Manage TB
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Lecture – 20
Approach to diagnosis of Pulmonary TB

Dear friends, very Good morning. In today's session we are going to talk about Approach to diagnosis Pulmonary Tuberculosis. I am Dr. Rupak Singla, I am heading the department at National Institute of Tuberculosis and Respiratory Diseases; New Delhi.

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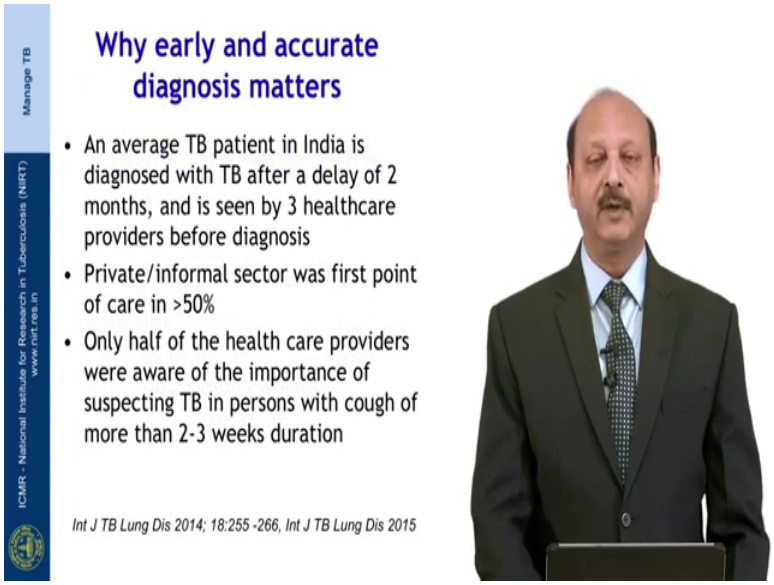

You see if you look at the private sector in India the TB diagnosis; an average TB patient in India is diagnosed TB after delay of 2 months and is seen by 3 healthcare professionals before the diagnosis of TB is made. And not only that the private sector was the first point of care in more than 50 percent of cases in several studies. And on top of that only half of the healthcare providers were aware of the importance of suspecting TB in person with cough more than 2 to 3 weeks, which we all know is the commonest symptom of pulmonary tuberculosis.

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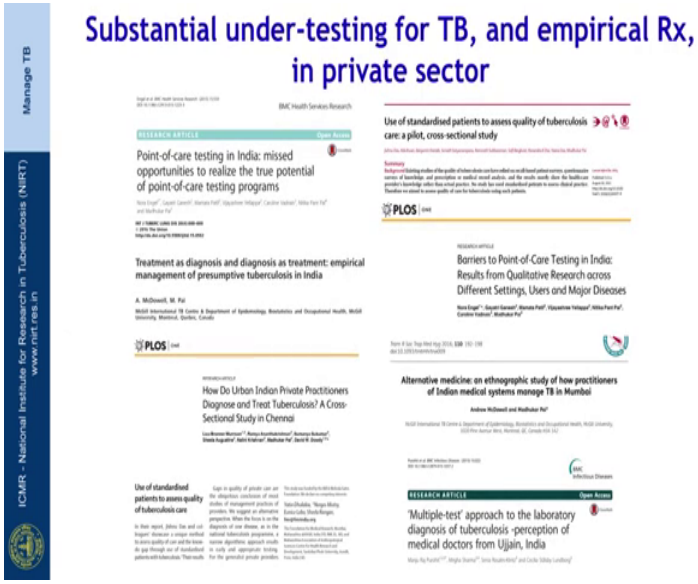

Several studies across the country have shown that in the private sector there is substantial under testing for tuberculosis and medical treatment is being started.

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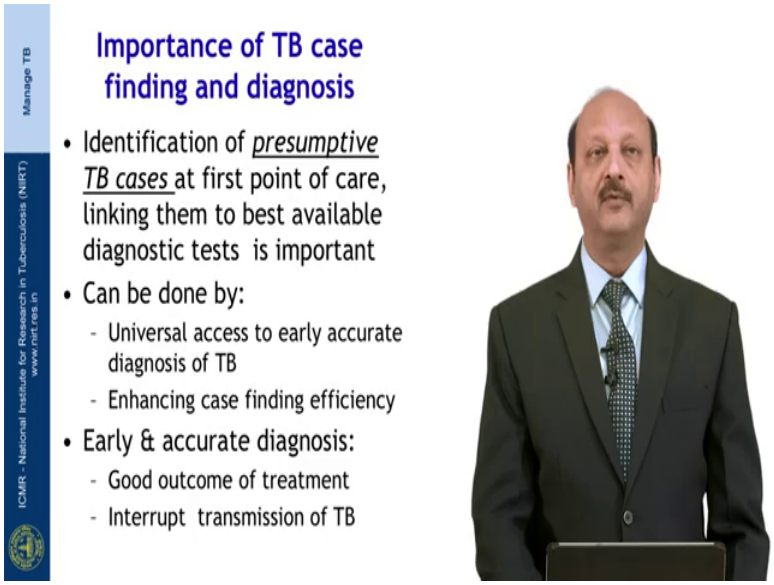

The importance of TB case finding and diagnosis cannot be over emphasized. Their identification presumptive TB cases at the first point of care and linking them to the best available diagnostic test; it can be done and can be done by universal access to the early and accurate diagnosis of TB and enhancing the case finding efficiency. The early and

accurate diagnosis of TB once we achieve it; it will lead to good often of treatment and also interrupt the transmission of TB to the others in the community.

