Manage TB
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Lecture – 53
Non-tuberculous Mycobacteria: Diagnosis & Clinical management
Session 2

Hello welcome to session 2 of Non-tuberculous Mycobacteria, I am Dr. Padmapriya. And I will continue with the diagnosis and clinical management of NTM.

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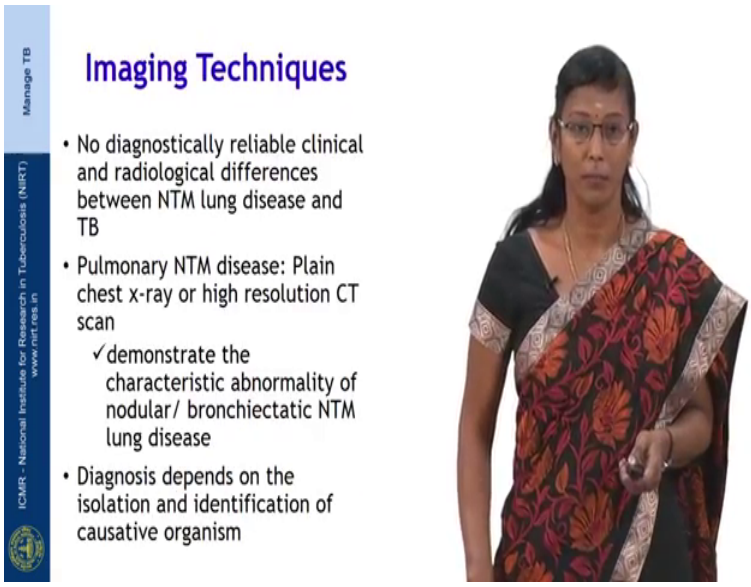

Imaging techniques there are no diagnostically reliable clinical and radiological differences between NTM lung disease and tuberculosis lung disease. Pulmonary NTM disease the plain chest x-ray, or high resolution CT scan will only demonstrate the abnormality, if it is either a nodular lesion or a bronchiectatic NTM lung disease or the presence of a cavitated lesion.

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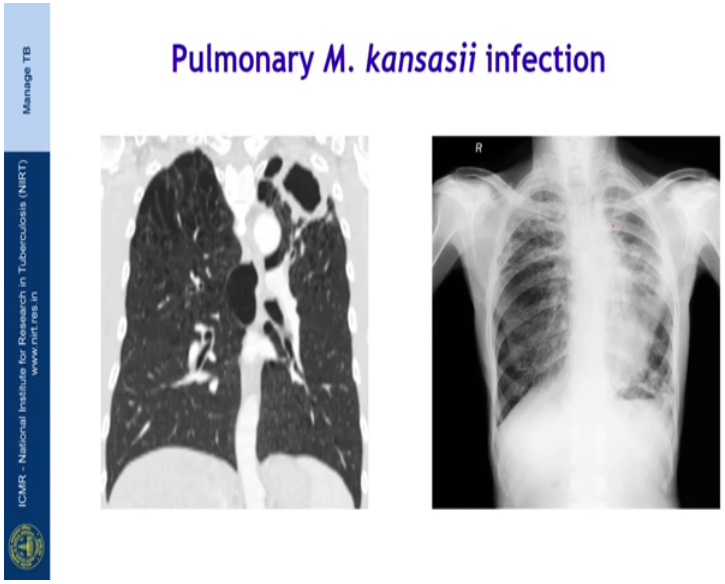

The final diagnosis depends upon isolation of the organism and identifying the species of the non-tuberculous mycobacteria. These are x-ray showing pulmonary M. kansasii as you can see the lesions are very similar to M tuberculosis and is very difficult to identify or differentiate between on an x-ray and CT scan difference between pulmonary M kansasii or pulmonary M tuberculosis.

