Manage TB
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Lecture – 52
Non-tuberculous Mycobacteria: Diagnosis & Clinical management Session 1

Hello I am Dr. Padmapriya and we will discuss about Non-tuberculous Mycobacteria its diagnosis, and clinical management in the next couple of slides.

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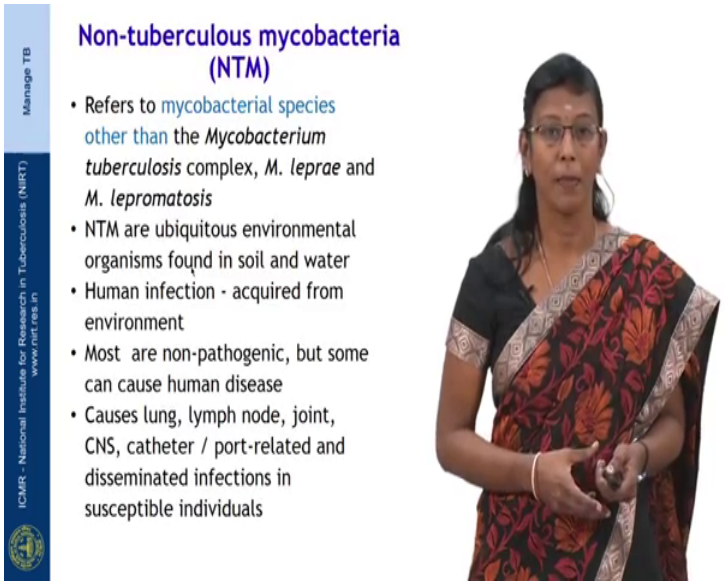

A non-tuberculous mycobacteria refers to mycobacterial species other than mycobacterium tuberculous complex, M. leprae and M. lepromatosis. These are ubiquitous organisms in the environment found in soil and water, and humans acquire the infection from the environment.

Most of them are non pathogenic, but some can cause human disease. They usually effect the lungs, lymph node, joints, CNS, infection is also been reported from catheter as well as laparoscopic port sites. They can also cause disseminated infection in susceptible, or immune compromise individuals.

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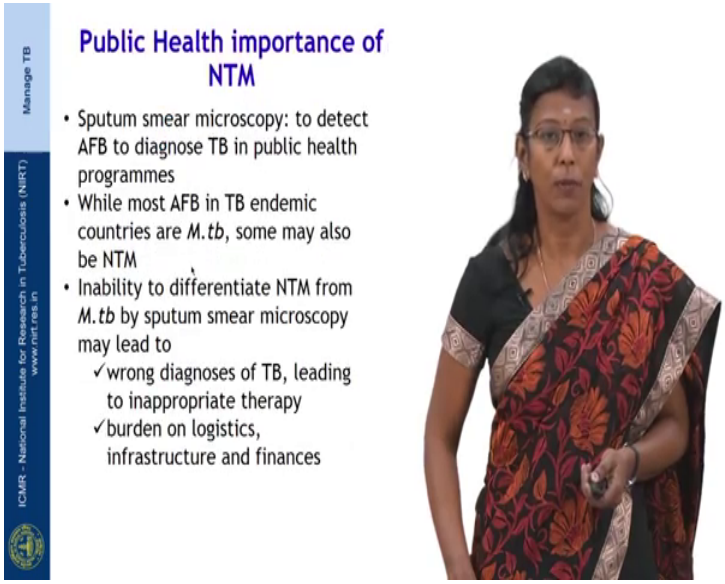

Now what is so important about these NTM's? Now sputum smear microscopy that is a corner stone of diagnosis of acid fast bacilli in public health programs can detect these NTM's as acid fast bacilli positive. The moment AFB positive is detected, this is diagnosis tuberculosis and in many they are treated for M tuberculosis.

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The inability to differentiate between NTM from M tuberculosis by sputum microscopy, may lead to wrong diagnosis, and resulting in inappropriate treatment, in turn increasing the burden on logistics infrastructures as well as finances. Now, NTM's are often

resistant to antibiotics and anti tuberculosis treatment that is commonly used in the national programs.

