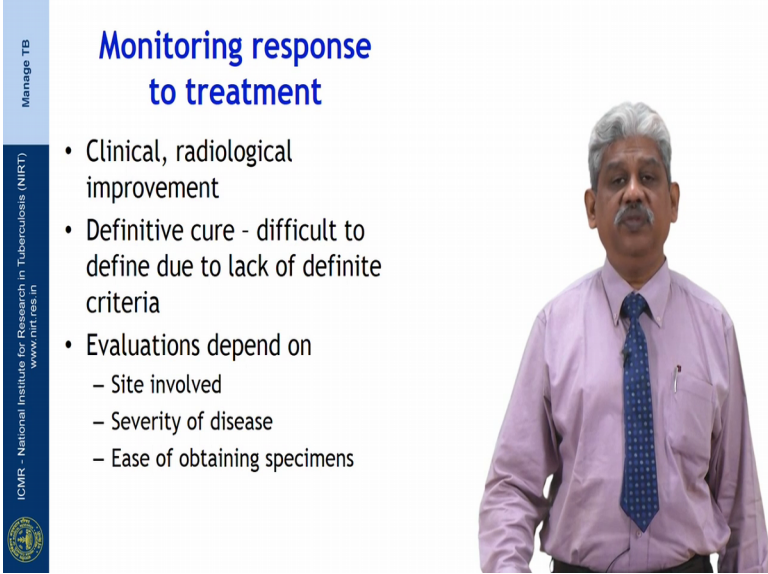


Manage TB
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Lecture - 39
Management of Extra Pulmonary TB Session – 02

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The slide features a vertical blue bar on the left with the text 'Manage TB' at the top, 'ICMR - National Institute for Research in Tuberculosis (NIRT)' in the middle, and 'www.nirt.res.in' at the bottom. To the right of the bar, the title 'Monitoring response to treatment' is displayed in blue. Below the title is a bulleted list:

- Clinical, radiological improvement
- Definitive cure - difficult to define due to lack of definite criteria
- Evaluations depend on
 - Site involved
 - Severity of disease
 - Ease of obtaining specimens

To the right of the text is a photograph of Dr. A. Mahilmaran, a man with grey hair and a mustache, wearing a light purple shirt and a blue patterned tie.

So, the next important thing is monitoring the response of treatment because you already do not have a microbiologically confirmed example my TB how will you monitor because there is no way of monitoring them through a microbiological response. So, we have to use our clinical knowledge and radiological improvement as a better way.

So, clinically every month you should see to that you monitor him on what is his weight, whether there is an increase of weight, whether his fever has settle, he is clinically better that as his appetite this code he is very active and whether he is size of his lesion has started reducing. Let us say a patient had a cervical node, whether the pain in the cervical node is reducing, the size is reducing, the patient is looking at an improvement.

Similarly, there are other method like radiological improvement, especially if you have a patient who has a spinal or TB with the bone joint involvement you can do all radiological methods like X-ray, you can take given a MRA or a CT scan to follow up your monitoring respond, whether the cold abscess is reducing, the inflammation in the bone is reducing all these things can be looked at.

The next important thing is when do you say it is a definitely cure, right? It is difficult to define a cure because we do not have microbiological confirm, all you have to base is on good radiological methods and good clinical acumen on how the patient is responding to your therapy.

Then evaluation depends upon what each one it is very different so, according to the site we differ. Let us say a patient has abdominal TB with nodes in the abdomen with mild a site is you have to follow up abdomen with ultrasound looking at how this ascites has reduced how is abdominal parasitic and perihepatic nodes have reduced.

So, how is his symptomatology how is his appetite all these things will be a better clue and let us say patient add some mind some sub acute intestinal obstruction whether he has a good improvement on the industrial obstruction whether his diarrhea is settled all these things is site specific. Similarly the severity of the disease we have access. So, let us say a patient has been bedridden for a spinal TB and if the patient tries to walk and he is improving then we know that the severity of the disease is over.

Similarly, a when a patient who had a epilepsy at the diagnosis of a tuberculoma if his epilepsy episodes have not come for the next 6 months then we are sure that the tuberculoma has responded.

Similarly, the ease of obtaining a specimen; let us say if you have a patient who has a cold abscess in the neck and let us say you initially in the cold abscess there was acid first basically is being demonstrated. And the next aspirate even if you do a culture from the cold abscess there is no growth then we are very definite to that the patient us responded well to our therapy ok.