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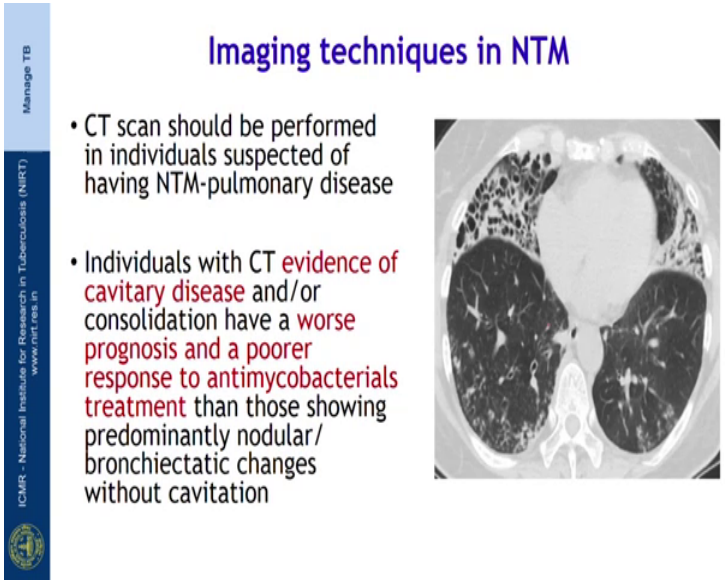

The imaging techniques in non-tuberculous mycobacteria does not vary much between the species also. Individuals with CT evidence of cavitary disease or consolidation they

have a worst prognosis to treatment and a poorer response to antimicrobial treatment than those showing a nodular, or bronchiectatic changes without any cavity.

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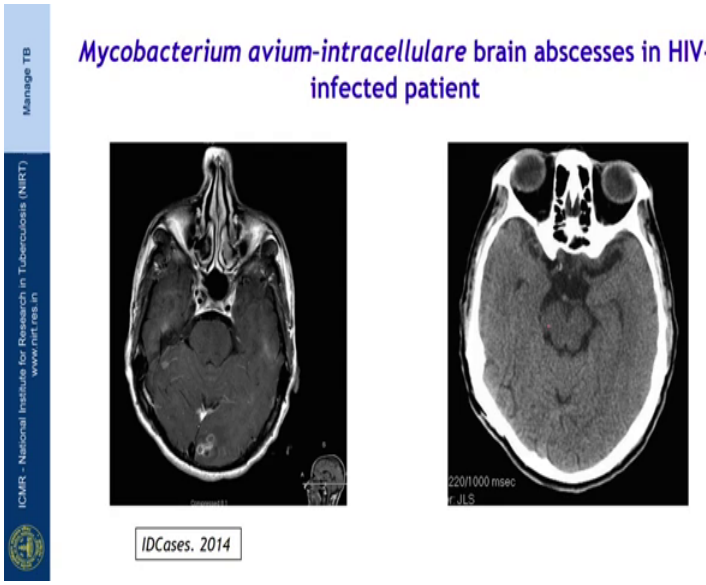

Now, these are few slide showing you various micro nontuberculous mycobacteria. This one shows you non mycobacterium avium intracellulare infecting the brain presenting in the form of brain abscess in a immunocompromised individual.

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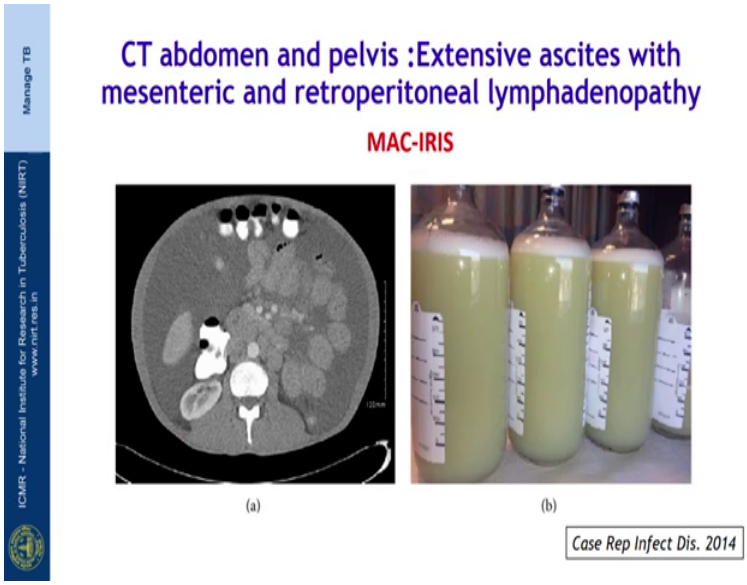

This is from a patient who has got nontuberculous mycobacterial infection of the abdomen presenting with the form of ascites and multiple lymph nodes of the abdomen.

