Manage TB
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Lecture – 49
Management of Adverse effects to anti-TB drugs Session 01

A very good morning to all of you; I am Dr. Vinod Kumar Professor of Thoracic Medicine and Deputy Superintendent of Government Hospital of Thoracic Medicine Tambaram Sanatorium. So, I will be I welcome you to the session on the Management of Adverse effects of anti tuberculosis drugs.

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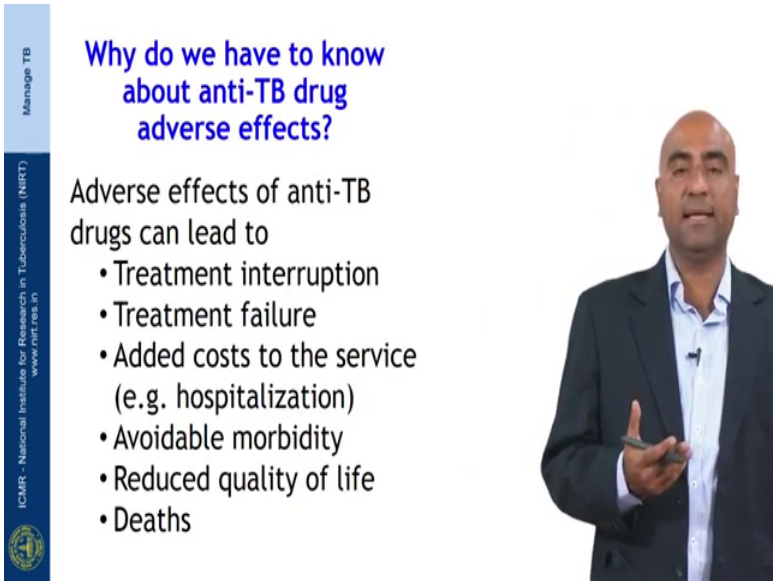

So, why should we know about anti-tuberculosis drugs adverse effects? As you all know we all come across patients who interrupt treatment for tuberculosis. It is not all patients who complete treatment for tuberculosis and many people who interrupt the treatment. The common one of the common reasons why they interrupt treatment is because of the adverse effect to TB drugs. So, what are the consequences of these adverse effects to TB drugs?

The adverse effects can lead to treatment interruption, treatment failure, added cost to the services that is more burden to the hospital in treating the tuberculosis, avoidable morbidity, reduce the quality of life, and even deaths. So, these are the reasons why we

should have t through working knowledge about all the adverse effects of each and every TB drugs. And how we can manage these adverse effects?

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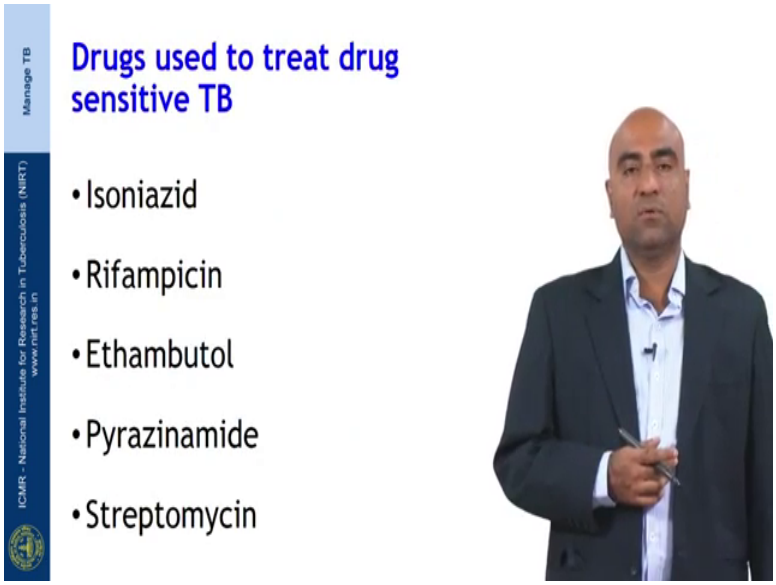

So, what are the drugs which are used to treat sensitive tuberculosis? So, all of us must be familiar with this right from our undergraduate days. These are the 5 drugs which we commonly use to treat drug sensitive tuberculosis. The 5 drugs are INH, or isoniazid, rifampicin, ethambutol, pyrazinamide, and streptomycin.

