Manage TB
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Lecture - 47
Treatment of Pediatric Tuberculosis-Session 02

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Once we have started therapy it is important to monitor it whether it is having an effect or not. So, when you start therapy it is good to have your first contact within 2 weeks because sometimes the parents may be confused may not understand one drug from the other, may not understand the right dosage child may be vomiting. So, they need to be seen earlier.

So, you see them within fifteen days to and make sure that they have understood the prescribed regime are they taking it well. This is important even if the patient is on DOT. When the patient is on DOT, the drug prescriber does not have the capacity to look at the other co-morbidities or response to therapy and therefore, it contact with the primary care physician is equally important. Having seen this child at 2 weeks then we see them at the end of 1 month and 2 months in every subsequent month till the treatment is over.

This is important because the assessment of response to therapy in children is largely clinical.

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What do we assess? We assess the clinical picture, resolution of symptoms, assess at the same time you assess adherence is the child vomiting, is the child taking all the drugs as the family understood the various drugs, which one is to be combined, the number of drugs which are to be used. You also look at other adverse effects other than vomiting.

So, this many of these drugs can cause drug induced liver injury about which will I will talk a little later and looking at weight measurement because this may require dose revision in some of the children.

We also monitor bacteriologically, at the end of intensive phase to see that this child has responded and there is a bacteriological conversion and you want that this has continued till the end of treatment and therefore, you would repeat that at the end of therapy also. It is equally important to monitor for other co morbidities be it HIV, where you could have drug interactions with ART you may decide to start a ART after about two weeks of giving HIV to decrease the risk of iris.

So, there are some detailing about how an HIV and TB combination should be treated which you will be taught in another lecture, but remember this is something which you need to look at. Similarly you need to look at what is happening to this severe acute malnutrition this child had. While you have taken care of the disease which may have contributed to malnutrition, but there may be other nutrition related issues which need addressing.

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Follow up radiology is used in children, but all is not routinely required in every child. It may be required at the end of continuation phase at the end of treatment as a baseline for future in all children. Otherwise at the end of IP, it is recommended only if there has been a slower result clinical resolution or; obviously, if there is any time child is showing any deterioration you would need a repeat radiograph.

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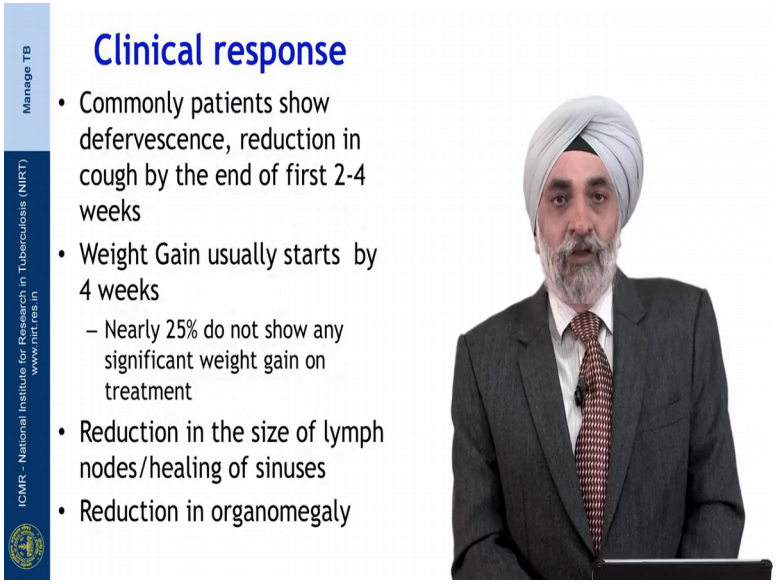

When we say clinical response it is important to know what is the common way this children respond. The commonly the patients would show a defervescence or reduction in cough in about 2 to 4 weeks time.

So, that is you do not expect a response before 2 weeks of the time in many a situations. Weight gain which is an important parameter to look at response to therapy is usually clearly evident by the end of 4 weeks. While the return of the lack of appetite which is often accompanied in this situation would go in about week or 10 days time, but in appreciable weight gain which is better seen by the end of 4 weeks of therapy initial 4 weeks of therapy.

What is equally important to remember is not all children will show you an increase in weight because it is basically recovery of the loss of weight. If a person did not have severe constitutional symptom has not have a loss of it they will not show you a weight increase you despite having a good response to therapy. So, this care should be remembered when you are looking at it.

There would be a reduction in organomegaly which may be seen, reduction in the lymph node size which may be seen. So, this is how a child who is the responding can be monitored, but it is also important to see at how to analyze a child who is not following this pattern of response what we call as a child who is not responding to anti TB therapy or a non respondent TB.