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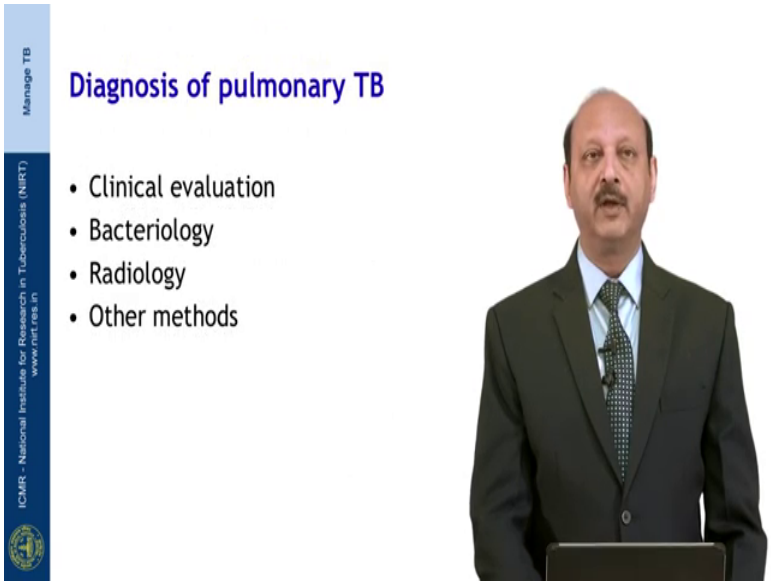

When we talk about diagnose pulmonary tuberculosis; always the initial thing is clinical evaluation, then bacteriology, radiology and other methods they come in to picture. .

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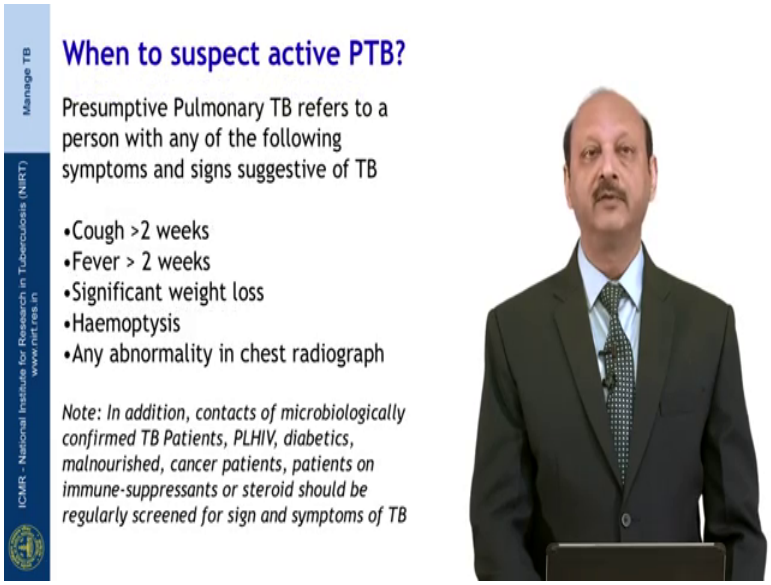

First thing is when to suspect permanent tuberculosis? So, they are called presumptive pulmonary TB it refers to a person with any of the following symptoms and signs which suggestive of tuberculosis; which includes cough for more than 2 weeks, fever for more

than 2 weeks, significant weight loss, haemoptysis or any abnormality in the chest radiograph suggesting tuberculosis. In addition, we need to remember that contacts of microbiological confirmed TB patients, people living with HIV, diabetics, malnourished, cancer patients, patients on immunosuppressive drugs or steroids they should be regularly screened for symptoms and signs of tuberculosis.