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Type of EPTB	Monitoring treatment response
Ocular TB	Level of inflammation in the eye after 3 months of ATT
TB meningitis	Clinical response at the end of intensive phase, end of treatment and over a 2 year period at regular intervals
CNS tuberculoma	Lesions increase in size or fail to reduce after 3 to 6 months of ATT - suspect treatment failure
Lymph node TB	<ul style="list-style-type: none">• Assess response to treatment at 4 months• Residual lymphadenopathy at the end of treatment<ul style="list-style-type: none">✓ If largest node <1 cm in size- no active treatment required✓ If residual nodes are >1 cm in size - partial responders. Patients should receive an additional 3 months of RHE, followed by a biopsy sent for histology and TB culture in patients who fail to respond
Cutaneous TB	Assess response at 4 to 6 weeks

So, how do you monitor? Normally we monitor ocular TB by what is a response within 3 months of therapy ok. So, we are very definitive that once the inflammation in the eye is reducing and the ophthalmologist could look at whether the waitress lesions and the retinal lesions are started disappearing we are very definitely. Similarly, TB meningitis we normally look it after 8 weeks on how the responses, but most of the TB meningitis we always follow them up for 2 years because some of them can develop a relapse.

So, it is very important in the national program that we follow all our TB cases for the next 2 years even after the treatment completion. Similarly cns tuberculoma you have to have a good response within 3 months to 6 months. So, you will follow up with that of with a CT or an MRI looking at whether the size of the tuberculoma is reduced and the inflammation or the edema is reduced and the patient is not having any sequelae like epilepsy or you let us say you had a monoparesis the monoparesis improved then we are very definitive that the tuberculoma has responded.

Lymph node TB similarly, you can have a node even persisting after 6 months of therapy, but depending upon the size their site we can decide on whether the response is good.

Let us say you have a node which is not painful and it is less than once 1 centimeter in size after 4 months of therapy we can be very definitely that the node is a good node which has responded, but let us say the largest node in that area is more than 1 centimeter and it is a little painful and all those things then we have to extend our therapy by

another 3 to 6 months and sometimes you can need to do a excision biopsy and even try to remove the node as a curative therapy and continue with the ATT. So, that is the way we have.

Similarly, cutaneous TB we have a good response very quickly because the acid fast bacilli load is very less, even 4 to 6 weeks there will be good response.

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Monitoring anti-TB treatment response	
Type of EPTB	Monitoring treatment response
Pleural TB	Follow-up x-ray at 8 weeks to assess progress
TB pericarditis	Assess response to treatment at 4 months
Abdominal TB	Assess response to treatment at 3 and 6 months
Urogenital TB	Assess response at 8 weeks
Female genital TB	Assess response at 6 months
Bone TB	Assess response at 5 months
Spinal TB	<ul style="list-style-type: none"> • X-rays of the spine every 3 months following ATT initiation to assess radiological healing. • MRI scans at 6, 9, 12 and 18 months following ATT initiation to assess healing • Follow up every 6 months for at least 2 years after treatment completion

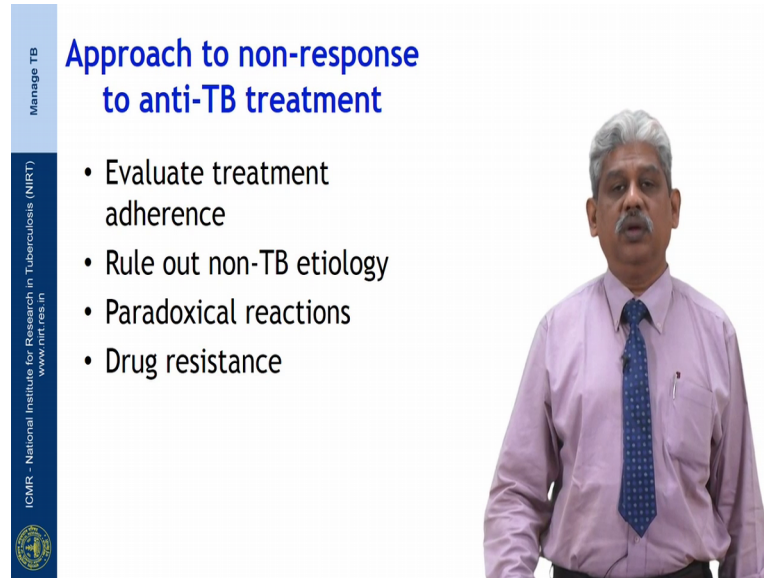
Pleural TB we always follow it up with the 2 months of 8 weeks after therapy we check an x-ray chest and see how the response is there. TB pericarditis he also has followed with the echo looking at whether the patient is trying to develop a constrictive pericarditis the response is always good within the next 4 months.