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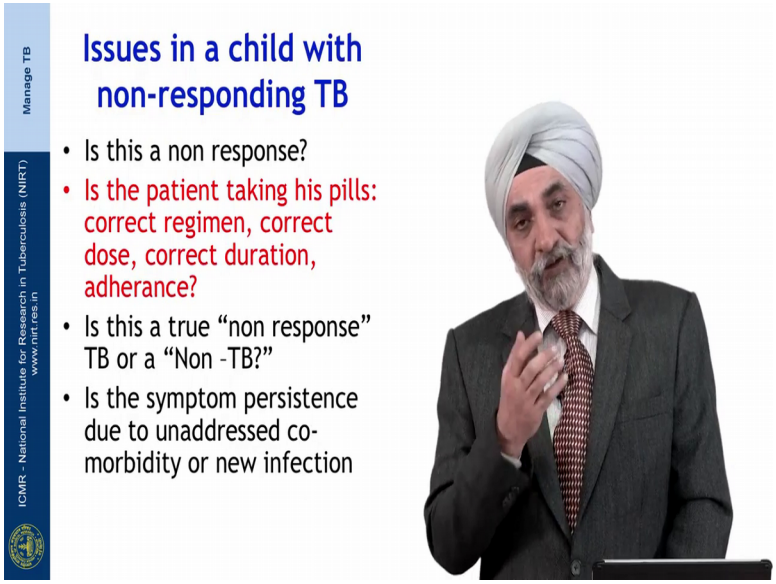

The first thing you need to know is this a non response. So, if we are looking for an in decrease in cough say or improvement in breathlessness in 2 weeks it may not happen.

So, we just now discussed that it can take up to 4 weeks for symptoms to disappear. So, look at that window period that it may still be some time before your patient would show a response though a large proportion of your patients would show significant clinical response by the end of 2 weeks with modern chemotherapy.

The second important thing when you do not see responses has the therapy been rightly understood and taken. So, such a patient is taking the correct regime, in the correct dose, is not vomiting out is something which is important to look at before you look for any other reasons for non response because this if the therapy has not taken rightly it will not have an impact.

Once you have decided that this all is something which is taken care of then you really need to know is this is a non response or non TB. What do I mean by this? If I started with the presumptive diagnosis of TB where it was not aesthetic a clinically diagnosed case of TB, where it was not a microbiologically confirmed this could there is a possibility this may not be TB at all and therefore, would not show you response to anti TB therapy.

So, in those clinically diagnosed cases of TB it is very important to say distinguish between a non response from a non TB. Once you have done that you are sure that your alternative diagnoses are dealt with, then the other reason for a non response could be an unaddressed co morbidity; child could have some other infection which may be what may have coughed because of bronchiectasis or are obese which may be an unaddressed we are just giving ATT.

So, once you will deal with those two symptoms were disappeared. It is only when these all are ruled out there is a possibility of two other reasons why you could have a change in symptoms or recurrence of symptoms.

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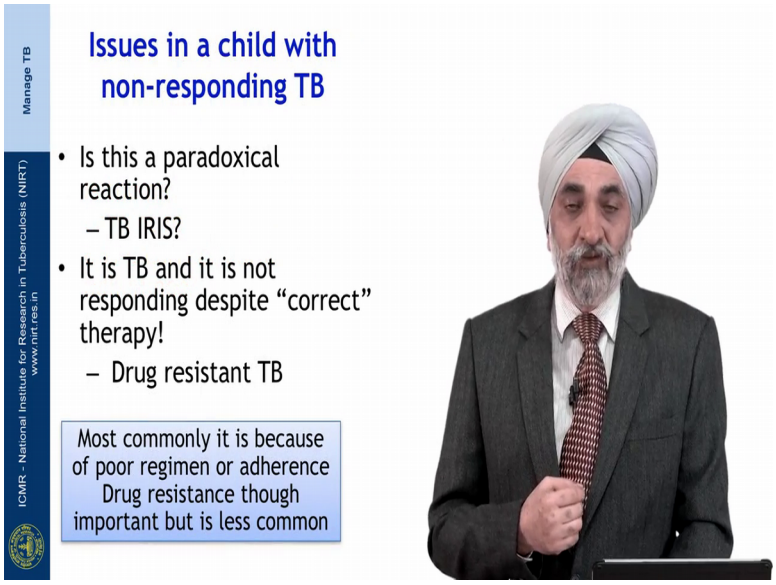

One of which is called a paradoxical reaction or TB iris which is a body's response to therapy and then there can be a overshoot response which leads to increase in the size of lesion because the local immunity improves and the cellular killing insights a local immunological reaction.

But this is a diagnosis of exclusion. What is equally important is that if everything was being done well. Your diagnosis was correct your treatment was correct and patient was doing taking it rightly then one important diagnosis which should always stay in your mind which is important to diagnose early is drug resistant TB.

It is only when you therefore, if the origin your diagnosis was TB the treatment was correct and treatment was taken and co morbidities are not there you start investigating for drug resistant TB. If the if there is no sign of drug resistant TB or the symptoms are not much then possibly you may be dealing with the paradoxical increase.

So, that is something which is important to remember, though our clinical experience shows the commonest reason for non responses poor understanding of a regime or poor prescription of a regime or poor adherence to a regime.