It can also be misdiagnosed as multiple multidrug assistant tuberculosis, when they do not respond to the regular anti TB treatment. Increasing notification of mycobacterial disease as either relapse of TB or drug resistant can also be because of increasing a non tuberculous mycobacterial infect.

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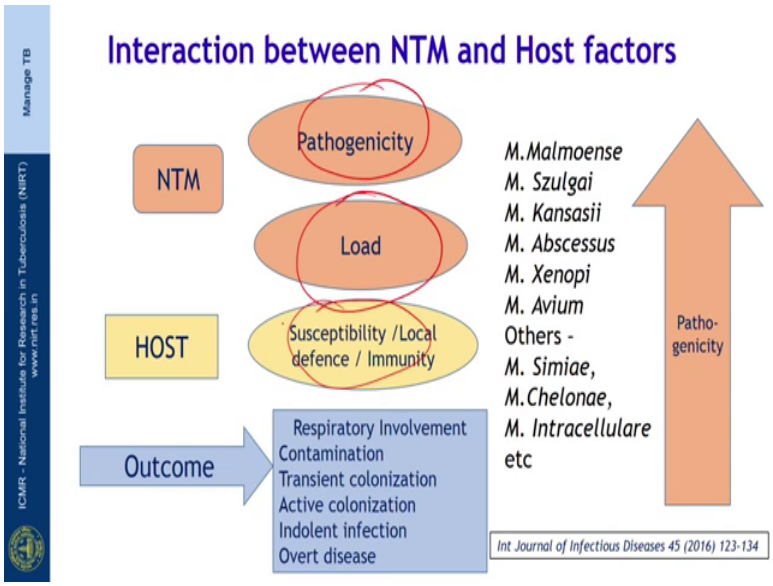

Now, what is a interaction between non tuberculous mycobacteria and the host factor? Now NTM pathogenicity depends upon the load of the organism in the effected host and also what the species of NTM that is causing the infection. In the host factor susceptibility of the host basically its immune compromise, or immune competent state as well as local defence mechanism plays a major role.

Now, both the interaction of NTM pathogen as well as the host or the bug and the host results in a variety of outcomes. It could be simple contamination of the respiratory tract, or a any of the body tracts or it could be a transient colonization it can also go on to overt disease.

Now, pathogenicity of NTM is what is listed on the right side of the slide? The pathogenicity increases from bottom to up it starts from intracellulare which is a least

pathogenic organism and as you see as it goes up kansasii, or malmoense is the most pathogenic organism causing human disease.

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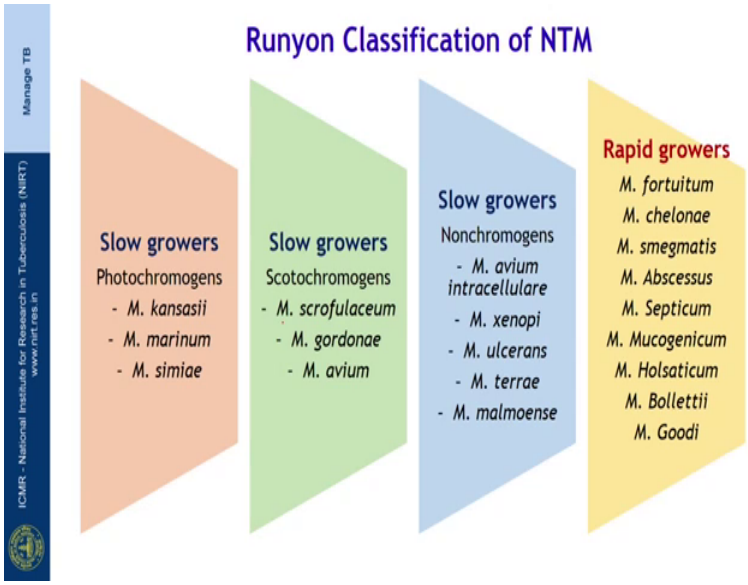

Runyon classification of NTM divides the non tuberculous mycobacteria into 2 groups; slow growers and rapid growers. Among the slow growers we have M kansasii causing pathogenic disease, scrofulaceum M avium, M intracellulare, M xenopi, all of these are commonly encountered in human human causing lung infections, or lung disease.