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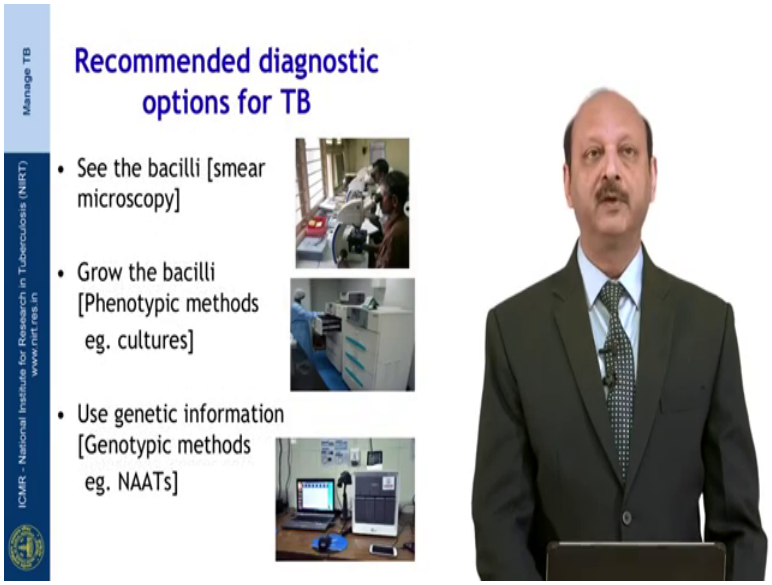

Once you suspect tuberculosis the recommended diagnostic options for tuberculosis are that we see the bacteria; that is smear microscopy or we grow the bacteria called phenotypictus like cultures or we use is the genetic information they are called genotypic methods.

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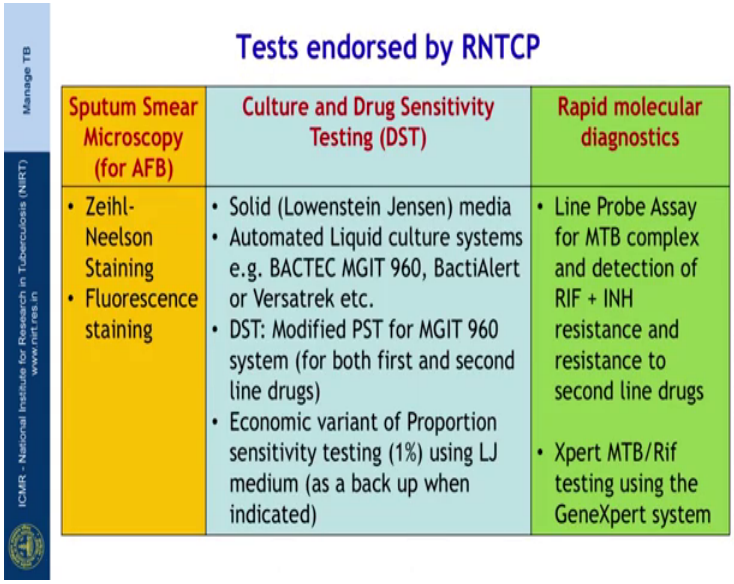

The test which have been endorsed by our national program that is revised national TB control program include sputum smear microscopy for AFB that is zeihl-neelson staining and fluorescent staining.

The culture and DST include the solid that is Lowenstein Jensen media. The automated liquid culture system that is BACTEC MGIT 960 or Bactialert or Versatrek; the DST includes modified PST for MGIT 960 system for both first line drugs as well as second line drugs or we can use economic variant of proportion sensitivity testing that is 1 percent using LJ media as a backup whenever indicated.

Among the rapid molecular test we have line probe assay for MTB complex, which helps in the detection of resistance against INH plus RIF remphasin and also against resistance to the second line drugs. Then we have expert MTB Rif testing using the genexpert system.

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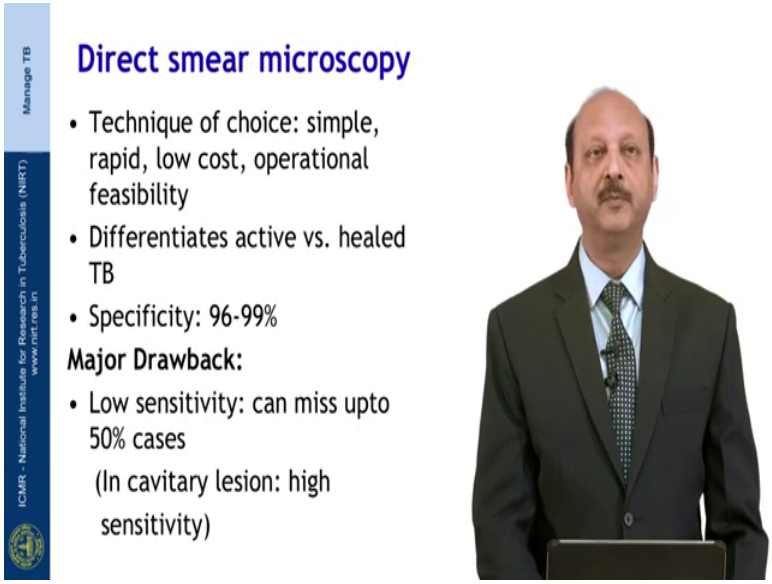

Coming to the direct smear microscopy; it is a technique of choice because it is simple, it is rapid, has a low cost and operational feasibility. It differentiates between active and healed tuberculosis and the specificity is very high to the tune of 96 or 99 percent, but it has some drawbacks; it has a low sensitivity and can mess up to 50 percent of cases although in cavitary lesions, the sensitivity is very high it can go up to 80 or 90 percent.