This is also immunocompromised patient where he was started on treatment and subsequent to the start of treatment he ended up collecting ascites. When the ascites were stabbed this what was found purulent fluid from the abdomen and these grew non-tuberculous mycobacteria.

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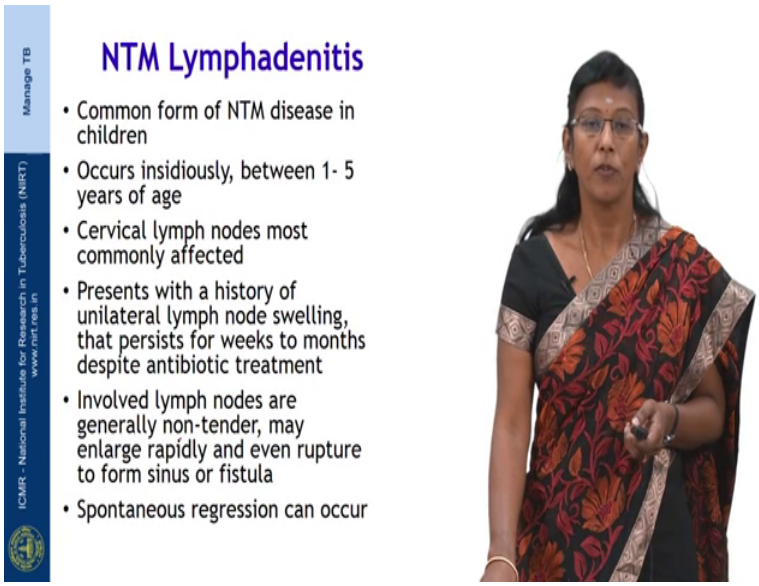

Another form presentation of nontuberculous mycobacteria is lymphadenitis this is one of the common form of NTM disease in children. It occurs insidiously between the age of 1 and 5 years among children, cervical node is most commonly affected though other groups of node can also be affected with nontuberculous mycobacteria.

We usually present with a history of unilateral lymph node swelling which persist 4 weeks and months and do not respond to antituberculosis treatment, or any other antibiotic treatment. The involve lymph nodes are non-tender, we can enlarge rapidly resulting in rupture and sinus formation spontaneous regression of these nodes have also been reported.

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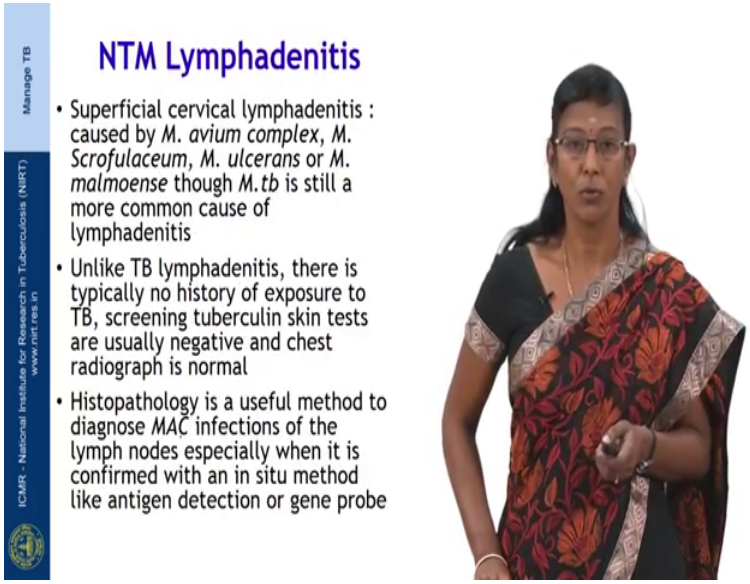

Since, the superficial cervical lymphadenitis is the usual mode of presentation of NTM lymphadenopathy. They can be the discharge can be taken up for biopsy and culture and many of them grow M avium complex, M scrofulaceum, or M ulcerans have also been identified. Now, one thing that we also remember is M tuberculosis still the common cause of lymphadenitis in TB endemic countries.

The difference here would be unlike TB lymphadenitis there is typically no history of exposure to tuberculosis the screening tuberculin skin test or the TST test are usually negative and the chest x-ray may be normal in such cases. Histopathology is a useful method to diagnose MAC infection as the lymph nodes confirm the presence of MAC can be confirmed with antigen detection or the gene probes in the lymph nodes.