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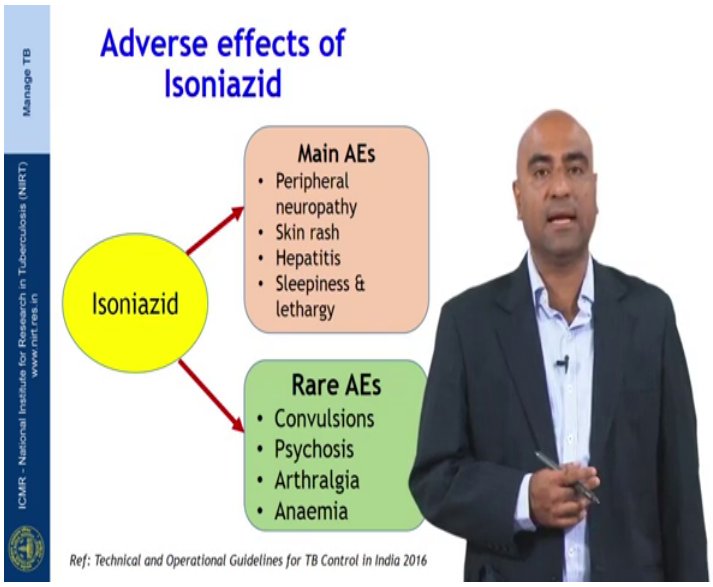

Let us see the adverse effects of each of these drugs one by one. The first let us take up isoniazid. So, what are the adverse effects of isoniazid? INH the main adverse effect is peripheral neuropathy this is something which we commonly see in clinical practice.

So, the other side effects are skin rashes, hepatitis, sleepiness, and lethargy. So, we will come to the management of these main adverse effects later. Some rare adverse effects which are associated with INH are convulsions, psychosis, arthralgia, and anemia.

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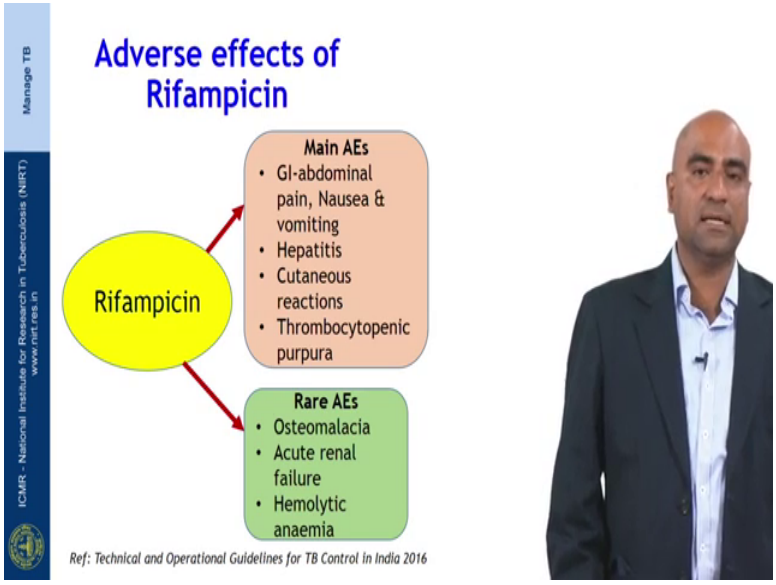

The next very important drug in TB regimen is rifampicin. So, the common side effects of rifampicin are mainly gastrointestinal, see the main problem with rifampicin is tolerance many of these patients developed acidity. And main thing is they develop abdominal pain, nausea, and vomiting. Other side effects which are associated with rifampicin include hepatitis, cutaneous reactions, and thrombocytopenic purpura.