Abdominal TB similarly within 3 to 6 months you will have good response, urogenital TB you will have within 8 weeks and female genital TB we have to look at after 6 months. Spinal TB is the most important thing which we have to keep on assessing, the response will be not immediate after 2 months, always you have to see it after 5 months and during the 3 months follow up of our ATT.

We have to assess the radiological clearing by an x-ray, let us say the spinal space has been reduced, what happened to the wedging rather the wedging is happening or calcification or let us say we do an MRI we have to treat 3 6 9 and 12 months, we have

to follow how far the cold abscess is reduce the peri retinal edima is reduced or the spinal lesion is reduced. So, everything we have to follow it up even after 2 years.

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Manage TB

Approach to non-response to anti-TB treatment

- Evaluate treatment adherence
- Rule out non-TB etiology
- Paradoxical reactions
- Drug resistance

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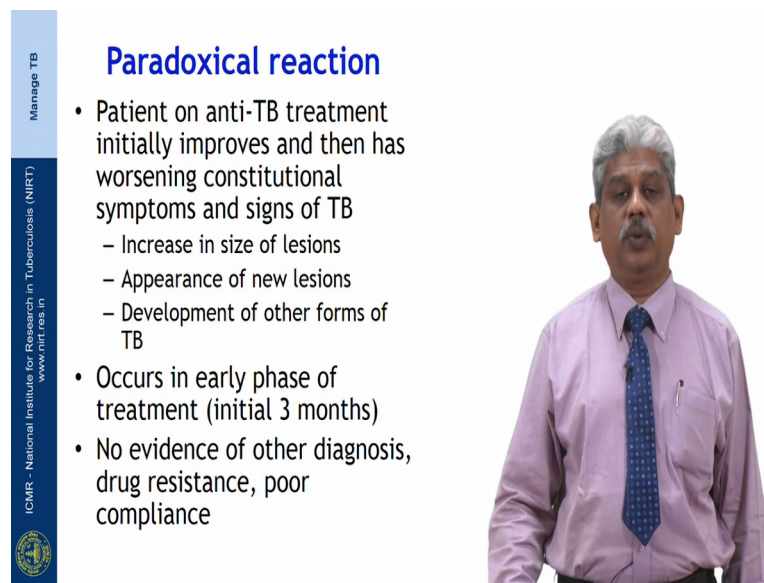
So, what is approach to a non response, how will you if know that there is a non response. So, you have to first evaluate whether he is following your treatment, whether he is adherently or therapy. So, do not at once jump it this might be a treatment failure. So, you have to get some good history from him whether he is adhering to its therapy by taking a regiment daily at the proper time and all the drugs at the same time.

Most of the patient will take let us say we give a fixed dose drug combination you will take one in the morning, one in the afternoon and one at night and if you space the drugs the efficacy of the drug is going to become lesser because we would have not attained the MIC; the maximal inability concentration. So, that is why the patient is not responding ok. Then we have to rule out whether it is not a TB itself. So, let us say we have no response, we have to reevaluate him, look whether it is a TB case or a non TB case.

Then the most important thing is paradoxical reaction because some of them which I will be telling you in the next slide can develop a paradox because of the dysregulation of our immune system because we had a very immune weak system before right. Then the last and important thing might be a drug resistance. So, do not jump to drug resistance immediately.

So, these are the first pathway you have to access first look at whether he is taking his drug regimen properly, next we evaluate him whether you are really TB you the TB patient, forth look at paradoxically reaction we are in the early stages of the therapy that is in the first 3 months if it happens and the fifth should be the drug resistance.