Among the rapid growers we have variety of organisms stratify M fortuitum, smegmatis, M abscessus, and M bollettii all of them resulting in pathogenic disease in humans.

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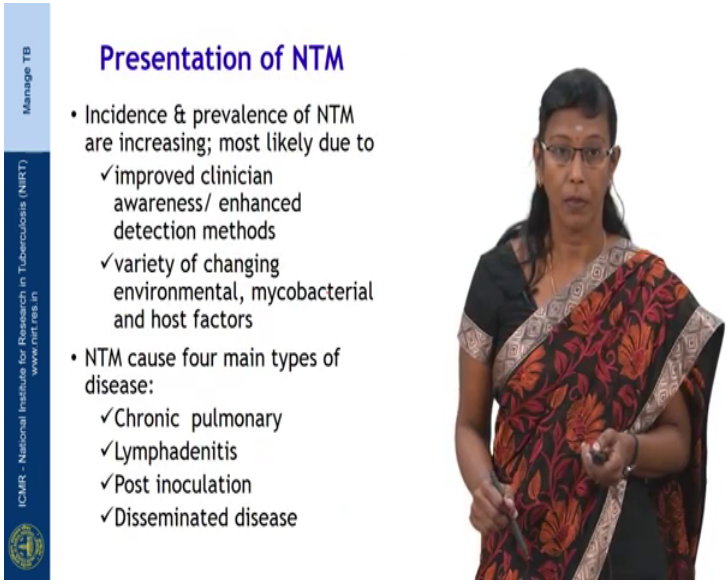

NTM can present either in the form of chronic pulmonary disease, or lymphadenitis, or it could be post inoculation either in form of laproscopic ports or catheter in catheter. It can also cause disseminated disease, increasing incidence and prevalence of NTM is commonly seen it mainly due to improved clinician awareness, or because of enhanced detection methods that is used to diagnose NTM and speciate them.

It is also due to variety of changing environmental factors, mycobacterial, and host factors.

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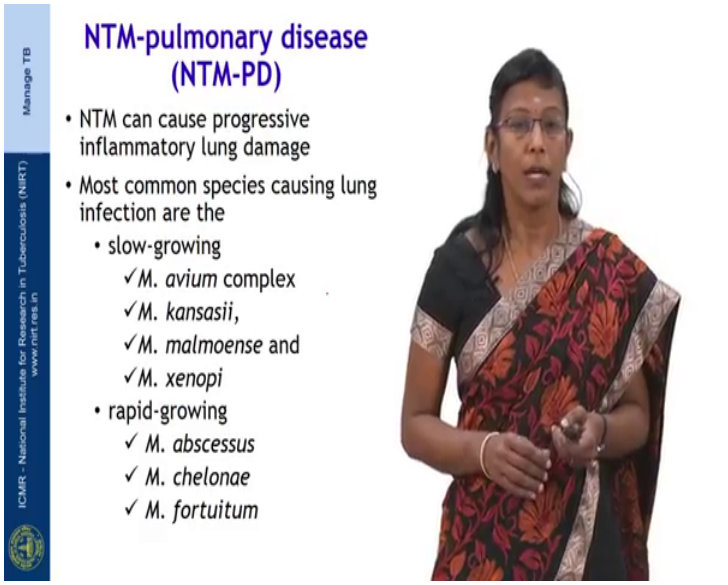

Now, since NTM pulmonary disease has a major impact on a public health scenario. I would like to discuss NTM pulmonary disease in the next few slides. NTM can cause progressive inflammatory lung damage, it can be due to both slow growing as well as rapid growers. Among the slow growers of clinical importance are M avium complex, M kansasii, and M xenopi and among the rapid growers we have M abscessus, and M chelonae along with M fortuitum.

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These vary in distribution not only between the countries, but also within the countries even there is a variation between the north and south of a country. The species also differ in the pathogenic potential, and most of them present with respiratory symptoms very again to tuberculosis.