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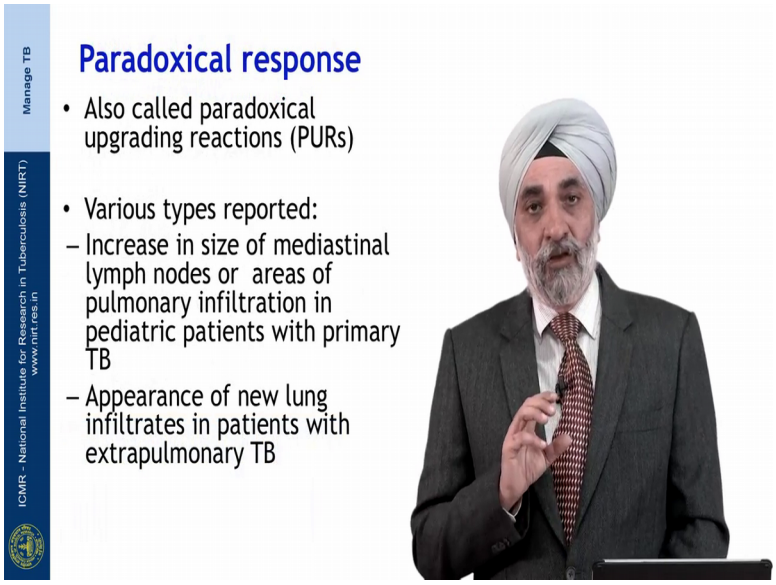

A word about paradoxical response, what do we mean by paradoxical response? As I said it is a disease this is an diagnosis of exclusion. Once you have ruled out drug resistance, ruled out co morbidities, ruled out an alternative diagnosis and you still see it think it is TB, studies have shown that you could have despite a drug sensitive bacilli right regime and increase in size of a lymph node, mediastinal peripheral increase in signs of parenchymal, lesion or even an appearance of a new parenchyma lesion in a patient who is adequately responding.

What will typically happen in this situation is they would very rarely have constitutional symptoms because they are otherwise responding. So, it is a clinically well child where your investigations are going bad, where you would keep a possibility of paradoxical increase in a child who is not otherwise immune compromised.

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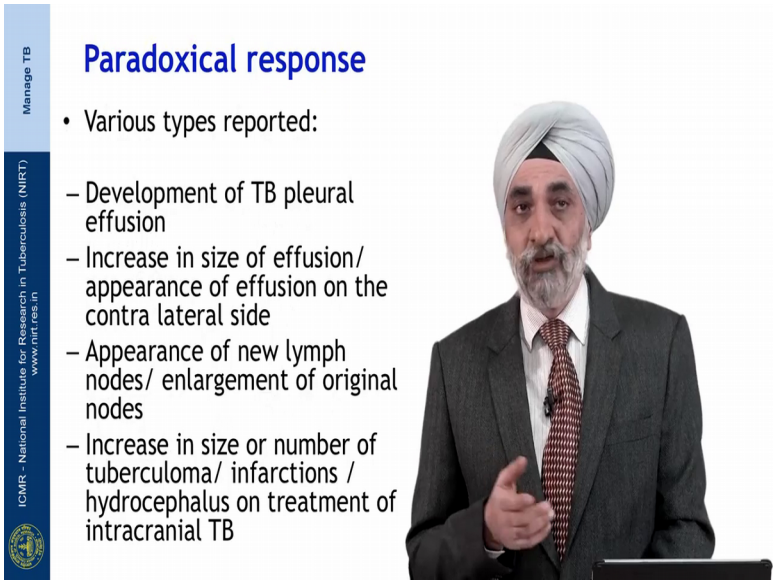

This could mean the element of pleural effusion or presence of a predator parenchyma lesion is in a child who initially had pleural effusion. It could mean an increase in size or a contralateral appearance of effusion; it could mean appearance of new lymph nodes or increases in size of tuberculoma.

A child with TB m may have a fresh lesion appearing, but if you have none of the other constitutional symptoms coming up then possibly and you have ruled out drug resistant TB where you would commonly have constitutional symptoms and possibly you are dealing with paradoxical increase.

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So, once you have looked at these entities how do you equally well look at the treatment adherence? The one the best way to ensure adherence is somebody else take charge of therapy, whether it is through counselling or through direct observation which may be family based, neighbourhood based or by a health worker it is something very important where a patient is contacted or counselled throughout for a complete adherence.

Remember as long as there are symptoms there is a reason for a patient or to continue therapy, but once the symptoms improve the motivation to continue therapy goes down and therefore, constant counselling is what you need and that is important for treatment adherence.

So, there may sometimes be reasons for the interruption may not be patient related it may be system related that their drug outages drugs are not available and that is something which we should ensure that every patient who is started on treatment his complete course is available right at the beginning and kept together and that is what is provided under the national TB control program.