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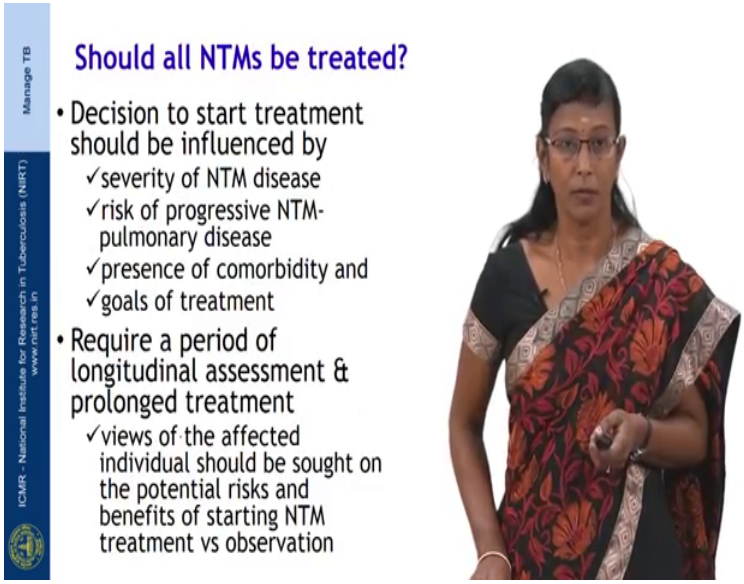

Now, moving on to treatment should all NTM cases be treated the decision to start treatment should be influenced by severity of the disease, the risk of progression of NTM pulmonary disease as well as the presence of comorbidity and the goals of treatment.

Now, why are we so particular about the severity or the risk of progression is? The duration of treatment for NTM is long drawn. It is something very close to MDR treatment, the infected patient has to continue treatment for a longer period of time with potentially toxic drugs and they need frequent monitoring as well as follow up.

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The factors that frequently associate with progressive NTM pulmonary disease are both patient related as well as the bug related. Among the patient patients with severe symptoms, low body mass index, somebody with a lung cavitation on a imaging techniques and the presence of comorbidity warrant treatment. Among the mycobacterial factors smear positivity presence of two or more positive cultures of the same organisms warrant treatment of this disease.

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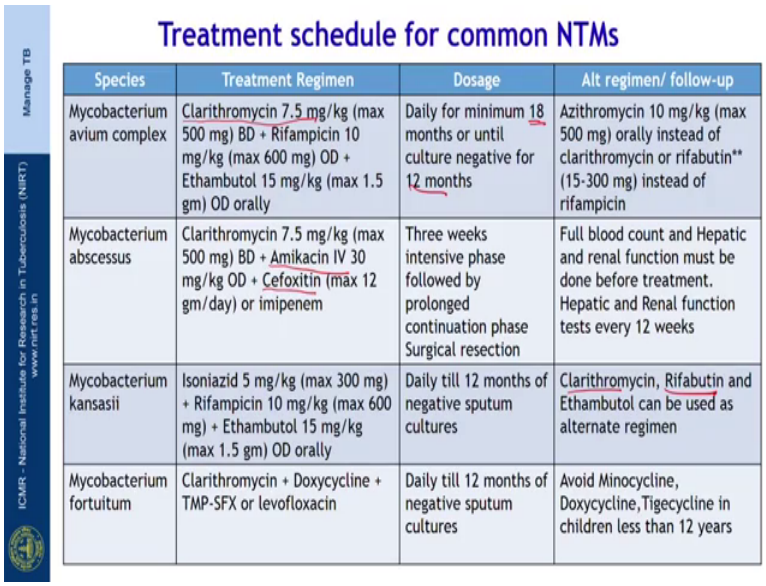