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Paradoxical reaction

- Patient on anti-TB treatment initially improves and then has worsening constitutional symptoms and signs of TB
 - Increase in size of lesions
 - Appearance of new lesions
 - Development of other forms of TB
- Occurs in early phase of treatment (initial 3 months)
- No evidence of other diagnosis, drug resistance, poor compliance



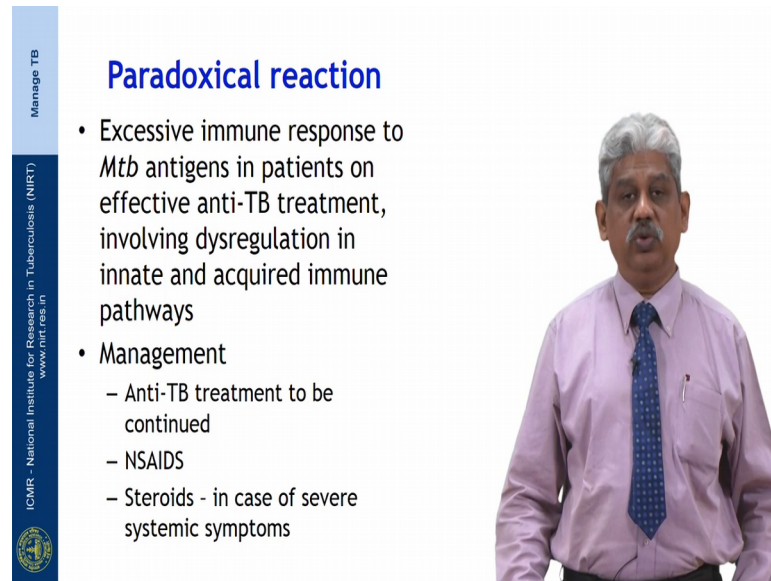
So, what is paradoxical reaction? Patient whose on anti TB drugs when he was very immune weak, especially now the most important group is HIV positive, but it can happen in all patients who are immune weak.

So, they allow initially improved then they are worsening of their constitutional symptoms and you can develop even new lesions right especially you can have an increase in the size ability. Especially in tuberculoma, you have a patient who add a tuberculoma, after 10 days he might develop a after a month you might develop a fits and if you repeat the CT you will see pre retinal edema around the tuberculoma.

This is a immune reconstitution where you will have a paradoxical reaction. Some of them can even have a new lesion coming up where you call it as a (Refer Time: 10:10) lesion. So, it will very common even in pulmonary TB where you love a new lesion coming up. So, that does not mean that he is still resistant. So, you have to he has done very well initially we have to consider it. So, this will very common during the first few months only.

So, maybe after 3 months you have a new lesion you have to suspect resistance, but let us say if it happens within 2 to 3 months of therapy you need to still suspect it might be a paradoxical reaction. So, it occurs very early and there is no evidence for other diagnosis you will always like resistance or non compliance problem you are always suspected it is a paradoxical reaction.

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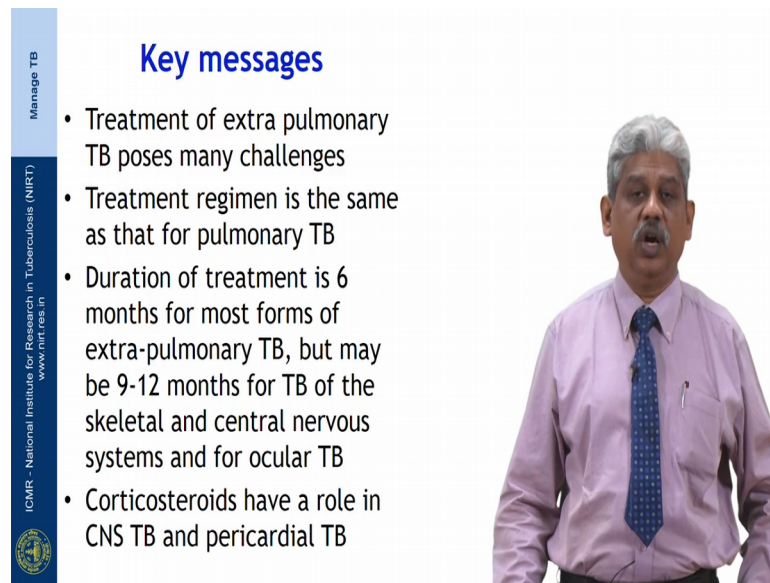
The slide features a vertical blue bar on the left with the text 'Manage TB' at the top, 'ICMR - National Institute for Research in Tuberculosis (NIRT)' in the middle, and 'www.nirt.res.in' at the bottom. The main title 'Paradoxical reaction' is in blue. The content includes a bulleted list and a photograph of a man with grey hair and a mustache, wearing a light purple shirt and a blue patterned tie.