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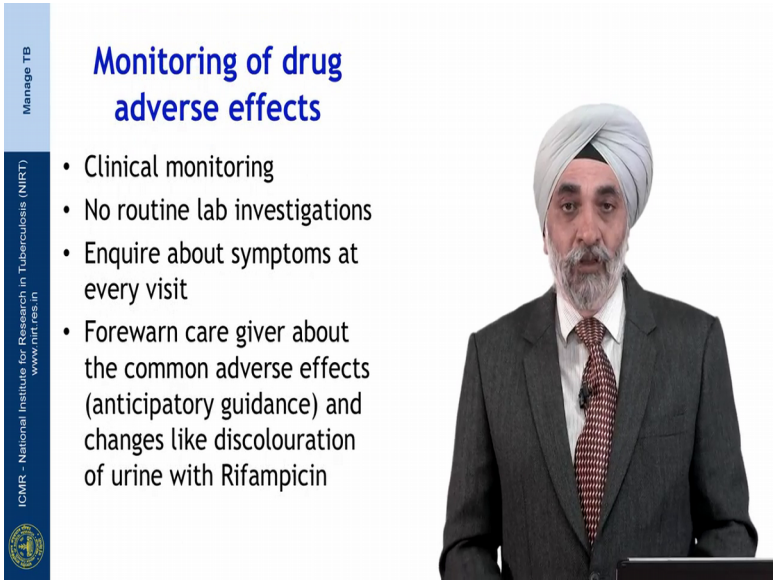

The other para face or facet of monitoring therapies if you looking at monitoring of the aiders adverse drug effects. Usually what you need is a clinical monitoring, there is no need for a routine lab investigation in every child, you do not need a baseline LFT or LFT every 4 weeks, you just enquire about symptoms at every visit; is there vomiting.

Remember to forewarn the care giver about some common things some anticipatory guidance about vomiting which may be because of gastritis, but one important thing is about discoloration of urine which happens because of a rifampicin and sometimes patients would discontinue considering that it may be blood in urine or it may be some effect adverse effect on their body.

So, if we forewarn or give the anticipatory guidance to the parents that this is normal, this is expected they would not stop therapy and they would adhere to it.

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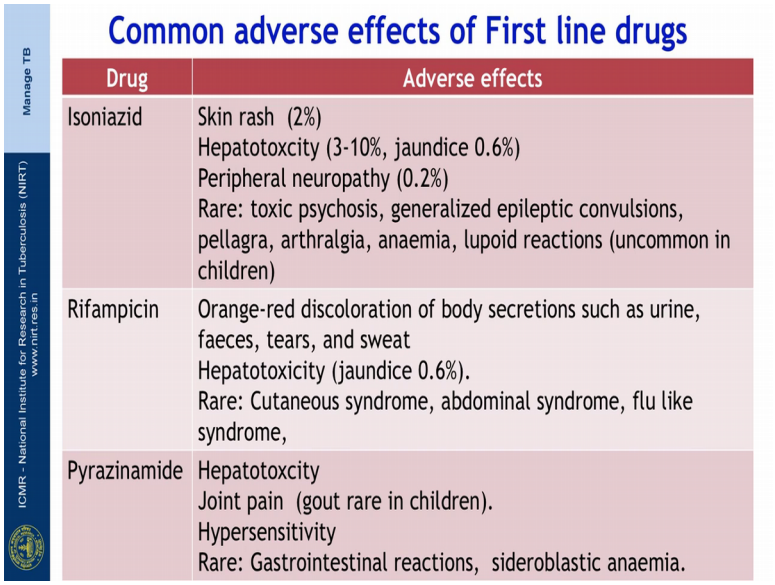

There is a complete module you where you would know about all the side effects of the various drugs which are used; isoniazid, rifampicin, pyrazinamide commonly have hepatotoxicity as an important common effect.

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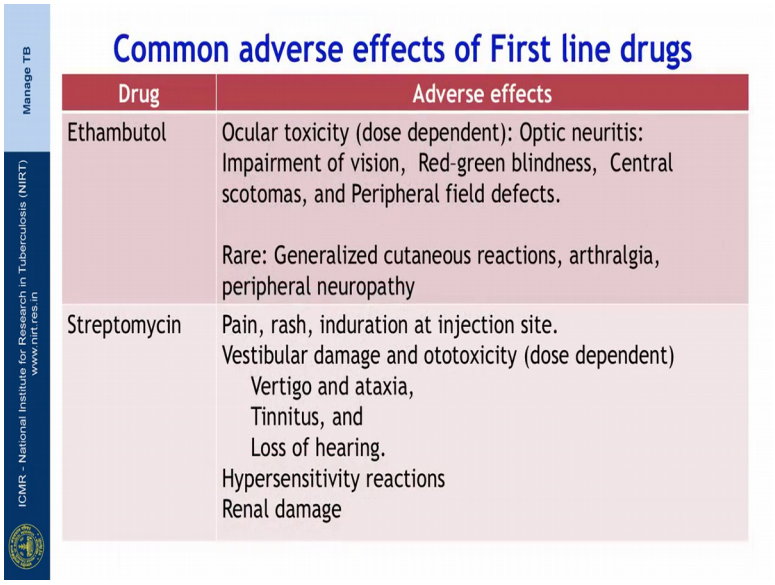

Ethambutol has ocular toxicity when used in higher doses say 20 to 25. They are relatively safe between the dose of about 20 milligram per kg in younger children, you could have vestibular effect with streptomycin.