Treatment schedule for common NTMs

Species	Treatment Regimen	Dosage	Alt regimen/ follow-up
Mycobacterium avium complex	Clarithromycin 7.5 mg/kg (max 500 mg) BD + Rifampicin 10 mg/kg (max 600 mg) OD + Ethambutol 15 mg/kg (max 1.5 gm) OD orally	Daily for minimum 18 months or until culture negative for 12 months	Azithromycin 10 mg/kg (max 500 mg) orally instead of clarithromycin or rifabutin** (15-300 mg) instead of rifampicin
Mycobacterium abscessus	Clarithromycin 7.5 mg/kg (max 500 mg) BD + Amikacin IV 30 mg/kg OD + Cefoxitin (max 12 gm/day) or imipenem	Three weeks intensive phase followed by prolonged continuation phase Surgical resection	Full blood count and Hepatic and renal function must be done before treatment. Hepatic and Renal function tests every 12 weeks
Mycobacterium kansasii	Isoniazid 5 mg/kg (max 300 mg) + Rifampicin 10 mg/kg (max 600 mg) + Ethambutol 15 mg/kg (max 1.5 gm) OD orally	Daily till 12 months of negative sputum cultures	Clarithromycin, Rifabutin and Ethambutol can be used as alternate regimen
Mycobacterium fortuitum	Clarithromycin + Doxycycline + TMP-SFX or levofloxacin	Daily till 12 months of negative sputum cultures	Avoid Minocycline, Doxycycline,Tigecycline in children less than 12 years

We have we have a British thoracic guideline on NTM recently released in November 2017, and the treatment schedule is very clearly explained and this is taken from that. I have I have kind of given the most commonly seen NTM species and causing various kinds of disease. M avium the corner stone with the treatment is clarithromycin 500 milligram twice daily along with rifampicin ethambutol.

The dosage has to be continued for at least 18 months or until 12 months after culture negativity. In case we find resistance to either clarithromycin or rifampicin alternate regimens can be given in terms of azithromycin, or with rifabutin instead of rifampicin. The treatment for M abscessus again is clarithromycin along with an injectable aminoglycoside and cefoxitin if available.

Now if patients complain about injectables, in 3 weeks of intensive phase is when injectable is given in this regimen for everyday for a period of 3 weeks and then it can be continued as a continuation phase without an injectable. Mycobacterium kansasii consist

of treatment consist of isoniazid, rifampicin, and ethambutol treatment to given every day for a period of 12 months after they become culture negative.

One thing to remember here is M kansasii we are seeing increasing number of resistant M kansasii resistant as same both the isoniazid as well as to rifampicin. In those cases we should look for alternate therapy for this patients. The alternate regimen includes clarithromycin or rifabutin and also ciprofloxacin, or any of the fluoroquinolones.

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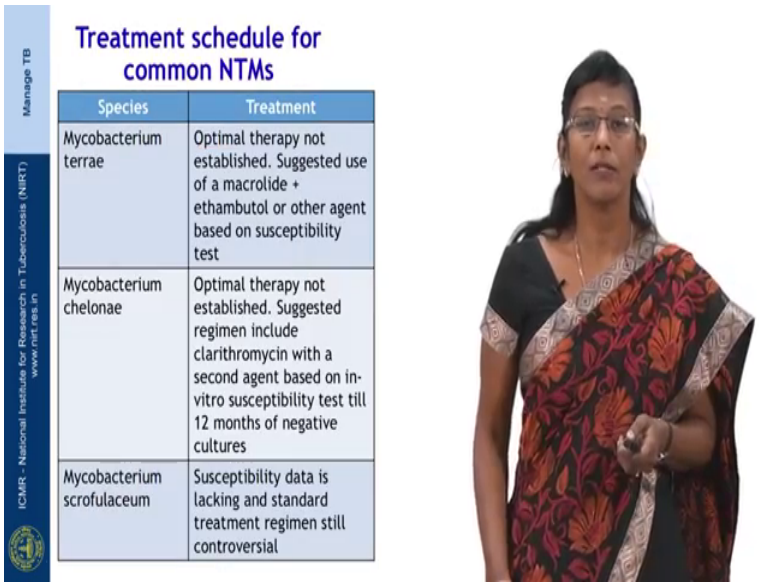

The guidelines also gives treatment for mycobacterium terrae, mycobacterium chelonae, and the scrofulaceum. Most important thing to remember here the treatment does not end with the patient becoming culture negative. Treatment has to continue for 12 months after the patient becomes culture negative to the species.