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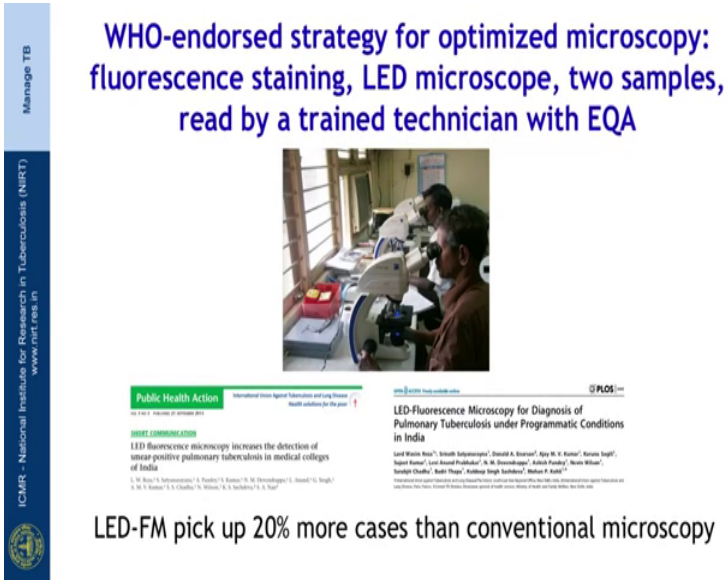

The WHO endorsed strategy for optimized microscopy includes fluorescent staining, LED microscope using 2 samples read by trained technician with the external quality

assurance. And it has been shown that led fluorescence microscopy it can pick up 20 percent more cases than the conventional microscopy.

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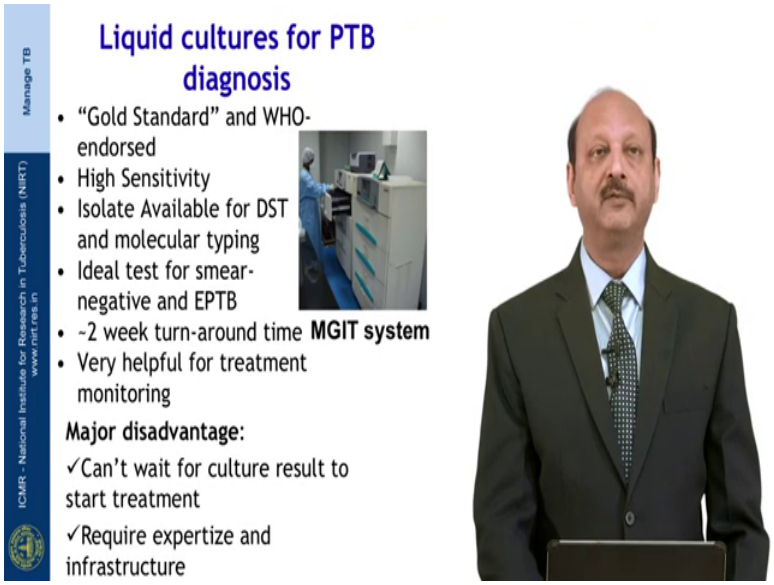

The liquid culture for the PTB diagnosis it is a gold standard and WHO endorsed, they have high sensitivity and the isolates are available for DST and molecular test typing as well and their ideal test for smear negative an extra-pulmonary tuberculosis.

However, they have 2 week turnaround time and they are very helpful in treatment monitoring also because you want to know whether the bacteria are dead or monitoring or not; however, they have some disadvantages that, most of the time treating position cannot wait for the cultural result to start the treatment and it can take 2 2 3 to 4 weeks and also the liquid culture they require expertise and infrastructure.

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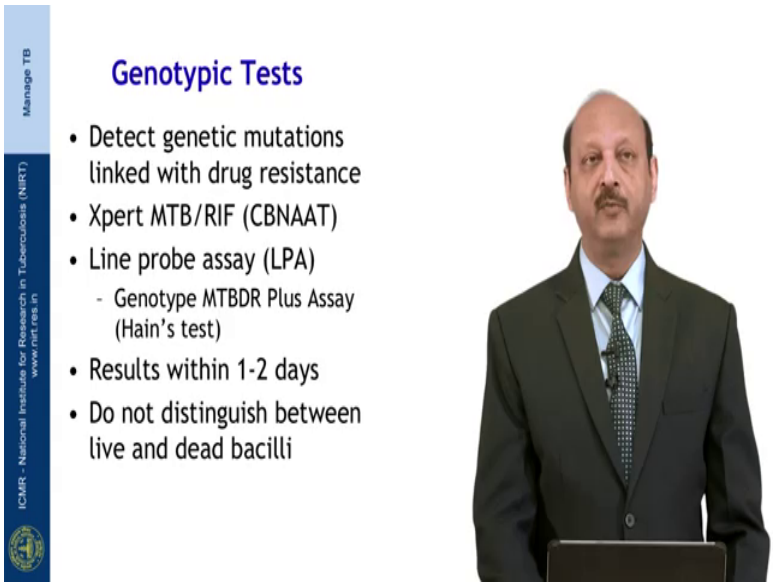

Coming to the genotypic test; they detect the genetic mutations which are linked with the drug resistance. And in this category we have export MTB RIF that is cartidridge space, nucleic acid amplification called CBNAAT and line probe assay called LPA and the genotypic MTBDR plus assay is also called hain test and the results are available within 1 or 2 days but they do not distinguish between live and dead bacteria.