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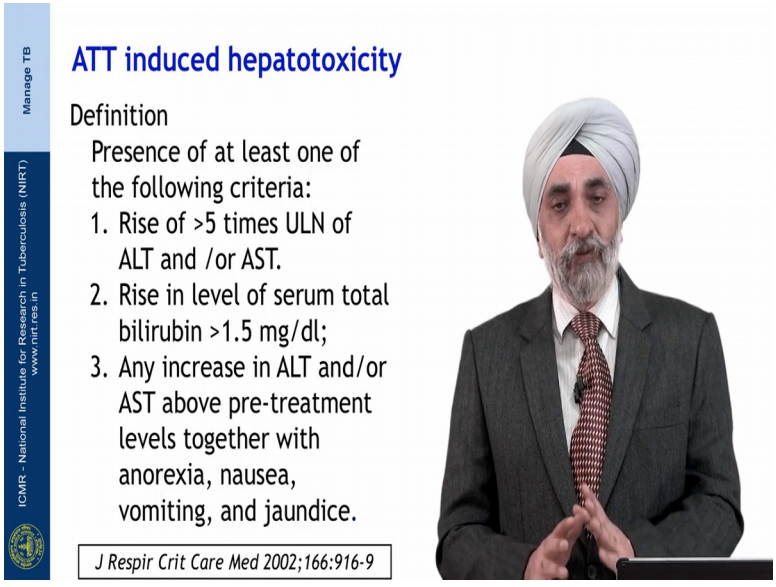

Let me quickly talk to you about one important cause of adverse effects with the ATT which is hepatotoxicity. What is a hepatotoxicity? It is difficult to recognize it if it is asymptomatic because rifampicin being an enzyme inducers would create some degree source of biochemical transaminase in every child, but this asymptomatic increase if it is more than 5 times the uppers limit of normal should be considered as a drug induced liver injury.

However, in the presence of symptoms like vomiting, loss of appetite, you your threshold will be lower. So, if it is more than 3 or at any time you have bilirubin increase or jaundice irrespective of whatever the level of transaminases maybe, you would consider this as a drug induced liver injury. Why we make this distinction is gastritis drug induced gastritis is a common cause for vomiting. There the transaminases are unlikely to increase above 3.

So, if you have transaminases which is less than 3 times and vomiting then considered drug induced gastritis as a cause and not a drug induced liver injury, but higher than that you have to be very sure very very particular about a hepatotoxicity.

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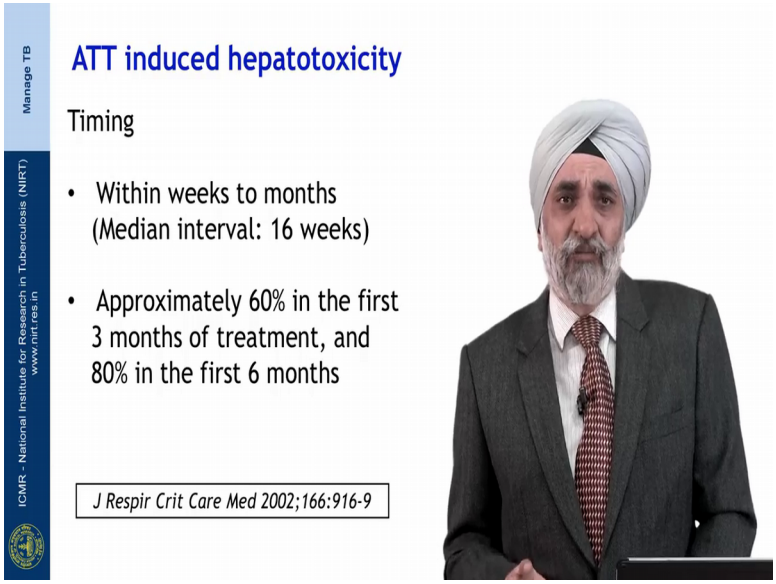

It can come anytime it the median interval is about 16 weeks and it takes most of the time it comes in the first 3 months because that is when you are using three hepatotoxic drugs.

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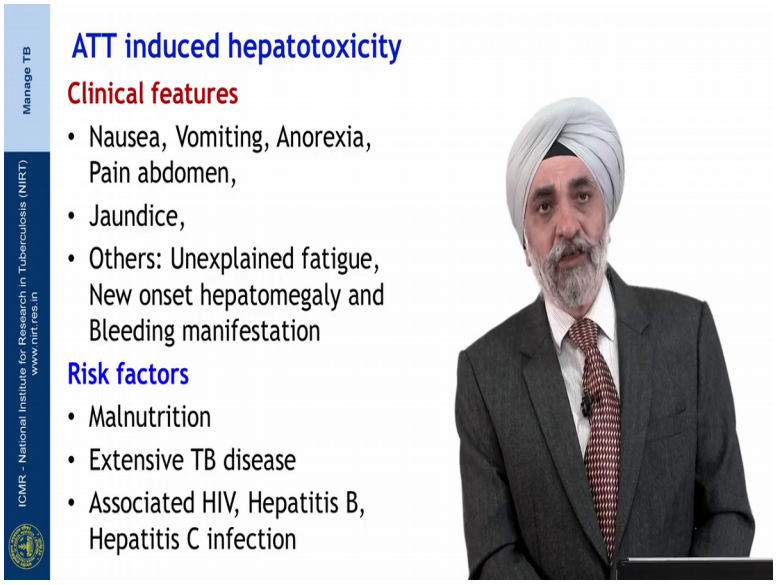

The clinical features are nausea, vomiting, anorexia. You can have unexplained fatigue and you can also have jaundice. Children who have extensive disease who are malnourished or have associated HIV or a background chronic liver disease or Hepatitis B carrier or Hepatitis C infected patient have a higher risk of developing the drug induced liver injury.