- Excessive immune response to *Mtb* antigens in patients on effective anti-TB treatment, involving dysregulation in innate and acquired immune pathways
- Management
 - Anti-TB treatment to be continued
 - NSAIDS
 - Steroids - in case of severe systemic symptoms

So, excessive immune response to a mycobacteria antigen when an effective anti TB regimen is involving dysregulation in the innate or the acquired immune immunity; So, management is to continue the anti TB drugs you can give non steroidal anti inflammatory drugs like ibuprofen or you can give even diclofenac for reducing the inflammation and steroids to have a roll when you have very severe forms where you have some problem of let us say, a patient has a node which is opening up very largely and producing him severe pain you can give steroids.

Similarly, patients who have a tuberculoma which has a new epilepsy coming up you can give him steroids. So, which will reduce the inflammation the duration will be for 4 weeks and though it will slowly titrate it off.

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The slide features a vertical blue bar on the left with the text 'Manage TB' at the top, 'ICMR - National Institute for Research in Tuberculosis (NIRT)' in the middle, and the website 'www.nirt.res.in' at the bottom. The main content is titled 'Key messages' in blue. To the right of the text is a photograph of a man with grey hair, wearing a light purple shirt and a blue patterned tie.

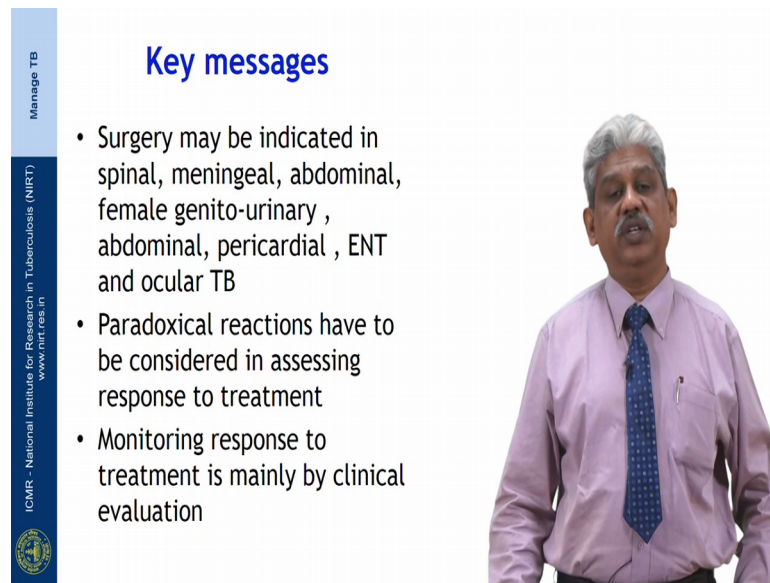
Key messages

- Treatment of extra pulmonary TB poses many challenges
- Treatment regimen is the same as that for pulmonary TB
- Duration of treatment is 6 months for most forms of extra-pulmonary TB, but may be 9-12 months for TB of the skeletal and central nervous systems and for ocular TB
- Corticosteroids have a role in CNS TB and pericardial TB

So, what are the key messages which we want to tell you is right the treatment of extra pulmonary TB is not very different from pulmonary TB, but the challenges are the duration of therapy is very important. So, you have to decide according to the clinical improvement how many months of therapy you have to continue as a continuation phase.

Then the treatment regimen it should be as same as for pulmonary TB, the duration of treatment can be from 6 months, you can extend it to up to 9 to 12 months. The corticosteroids have a role in CNS TB especially it is proven. So, all your patients with TB meningitis should have cardio steroids during the first 4 weeks and then taper it off within the next 4 weeks.

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Key messages

- Surgery may be indicated in spinal, meningeal, abdominal, female genito-urinary , abdominal, pericardial , ENT and ocular TB
- Paradoxical reactions have to be considered in assessing response to treatment
- Monitoring response to treatment is mainly by clinical evaluation



Surgery is indicated in some of your cases especially when you have structures like in abdominal or in a urogenital. Similarly, when you have CNS TB with hydrocephalus being developing; similarly when you have pericardial effusion leading on to a patient who is going to develop a constrictive pericarditis and in ENT when you have a parapharyngeal abscess you have to definitely drain it an ocular TB.

Paradoxical reaction has to be considered in assessing response to any treatment with TB especially within the first 3 months where you have initially good clinical response and the patient is doing well. But there is a market problem of increasing in problem of the lesion you will still consider paradoxical scale reaction, if the patient has been taking the therapy very properly and you are very sure he has had a good therapy and monitoring response to treatment is mainly by critical evaluation.

Thank you.