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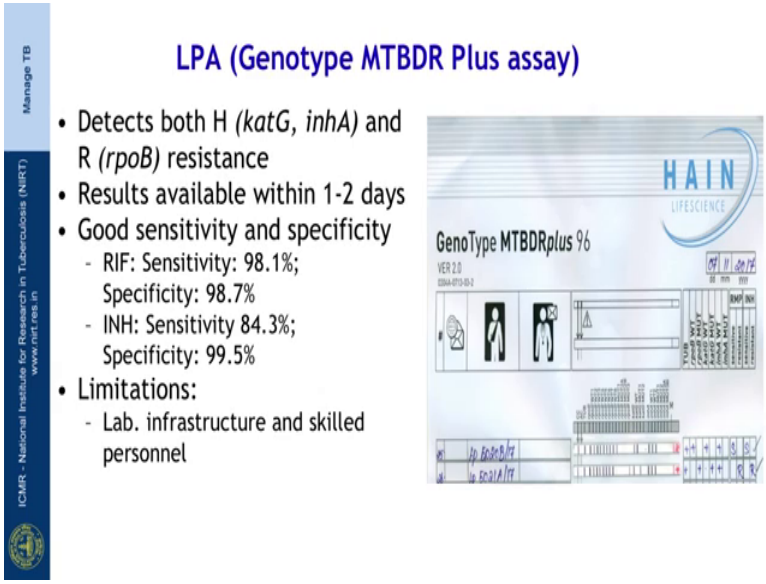

Coming to the LPA that is genotype MTBDR plus assay it detects both INH as well as RIF resistance INH based on the cardigan inhA mutations and RIF resistance based on

the rpoB beam gene mutations; the results of the available within 1 or 2 days the good sensitivity and good specificity, for rephampicin sensitive ors to the tune of 98 percent and specificity also almost 99 percent.

For INH this sensitive was low to the tune of around 84 percent with a very high specificity almost reaching 99.5 percent, but the limitations are that the LPA it needs lab, infrastructure as well as skilled personnel.

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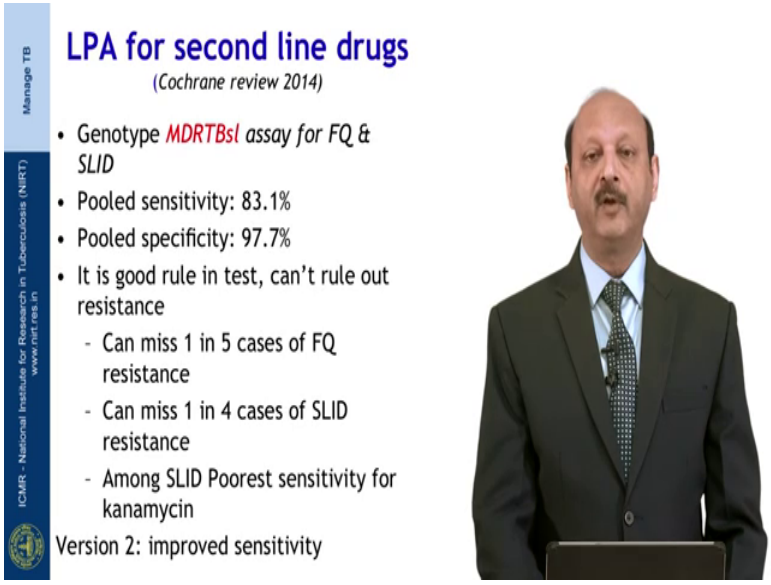

Then we also have a LPA for this second line drugs the cochrane reviews 2014; it showed that this LPA for second line drugs also called MDRTB second line assay for fluoroquinolones and second line injectable drug that pooled sensitivity of 83 percent and pooled specificity of almost 100 percent.

It is a good role in test, but cannot rule out the resistance; that means, in case LPA is tells it is resistance it is resistance, but if it says it is sensitive; it may not be sensitive. DLP can miss 1 and 5 cases of product non resistance, it can miss 1 in 4 cases of second line injectable resistance and among the second line ejectibles the poorest sensitivity is for the kanamycin. And there is version 2 now available in the market and our national program using version 2, it has improved sensitivity to the tune of up to 90 percent.