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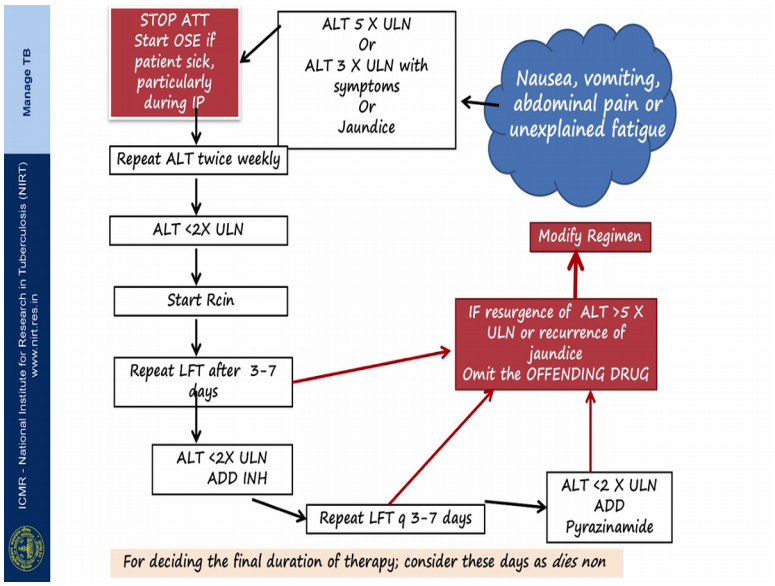

So, once you have a patient who has nausea vomiting abdominal pain or unexplained fatigue, you look at the transaminases level. If it is with symptoms more than 3 times, without symptoms more than 5 times or presence of jaundice irrespective the symptom you will stop ATT, you will not give anti TB drugs to this child.

Now, in a seriously ill child you may need to use alternative hepato safe therapy and that is what we recommend is a fluoroquinolone plus a streptomycin and ethambutol only in sick children. If you have such just a peripheral lymphadenopathy you may put them off therapy till their drug induced liver injury improves, you follow them up. In about 2 weeks time usually these ALTs will go up. So, you monitor their ALT, once these transaminases or SUT or ALT is less than 2 times the upper limit of normal then we start the rifampicin.

If that is your first drug you add. You repeat the levels of the transaminases after 3 to 7 days and if they are normal you introduce the next drug which is INH and that is how we sequentially reintroduce the therapy adding pyrazinamide last. At any point of time if you see resurgence of ALT after introduction of drug then possibly you would have to modify the regime this child would not be able to tolerate that particular drug.

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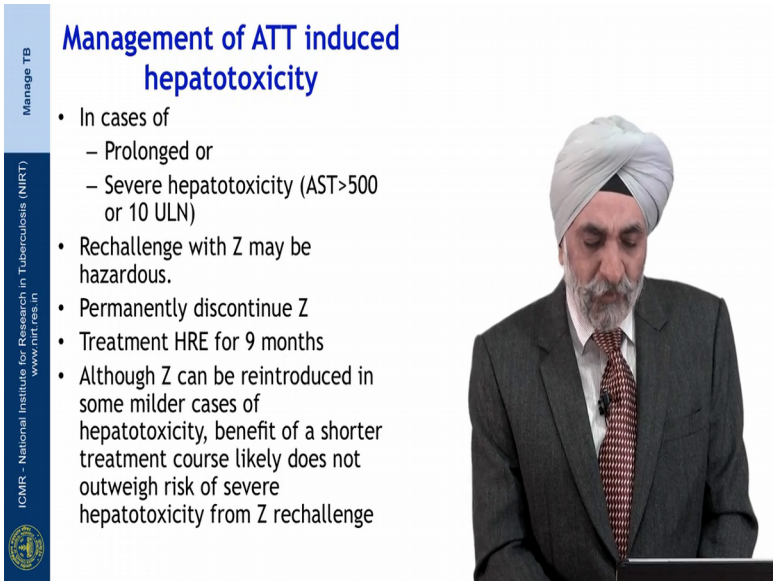

This happens very commonly with I mean it happens more commonly with pyrazinamide, though I must say that most children are able to tolerate the INT first line therapy better than adults and it is possible to reintroduce all the 4 drugs in most situations.

But in the child who may have on reintroduction of pyrazinamide any increase in transaminases which is huge or have a persistent liver injury which is not going down or

a background liver disease one may not use pyrazinamide at all and you would have to use an alternative regime.

One of the alternative regime which is available to you is HRE for 9 months. What do you do about the period when you had used that alternative hepatocyte safe drugs and you were not using the first line drugs. Remember in your total therapy duration you will not count that duration of alternative regime.

It is only the total duration of the first when the first line dose were given which are taken into account for the purpose of defining whether a patient has received the complete duration of therapy or not, this is something important to remember.