The rare adverse effects which have been associated with rifampicin are osteomalacia acute renal failure and hemolytic anemia. So, we should all have a knowledge that rifampicin can cause these side effects even though it is not very common and we do not see such things in common practice. But it is necessary that we have a knowledge of all these adverse effects.

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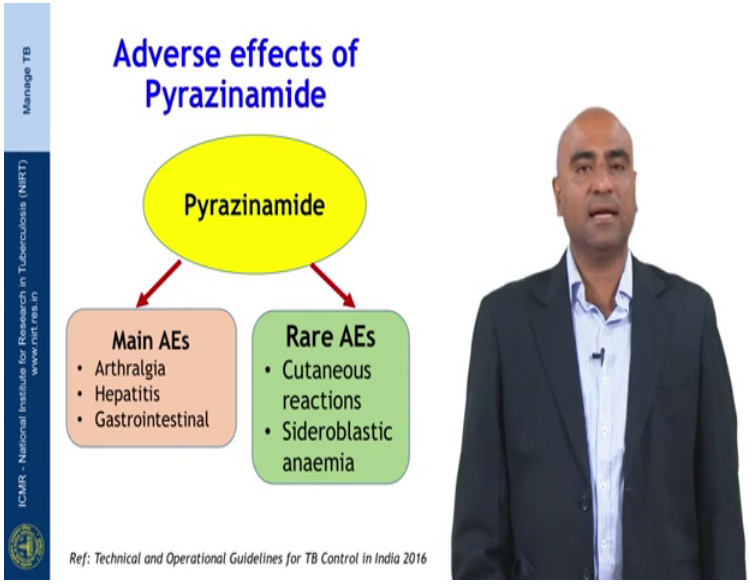

Coming to the adverse effects of pyrazinamide the main adverse effect with the pyrazinamide is arthralgia. Usually arthralgia and pyrazinamide is transient which last for around 2 to 3 weeks and then it disappears on its own. But other side effects with pyrazinamide include hepatitis and GI intolerance rare adverse effects of pyrazinamide are cutaneous reactions and sideroblastic anemia.

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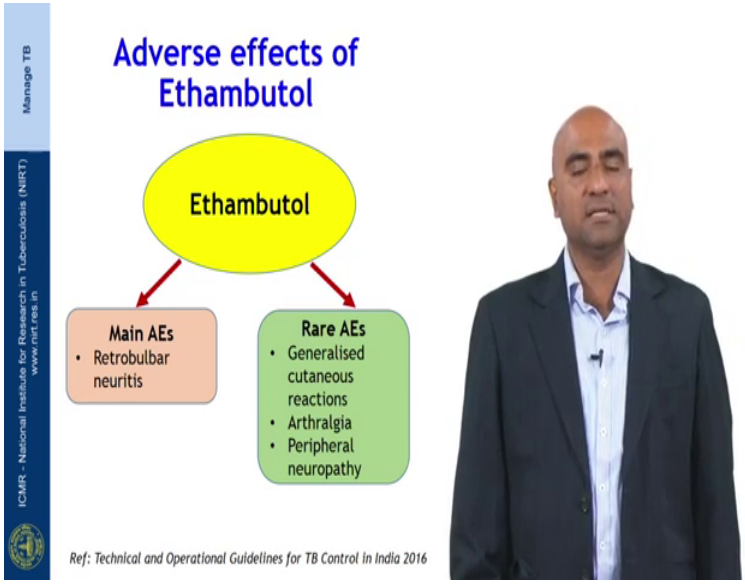

Coming to the adverse effects of ethambutol; so the main adverse effect with ethambutol is retrobulbar neuritis that is why it is always imperative that we monitor the vision of

the patient when the patient is on tuberculosis treatment. And rare adverse effects include generalized cutaneous eruptions, arthralgia, and peripheral neuropathy.