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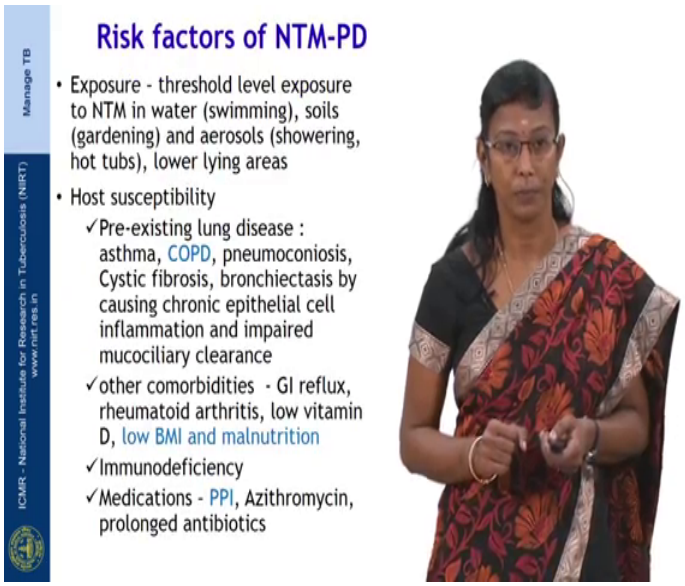

So, the non tuberculous mycobacterial pulmonary disease there are various risk factors both among the exposure as well as in the host factors. Among the host factors a most important of pre existing lung disease like asthma, COPD, pneumoconiosis, or bronchiectasis.

Other comorbidities like rheumatoid arthritis, or low vitamin D, low body mass index malnutrition all of them can contribute to a person getting infected with NTM's. Some of the medication that are commonly used that proton pump inhibitors, or prolonged use of antibiotics can also make an individual susceptible to NTM.

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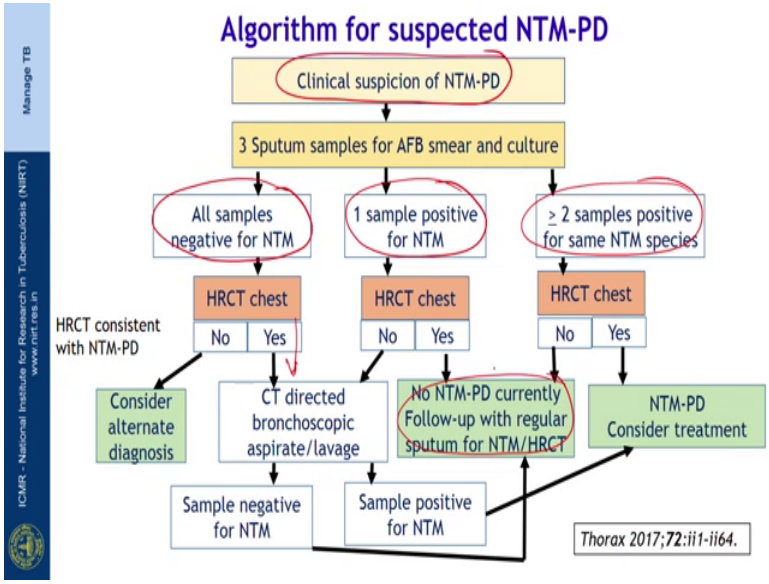

So, how do we diagnose NTM pulmonary disease? When an individual presence to a clinician with symptoms of cough, and fever and not responding to the regular anti tuberculous, or anti bacterial treatment. There should be high suspicion of NTM pulmonary disease three sputum samples are collected and sent for acid fast bacilli by smear microscopy and also culture.

Now if all the three AFB smears comes negative in the culture for NTM, but the clinical suspicion still persisting. Then a CT scan chest it is in order city scan chest is suggestive of NTM, you can do a bronchoscopic aspirate and lavage send it for culture again. If the city scan chest is negative for lung pathology consider alternate diagnosis.

The same time if all the two if any two of the three sputum comes is positive for NTM species you can still order a HRCT. And if the HRCT is positive for NTM then you consider treatment for non tuberculous mycobacteria. If HRCT is negative then you think for other diagnosis alternate diagnosis of this pulmonary infection.