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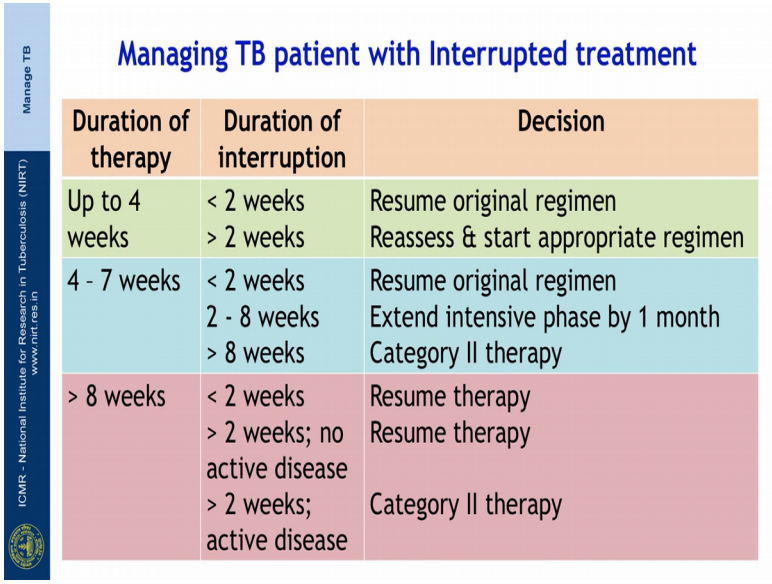

You may have other reasons for interruption of therapy also and this chart tells you that what to do in that situation.

If this interruption is less than 2 weeks at any point of time you are able to resume therapy in most situations. If it is between 2 to 8 weeks of interruption and it happens in the intensive phase then you would need to perhaps restart or extend the intensive phase by 1 month.

If it happens after 8 weeks of therapy and the interruption is more than 8 weeks and there is an active disease this is a child who would qualify as a treatment after interruption or a

defaulter, who would need to be given a retreatment regime and that is something we need to remember.

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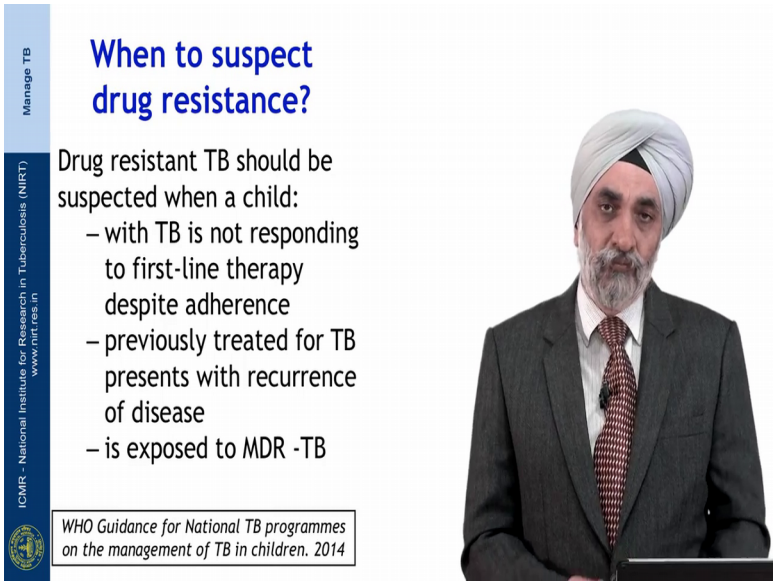

So, far we looked at the monitoring. One of the issues which is left behind is patient who on monitoring does not have a response, who could harbour or drug resistance. Is that the only situation we will consider drug resistance? No. There are other situations also you may up front think of drug resistant TB and they are a child who is not responding to first line is one and the other is a child who has a recurrence on a previously treated child who delays a recurrence of disease.

You would also suspect drug resistance if this child is exposed to a contact with MDR to begin with. In these situations you have to seek help of the experts what you need to give is a combination therapy with much toxic regimes like kanamycin, liver flucloxacillin, ethonomide, ethambutol, pyrazinamide and cycloserine. When it comes to treatment of MDR or in XDR in children it is something where you need to refer this patient to the local DR TB plus committee and where wherever your PMDT facilities are there. And this is where an expert should always be involved.

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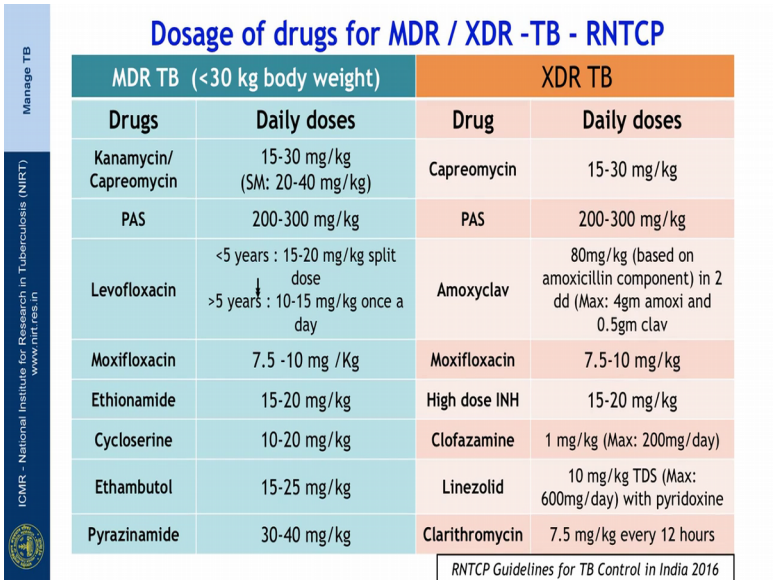

Here are the drugs just for your guidance as I said what is important is this therapy should be done under PMDT with an expert evaluation.