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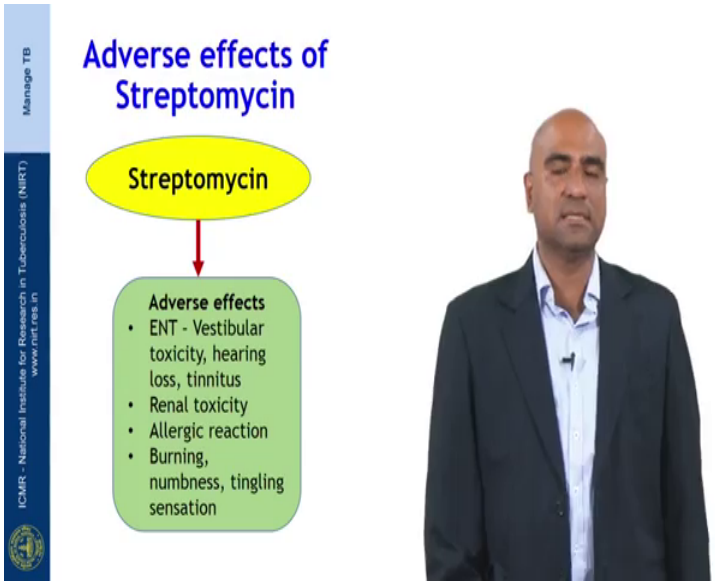

The adverse effects of streptomycin include they are mainly ENT, that is they are mainly vestibular toxicity in the form of either giddiness, or dizziness, or hearing loss, or tinnitus. These are the common side effects of streptomycin, the others are renal toxicity allergic reactions, and sometimes people can have some burning numbness or tingling sensations in the body.

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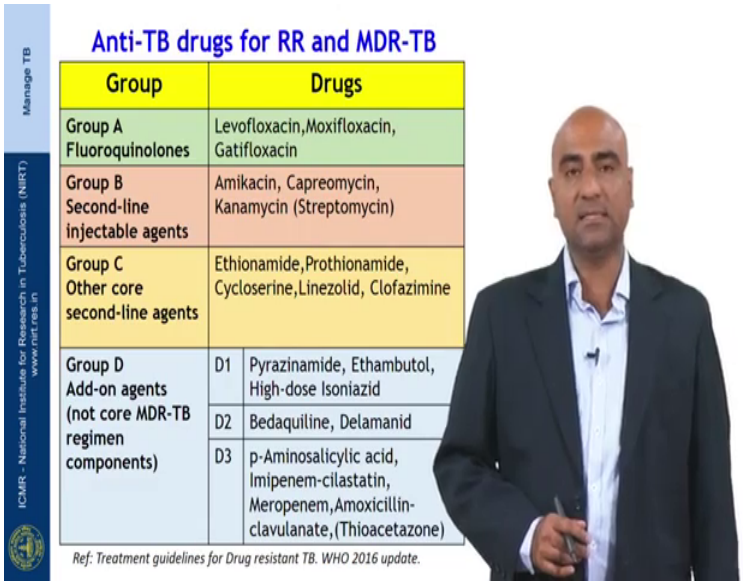

Let us now see the various group of drugs which are used for the treatment of rifampicin resistance, and multidrug resistant tuberculosis. The recent WHO classification in 2016 has the following group of drugs in group A are included the fluoroquinolones. The fluoroquinolones which are used for the dresses for the treatment of rifampicin resistance and MDR TB include levofloxacin, moxifloxacin, and gatifloxacin.

So, these three are the drugs which are used in group used as group A for treatment of rifampicin resistance and MDR TB. In group B, you have the injectable drugs the injectable agents include amikacin, capreomycin, and kanamycin, SM that is streptomycin is used if it is sensitive.

In group C, you have other core second line agents which include ethionamide, prothionamide, cycloserine, linezolid, and clofazimine. In group D, you have agents which are used as add on agents they are not that is they are not core MDR TB drug regimen components, but we have three subclasses in that the first D 1 includes pyrazinamide, ethambutol, and high dose of INH.