Now, of the 3 sputum samples what to do if we have only one sputum sample that is positive for NTM? These are the cases where HRCT is recommended strongly, if HRCT is negative for NTM, CT directed bronchoscopy is very much warranted the aspirate or lavage is sent for NTM culture. At the same time if HRCT shows positivity, then the patient cultures are negative it is warranted to follow up the patient regularly with repeats

sputum, and HRCT. And if any of those culture becomes positive patient has to be treated for NTM pulmonary disease.

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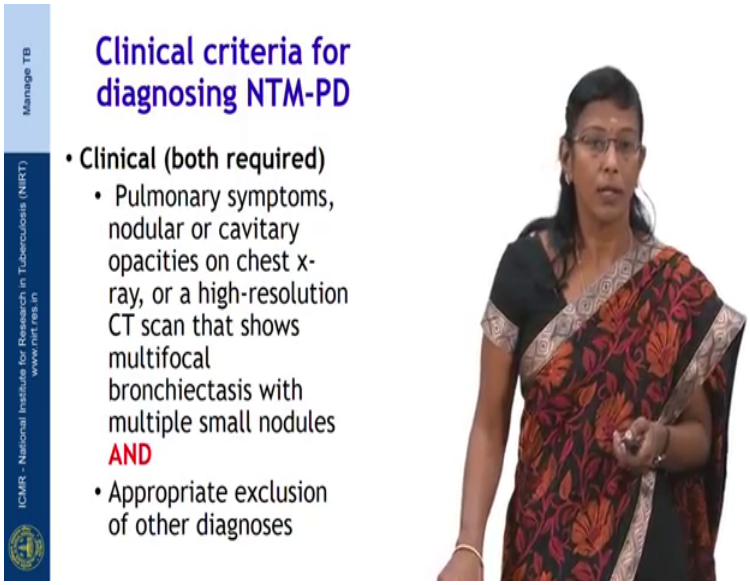

What are the clinical criteria for diagnosing NTM pulmonary disease? So, this is from the ATS guide lines as well as the British Thoracic guidelines for management NTM disease. In clinical there are clinical criteria as well as microbiological criteria.

The clinical criteria all the all the criteria should be positive and they are pulmonary symptoms plus chest x-ray showing nodular, or cavitary opacities, AND city scan showing multifocal bronchiectasis, with multiple small nodules, all of this plus exclusion of other diagnosis of pulmonary disease.

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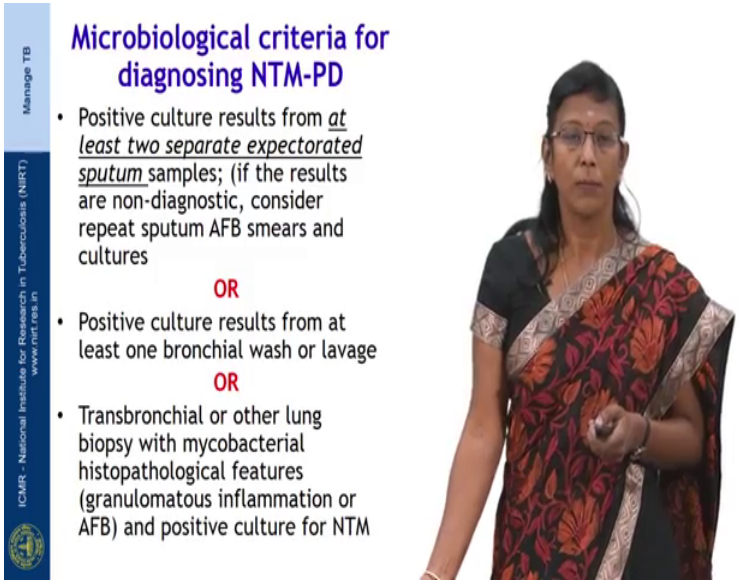

Looking at the microbiological criteria we have three criterias and they are alternate criterias. We should have positive culture from at least two separate expectorated sputum sample, or one positive culture from bronchial wash or lavage, or a transbroncial or other lung biopsys with a mycobacterial histopathological features, and positive culture for NTM.

So, we need to have a clinical criteria as well as some microbiological criteria positive to diagnose a case of NTM.