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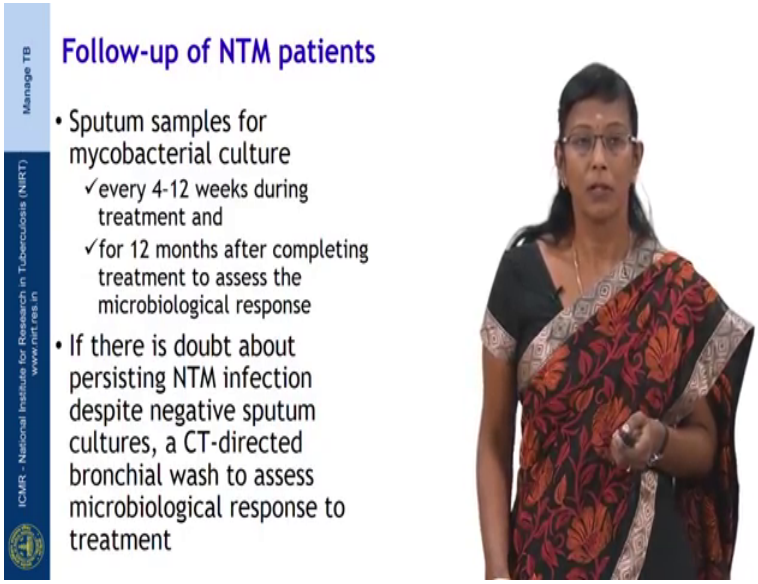

Since, these patients are taking treatment for more than 12 months they have to be followed up regular intervals for two important points, one is look for toxicity of these drugs, second to see for the sputum culture conversion. The sputum samples for mycobacterial culture during follow up period has to be con taken every 4 to 12 weeks for 12 months after completing treatment to assess for the microbiological response

At any time period if there is a doubt about persisting NTM infection though the sputum smear and cultures become negative, a CT directed bronchial wash can be done to assess for the microbiological response to treatment.

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Now, moving on to drug adverse event monitoring the three commonly used drugs include aminoglycosides, ethambutol, azithromycin, besides rifampicin, and isoniazid auditory and vestibular. Monitoring has to be done frequently when a patient is on aminoglycoside group of drugs, ocular toxicity should be monitored when someone is getting ethambutol for beyond 6 months and these drugs have to be given every day for almost 12 months of culture negativity.

Hence periodic ocular testing as well as audiometry testing is mandatory for these patients on a long drawn course of ethambutol, or dollar aminoglycoside. The group of azithromycins including clarithromycin can cause gastrointestinal disturbances mainly in the form of severe abdominal achesM and pancreatitis. As a GI side effect has to be monitored frequently at least once in 3 months for the entire period of treatment.

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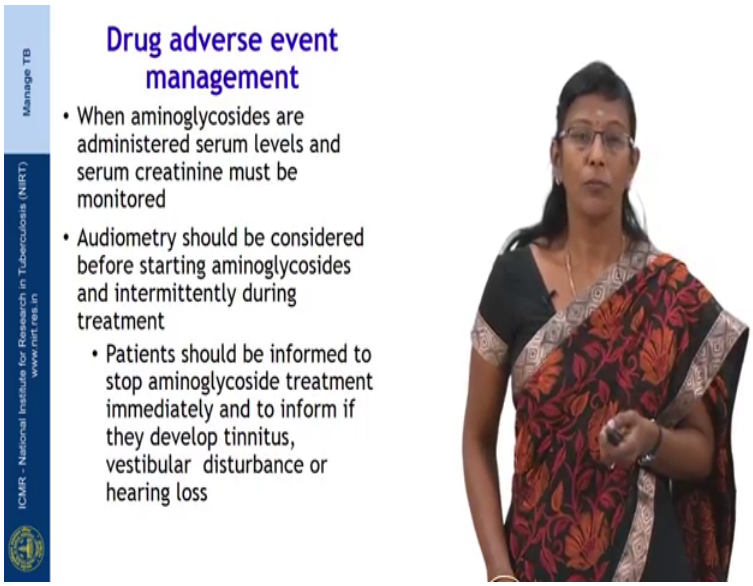

We also have to monitor the serum levels for aminoglycoside if feasible if not at least look for serum urea, and creatinine during the follow up period when a patient is an aminoglycoside containing regimen. Patient can also be informed to stop aminoglycoside in the presence of tinnitus, or vertigo and inform to the medical officer immediately to look and then patient can be followed up for further investigations.