In D 2 you have bedaquiline, and delamanid and D 3 you have para aminosalicylic acid, imipenem, cilastain that is imipenem cilastatin combination, meropenem, and amoxicillin clavulanic acid with thiacetazone. So, when you formulate a regimen for MDR TB you usually choose from different groups.

So, I think some other speaker will be other speakers will be teaching you on how to take up drugs from these regimen, but I will confine my task to discussing about the adverse effects of these drugs

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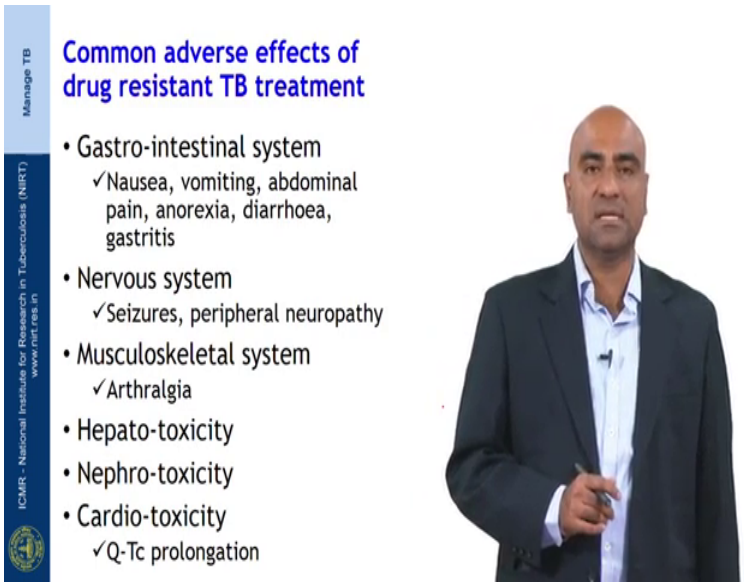

Coming to the common adverse effects of drug resistant TB treatment, the main adverse effect which we encounter is gastrointestinal intolerance. So, usually people have some minus in terms like nausea, mild abdominal pain, and other symptoms which can happen include vomiting, anorexia, diarrhea, and gastritis. So, these are some of the commonest adverse effects which we encounter.

In nervous system people can have seizures and peripheral neuropathy. We will come to the management of these later. Musculoskeletal system generally there can be a transient arthralgia, hepato-toxicity, nephrotoxicity, cardiotoxicity in the form of Q-Tc prolongation. So, these are the common adverse effects which we generally encounter while treating a patient with drug resistant tuberculosis.

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The other side effects include psychiatric manifestations like depression, psychosis, and suicidal ideation. In ENT, you can have manifestations like dizziness, vertigo, hearing disturbances, and tinnitus.

Visual disturbances and cutaneous reactions can also happen the cutaneous reactions can be in the form of either minor allergic reactions like itching or it can be like rashes, hypothyroidism, electrolyte disturbances. So, these are the adverse effects of which are the these are the common adverse effects of drug resistant TB treatment.

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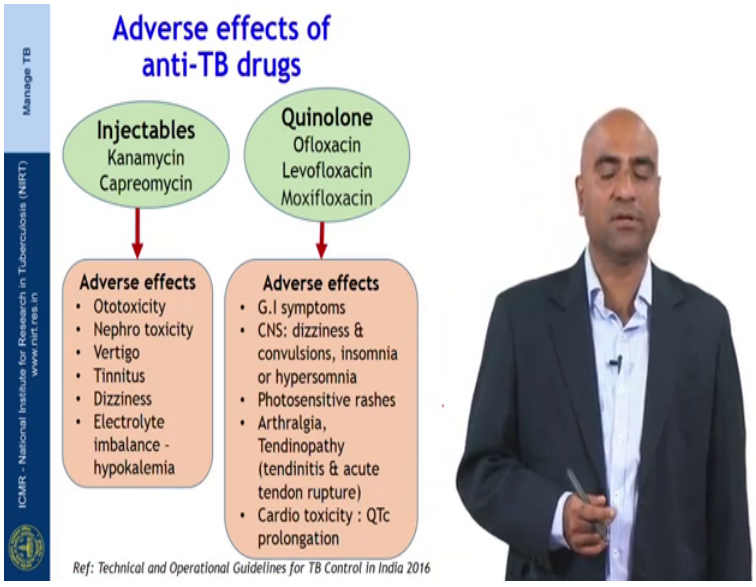