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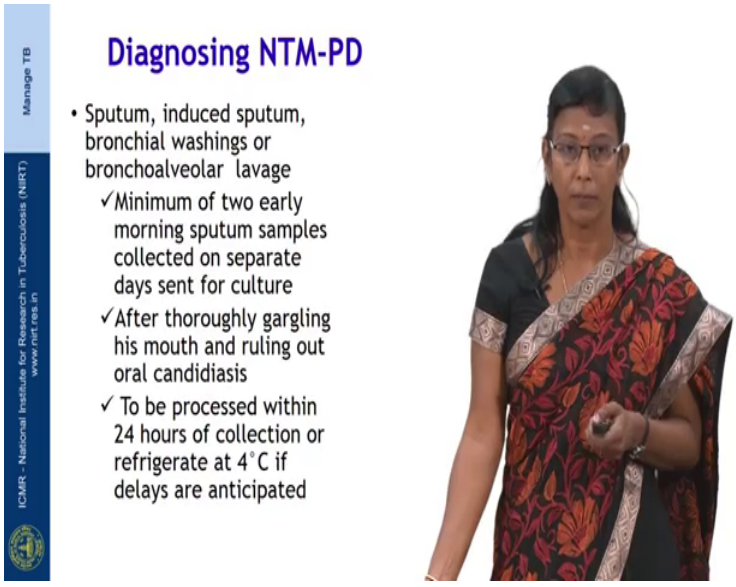

The sputum could be an induced sputum and the induced sputum you need to have minimum of two early morning sputum samples collected on two separate days and sent for culture. Now, the sputum collection to be done after thorough thoroughly gargling his mouth, and ruling out oral candidiasis.

Now, if you remember immune compromised state is one of the very important state where you diagnose NTM pulmonary disease, therefore, it is very important to rule out oral candidiasis before a sputum is collected for NTM. The sample collected to be processed within twenty four hours of collection and if it is not possible to refrigerate the sputum sample at four degree if delay is anticipated ah.

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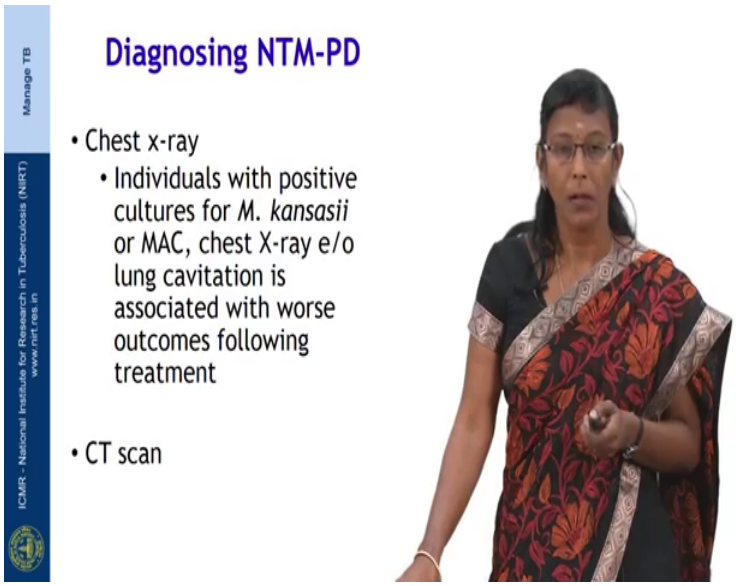

Looking at the investigations chest x-ray is a mandatory investigation for NTM pulmonary disease individuals with positive cultures of M kansasii or MAC, chest x-ray evidence of lung cavitation is an important prognostic factor during the a treatment follow up.