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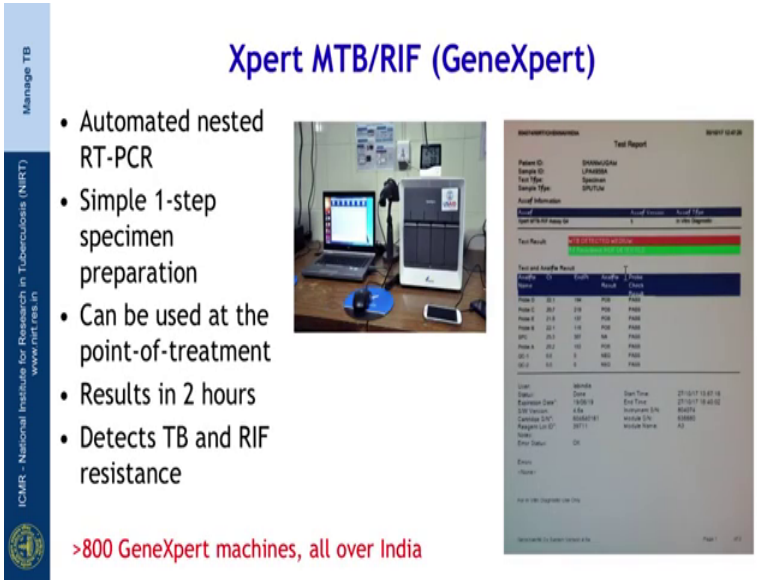

The Xpert MTB RIF is also called GeneXpert it is a automated nested RT-PCR. It is a simple one test specimen preparation that can be used at the point of treatment that is wherever the treatment is being planned, it can be used there. The results are available within 2 hours and detects TB and RIF resistance, but does not tell us about the INH resistance.

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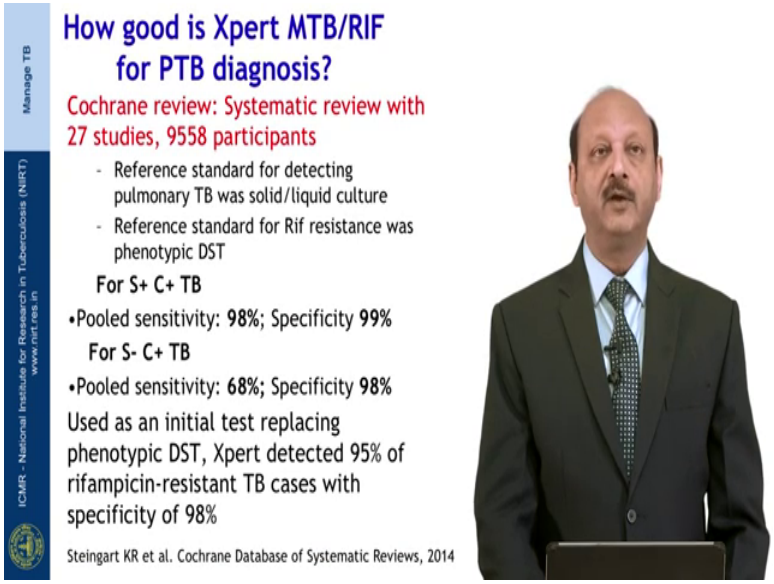

Then looking at the how good is GeneXpert for PTB diagnosis, a cochrane review including 27 studies and almost 9500 patients, it showed that using the reference

standard for detecting TB as a liquid culture. And reference standard for RIF resistance as a phenotypic DST for smear positive and culture plus tuberculosis the pooled sensitivity are 98 percent and specificity 99 percent.

Even amongst smear negative culture positive cases, the sensitivity was 68 percent specificity 98 percent. So; that means, even if person is sputum smear negative where LPA cannot be used it could detect up to 70 percent of patients and used as an initial test replace in phenotypic DST, Xpert detected 95 percent of rifampicin resistance TB cases with specificity of 98 percent.

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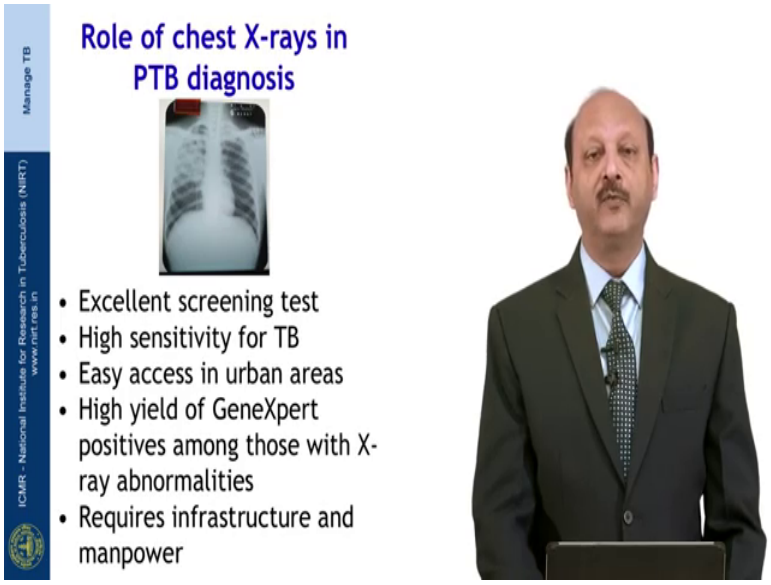

Coming to the role of X-ray in the PTB diagnosis; it is a excellent screening tool it has a high sensitivity for the tuberculosis and has easy access in the urban areas. And among those with X-ray abnormalities the gene expert can have very high yield; however, as we all know it required infrastructure and manpower.