So, let us see the side effects of each of these drugs. So, coming to the injectables the commonly used injectibles include kanamycin, and capreomycin. The main adverse effects of these include ototoxicity, nephrotoxicity, vertigo, tinnitus, dizziness, electrolyte imbalance, and hypokalemia.

The next group of drugs are the quinolones the quinolones which are commonly used are ofloxacin, levofloxacin. So, the adverse effects of these are mainly gastrointestinal in the form of just like nausea, vomiting, or minor intolerance.

Then there can be some CNS manifestations like dizziness, convulsions, or insomnia, or even sometimes hypersomnia, then photosensitive rashes can happen, then arthralgia tendinopathy and cardiotoxicity in the form of Q-Tc prolongation. These are the main adverse effects which you encounter while treating a patient with quinolone.

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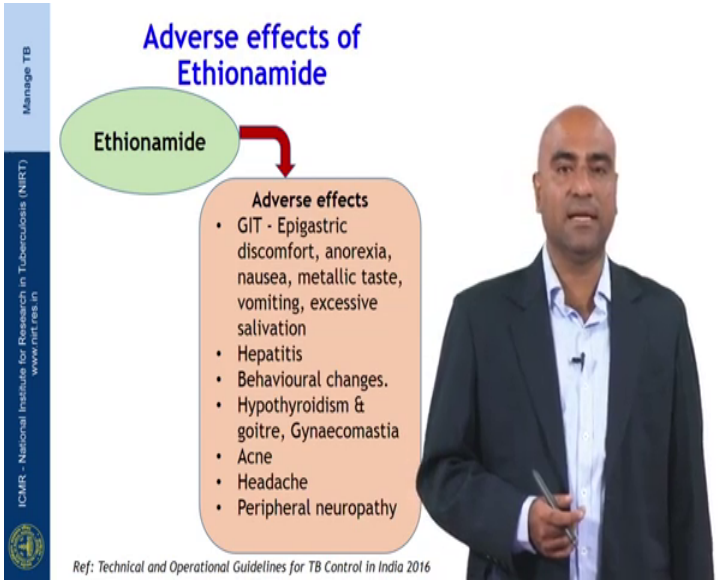

Coming to the next main drug which is used in the regimen ethionamide, the main adverse effects of ethionamide like all the TB drugs, there it is mainly gastrointestinal. People can have some epigastric discomfort some anorexia, some vomiting, metallic taste, and excessive salivation these are some of the known GI side effects of ethionamide.

The other thing which we should be careful about is hepatitis. So, left monitoring is required then behavioral changes can happen, then people can have hypothyroidism,

goiter, and gynecomesia which are endocrinological manifestations of ethionamide. Then some of them can develop acne, and CNS manifestations like headache and peripheral neuropathy are also known to happen with ethionamide.