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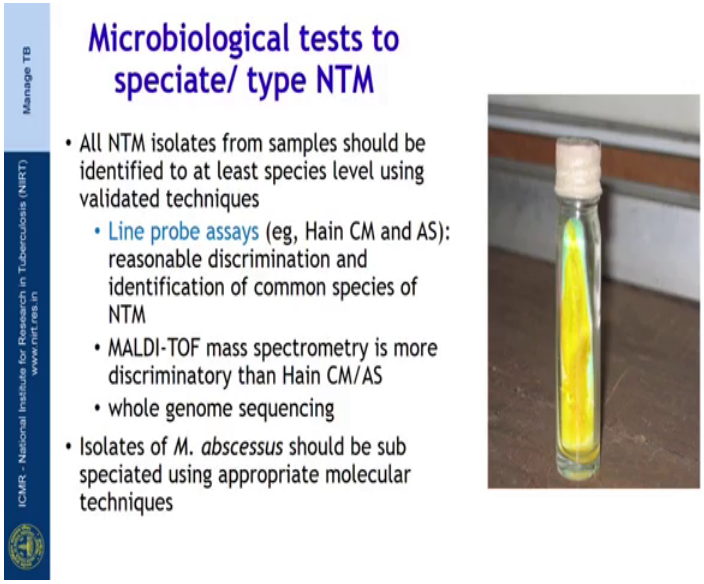

As we discussed before CT scan is another important diagnostic tool for NTM pulmonary disease. Now, coming to the microbiological test most important test for diagnosing NTM is the identification of the species.

All NTM isolates from the sample should be identified at least to the species level using validated techniques, few of the techniques that are commonly used are line probe assays, and MALDI TOF mass spectrometry.

These two tests help us to identify the species level of non tuberculous mycobacteria. Whole genome sequencing is also now being more commonly used more detail of these test where discussed in the previous lecture on diagnosis of M mycobacterium.

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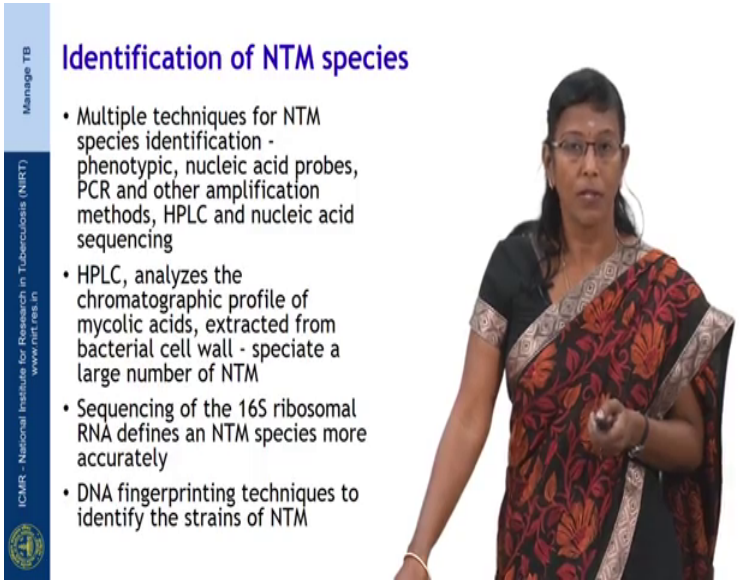

Now, the yellow yellow picture that you see on this slide is nothing, but a culture of M kansasii. Now, multiple techniques have been used to speciate these which includes as I said PCR technique, or HPLC methodology these. And also 16S ribosomal DNA defines NTM species more accurately many of these test may not be available in all centres. But they can always be sent to a tertiary level before we start treating a patient of NTM pulmonary disease.

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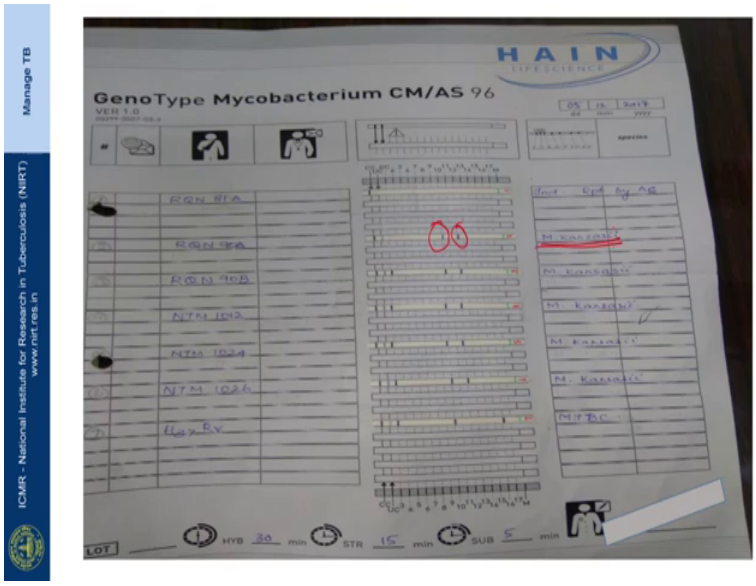

This slide shows various banding so these are the bands that you see these are very fixed bands on a line probe assay. And they diagnose it is a predefined bands which diagnose the species of the NTM.

