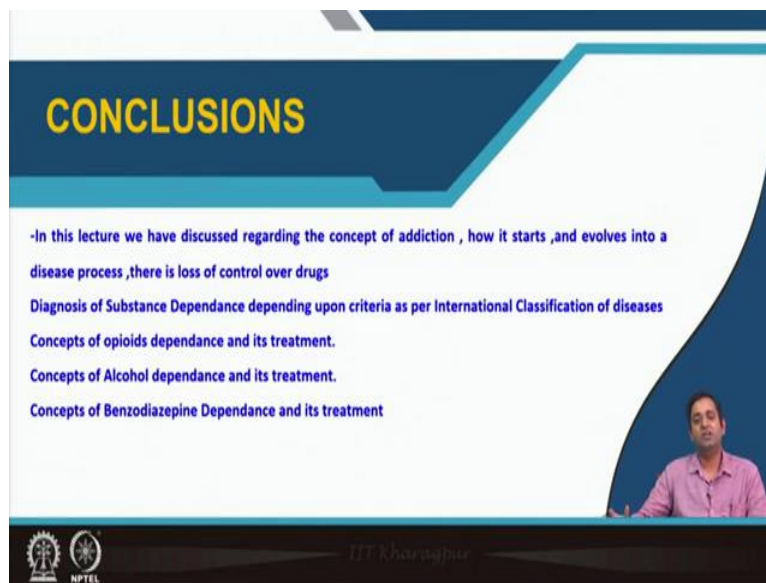
- Evaluate and treat medical and psychiatric condition
- Obtain drug history and urine and blood samples.
- To determine the dose required for stabilisation from history obtained, clinical presentation.
[Most symptoms occur on first 3 days of abstinence and seizure on 2nd or 3rd day]
- Hospitalise if there is poor social support, polysubstance dependence and /or medical problems.
- Long acting benzodiazepines preferred.
- After stabilizing reduce dosage by 30 % on second and third day
- Tapering of the dose should be done depending upon the symptoms present by counteracting them
- Psychological intervention assist patients in managing related anxiety.

The slide features a background with a stylized tree of icons and a blue wave on the right. A presenter is visible in the bottom right corner. The NPTEL logo and 'IIT Kharagpur' are at the bottom.

What are the guidelines of the benzodiazepines withdrawal? To evaluate the condition first, obtain a prior drug history, blood urine samples. To determine the dose required for stabilization history has to be obtained from how long the patient was taking, what those the person was taking and for what was the frequency, what were the number of tapers the dose which the patient was taking.

Hospitalized, is the patient is not having any family members that is when the social when the social factors is actually more prevalent in this patients then we need to hospitalize. After stabilizing the reduction of the dosage is by 30 percent on second and third day. The tapering of the dosage should be done depending upon the symptoms because some sometimes it is seen that when we are decreasing the dose for benzodiazepines dependence patients there is resurgence of the symptoms, so there we need to increase the dose again and thereby tapering it very slowly. Now, psychological intervention is sometime given for patients who are undergoing irritation, agitation, headache or sometimes they are perceiving anxiety as well.

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CONCLUSIONS

- In this lecture we have discussed regarding the concept of addiction , how it starts ,and evolves into a disease process ,there is loss of control over drugs
- Diagnosis of Substance Dependence depending upon criteria as per International Classification of diseases
- Concepts of opioids dependence and its treatment.
- Concepts of Alcohol dependence and its treatment.
- Concepts of Benzodiazepine Dependence and its treatment

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Now, what have we learned in this lecture? We have discussed regarding the concept of addiction, how it starts, evolves into a disease process, a brain disease and thereby losing control over the drugs, the diagnostic criteria for substance dependence and benzodiazepines dependence, opioids dependence along with its management and treatment. Thank you.