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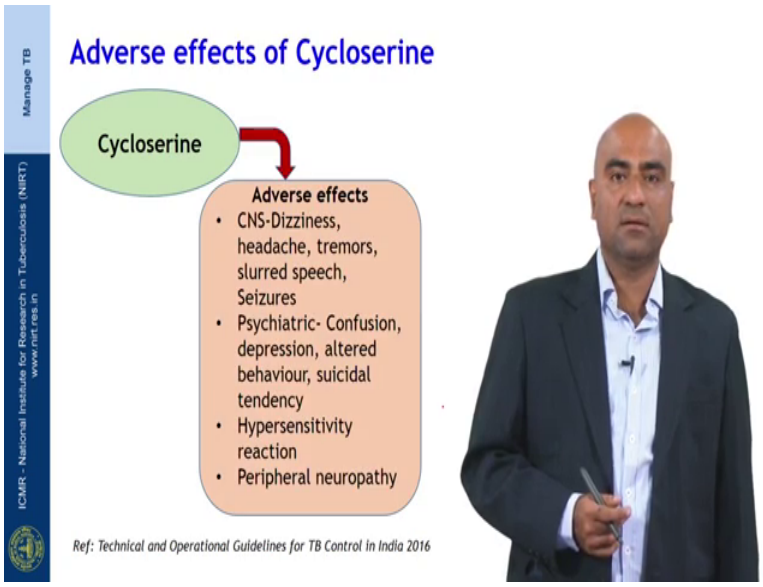

Coming to cycloserine cycloserine the main adverse effect is CNS manifestations like dizziness, headache, tremors, slurred speech, and seizures. Then psychiatric manifestations in the form of confusion, depression, altered behavior, and suicidal tendency can happen.

Hypersensitivity reactions are also known to happen with cycloserine. And peripheral neuropathy especially when it is combined with other drugs peripheral neuropathy can happen.

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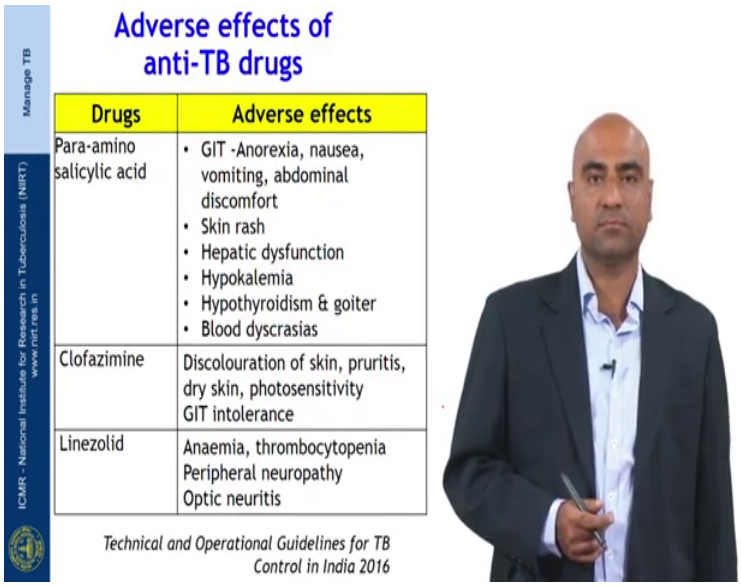

Coming to other drugs in the regimen let us take a para aminosalicylic acid. So, para aminosalicylic acid the main adverse effects are again gastrointestinal; So, the main adverse effect being like anorexia, nausea, vomiting, and abdominal discomfort. Skin rashes, hepatic dysfunction, hypokalemia, hypothyroidism, and goiter, and blood dyscrasias these are also associated with pas use.

The next drug is clofazimine it has a unique adverse effect in the form of discoloration of the skin, and pruritus dry skin and photosensitivity. So, these are very peculiar manifestations of clofazimine. The next drug is linezolid, the linezolid is mainly associated with side effects are anemia, thrombocytopenia, peripheral neuropathy, and optic neuritis.