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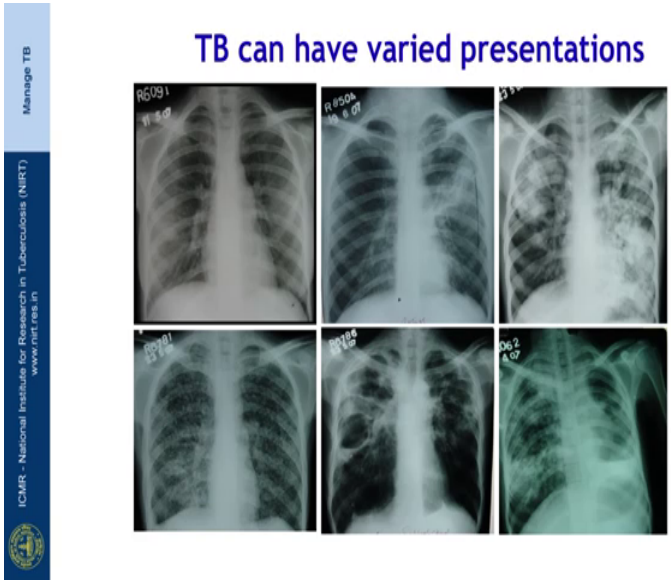

And we know the TB can have varied presentation it can be minimum involvement, it can have consolidations, it can have bilateral (Refer Time: 09:34) consolidation with fibroses, it can have miliary shadows, it can have cavitary shadows, it can have also involve the pleura with (Refer Time: 09:42) and we all need to remember TB can be make anything and anything make tuberculosis.

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The RNTCP recommendation on chest X-ray use are that the chest X-rays to be used as screening tool; to increase sensitivity of the diagnostic algorithm. And any abnormality

in chest X-ray should further be evaluated for TB including the microbiological confirmation. And diagnosis based only on the X-ray can result in significant over diagnosis and some amount of under diagnosis as well.

In the absence of microbiological confirmation, we require a careful clinical assessment for TB diagnosis and diagnosis of TB based on X-ray is labeled as clinically diagnose tuberculosis.

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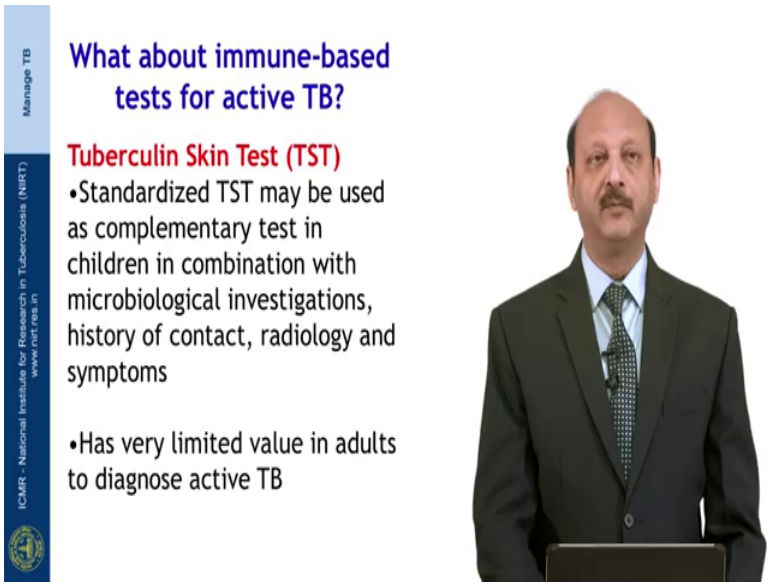

What about the immunological based test for a active tuberculosis? First coming to the tuberculin skin test also called as TST. In children this standardized TST may be used as a complementary test in combination with microbiological investigations, history of contact, radiology and other symptoms by it is limited value in adults to diagnose active tuberculosis.

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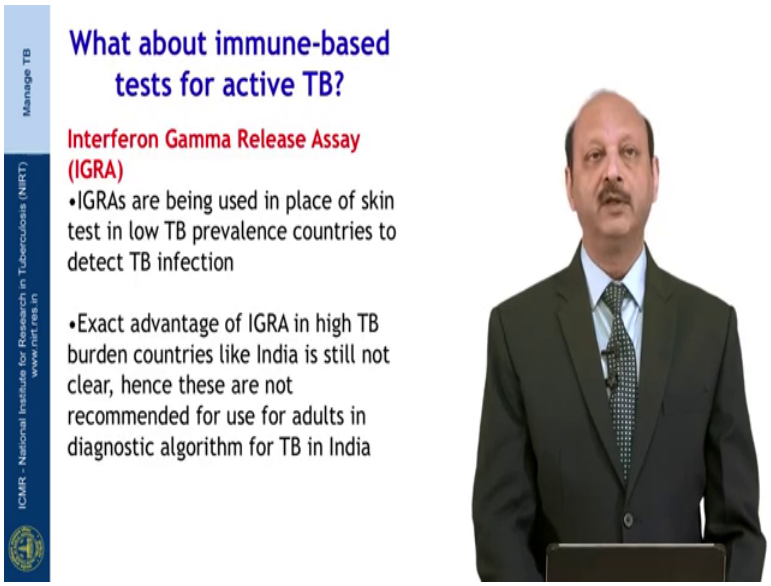