Visual acuity both in the form of color vision as well as any distance vision has to be monitored frequently. Serum ether module levels can also be monitored in case of suspected drug toxicity.

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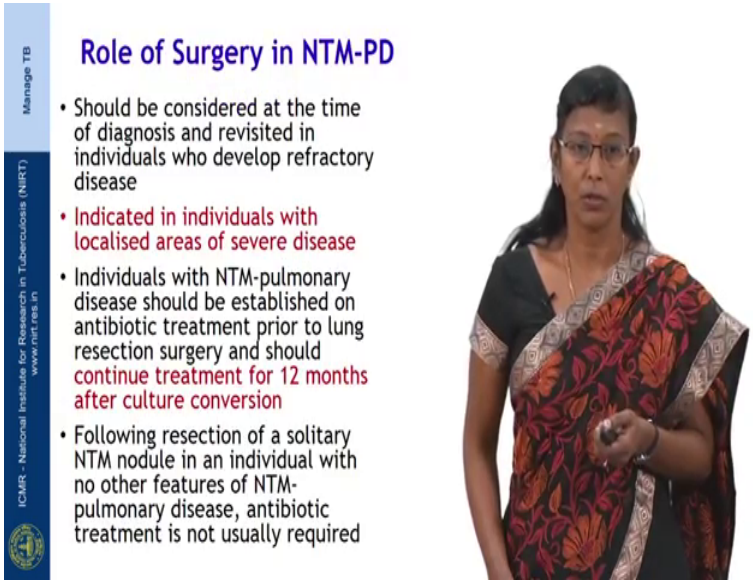

Is there a role of surgery in NTM pulmonary disease? Yes, surgery should be considered at the time of diagnosis and again revisit when the patient becomes refractory to treatment after 6 months of appropriate regimen.

It is usually indicated in individuals with localized areas of severe disease, individuals with NTM pulmonary disease should be established on antibiotic treatment prior to lung resection. They should also continue the same treatment for 12 months after culture conversion. In case the patient continues to have smear positivity and you are waiting for the culture results the antibiotic to be continued even in the post surgical period.

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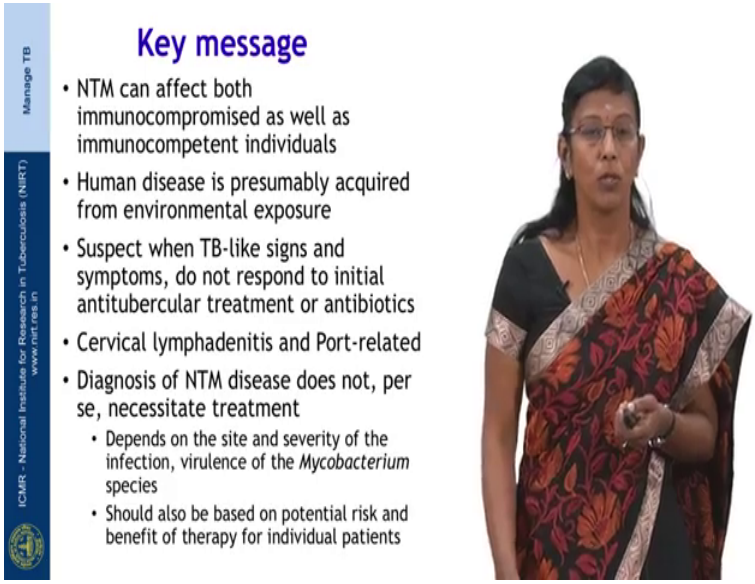

ah So, we to end our session on NTM pulmonary disease as well as other NTM disease the key messages from this lecture we would like to inform that NTM can affect both immunocompromised as well as immunocompetent individuals. Human disease is specifically acquired from the environmental exposure, suspect NTM disease when TB like signs and symptoms do not respond to initial antitubercular treatment or antibiotics.

Cervical lymphadenitis and port related NTM disease are being more frequently seen and have to be suspected when they do not respond to the regular treatment. Diagnosis of NTM disease is laboratory based it does not per se necessitate treatment.

The treatment of NTM disease depends upon the site, the severity of the infection as well as the virulence of the organism. Hence, identification of the speeches of mycobacterium is the cornerstone for the management of NTM disease, and once identified treat the species appropriately with the given regimen with this we come to the end of NTM session.

Thank you.