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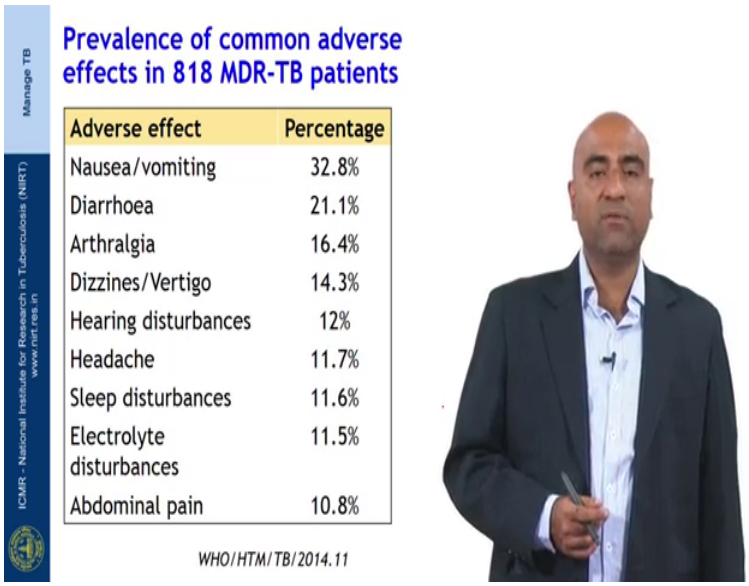

So, how prevalent are the adverse effects with MDR TB drugs? So, based on pre various studies the WHO has found that the side effects which are common with MDR-TB drugs are as follows. The main side effect is again GI intolerance that is nausea and vomiting, which happens in roughly about 32.8 percentage of the patients that is one-third of the patients can have nausea and vomiting.

The other side effect is diarrhea which happens in about 21.1 percent, arthralgia which is usually transient in about 16 to 16.4 percentage, dizziness and vertigo in about 14.3 percentage of patients. Hearing disturbances in 12 percent, headache in 11.7 percent, sleep disturbances in 11.6, electrolyte disturbance in 11.5, and abdominal pain in 10.8 percent. So, these are the prevalence of the adverse effects with MDR TB drugs.

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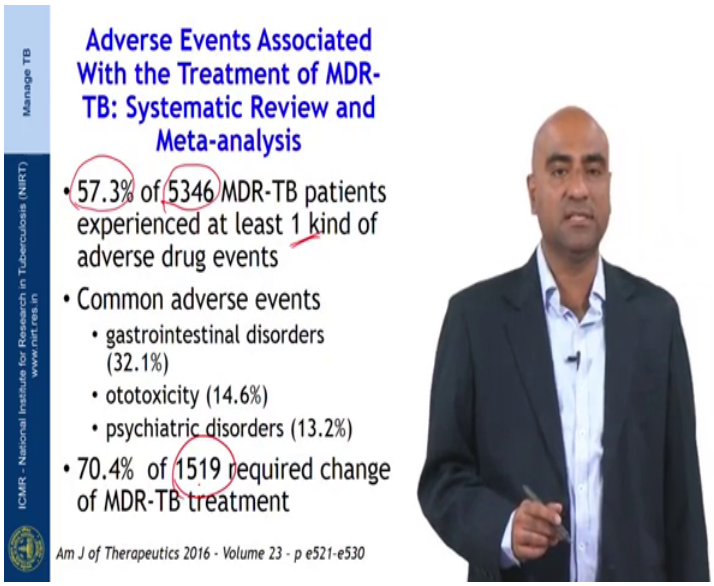

So, there has been studies on the adverse effect of MDR TB regimens, and there are also systematic analysis and meta analysis which was published in 2016 which has reported that out of 5346 MDR India people TB patients treated would about a half that is about 57.3 patients 3 percentage of the patients have at least one adverse side effect.

So, it may be in the form of nausea vomiting. So, almost half of these patients develop some minor adverse reactions and the common adverse reactions which are noted and as already we discussed it is mainly about GI, that is gastrointestinal disorders in about 32 percentage that is one-third of the patients.

And ototoxicity can happen in 14.6 percentage, and psychiatric manifestations in 13.2 percentages of the patients, so these are major effects the side effects which can be managed clinically. There are some cases where there may be a requirement for a change in the regimen the study found that out of 1519 people who had a documented change of a treatment of MDR, it was due to side effects taking about 17, 70.4 percentage of the people. With this we have completed the description about the various adverse effects of the TB drugs.

I Thank you and we will continue with the management in the in another session.