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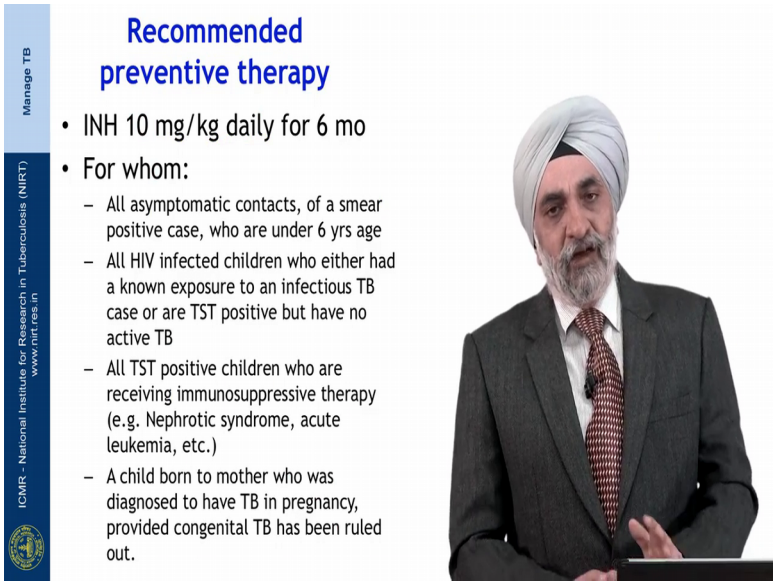

Finally, I come to the last part of my talk which is about preventive therapy. A lot of children when they get infected and has yet have not developed disease or asymptomatic or are asymptomatic exposed children below 5 years of age to a child or to and to a case who is infected.

So, smear positive pulmonary case family members who are below 6 years of age and are asymptomatic would benefit for preventive therapy. What we recommend in our

country is INH for 10 milligram per kg per day for 6 months. So, all asymptomatic contacts of a smear positive case, in addition any HIV case who has been exposed and does not have an active TB. All TST positive patient which shows infection, but no disease and are on immunosuppressive therapy should be given preventive therapy. This is a very good method to decrease occurrence of disease in children.

So, remember preventive therapy with INH single drug 10 milligram per kg for six months is recommended for this category of patients. So, this brings us to the end of whole gamut of treatment of childhood TB.

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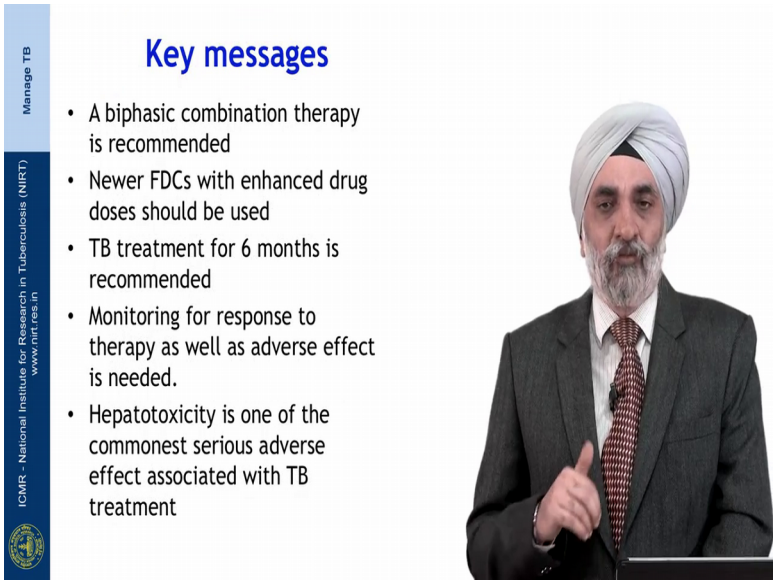

Remember what I told you was the childhood TB is treated with a biphasic combination therapy which is usually given for 6 months except when you are treating austerity clot and TB meningitis when it is treated for 12 months.

Remember that you need the right combination of fixed drugs. The newer FDCs with the nr higher drug doses in the right ratio should be used. When you monitor these children for clinical improvement remember hepatotoxicity as an important cause. It is important to remember hepatotoxicity also because commonly parents would identify hepatotoxicity by high coloured urine.

When you are giving rifampicin that is no more a distinctor or something which can be used as a pointer towards the liver injury and therefore, one has to focus on loss of

appetite, persistent vomiting which should bring into focus whether this child is having any drug induced liver injury or hepatotoxicity. It is important to respond monitor for response to therapy as well as an adverse affect as needed.

Thank you very much for your kind attention. I hope this lecture has helped you learn all about the different aspects of treating children with TB.

Thank you.