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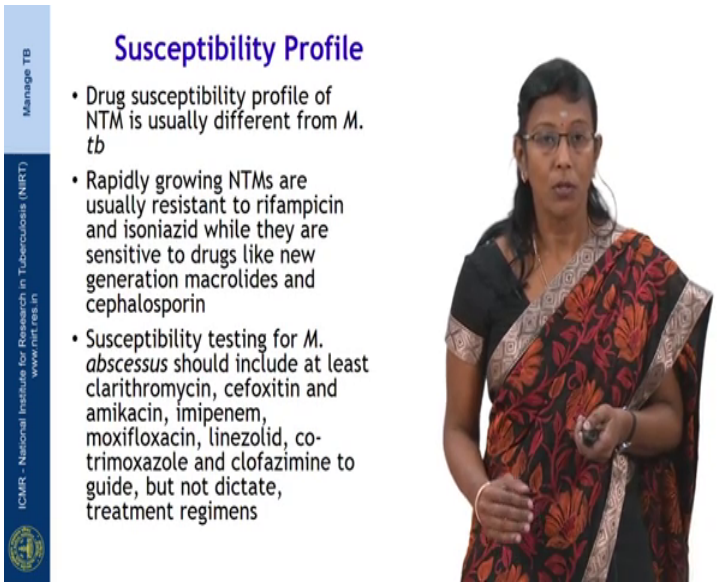

So, we cannot stop just with that identification of the species of non tuberculous mycobacteria. What we also have to do is? Drug susceptibility profile of these NTM because they vary for each organism and they are very much different from M tuberculosis.

The rapidly growing NTM are usually resistant to rifampicin and isoniazid; while they are sensitive to other kinds of macrolides and cephalosporins. Susceptibility testing for M abscess also varies and they need to have a larger group of drugs where a DST has to be ordered.

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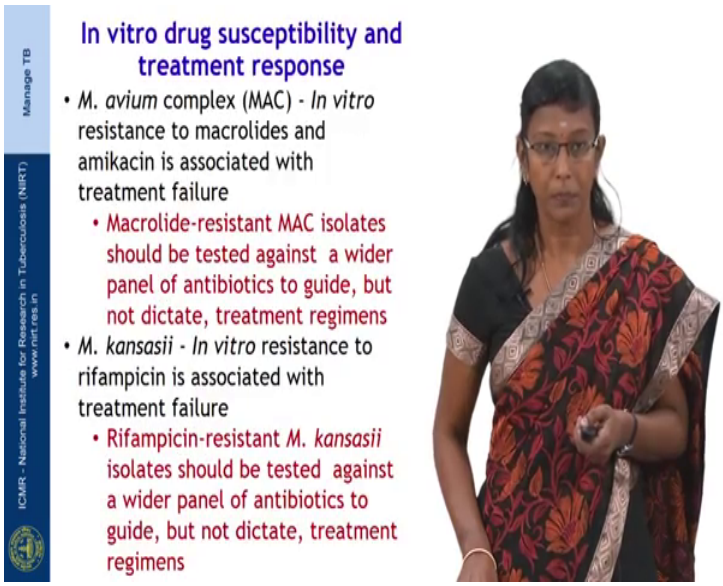

Other important reason why you should have a drug susceptibility profile? Some of the drug susceptibility pattern may not correlate so well with the clinical response of a patient. And they also form a prognostic indicator for the treat for the management of these patients.

Especially in cases of MAC or M avium complex resistance to macrolide as well as to amikacin is has been shown to be associated with treatment failure. Also M kansasii the in vitro resistant to rifampicin is a very high prognostic marker for treatment failure to M kansasii pulmonary disease.

Thank you with this we come to the end of session one.