Talking about the interferon gamma release assay is called IGRAs they are being used in place of skin test in low TB progress countries to detect TB infection not the disease is an exact advantage of IGRAs in high TB burden countries like our country. It is still not clear and hence these are not recommended for use for adults in diagnostic algorithm for TB in India.

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And in India the serological test are banned for TB diagnosis in 2012 the Government of India released a gazette notification where they banned the manufacture, importation,

distribution and use of currently available commercials serological test for diagnosis of tuberculosis.

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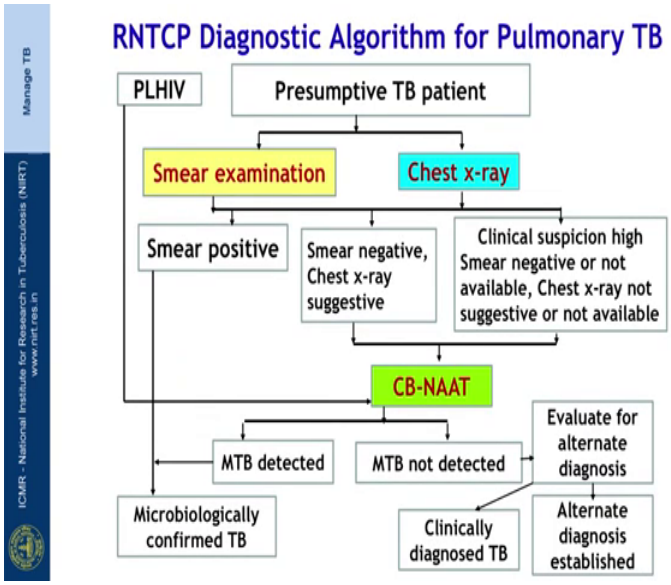

Coming to the RNTCP our national program diagnostic algorithm for pulmonary tuberculosis; first step is the whenever we suspect tuberculosis on clinical ground that is called presumptive TB patient; we offer smear examination and chest X-ray whenever it is a variable. If the smear shows smear positive this patient is labeled as microbiologically confirm tuberculosis.

If smear is negative or the chest X-ray suggestive tuberculosis or another scenario technical suspicion is high, but smear is negative or not available and chest X-ray is not suggestive or is not available then they are offered the CB-NAAT. In people living with HIV then they are offered the CB-NAAT examination up front, after CB-NAAT either we can have MTB detected again the diagnosis microbiologically confirmed tuberculosis in case MTB is not detected these patients are offered other test and where were for alternative diagnosis. After these test we can have clinically diagnosed tuberculosis or we can have alternative diagnosis established.

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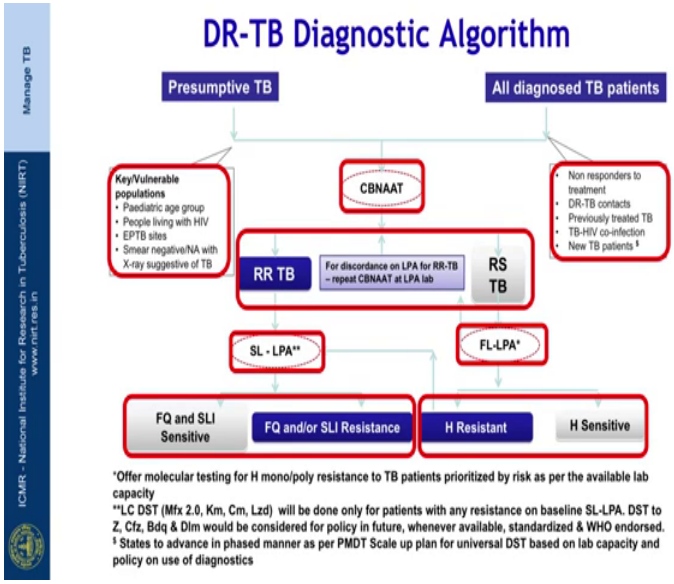

Coming to the algorithm diagnostic algorithm for drug resistance tuberculosis so one is the presumptive pulmonary tuberculosis cases where we offered the CB-NAAT upfront or we have clinically the all the diagnosis case tuberculosis. Among presumptive TB cases like paediatric age group, the people living with HIV or we have extra pulmonary tuberculosis or EPTB cases in these cases upfront CB-NAAT is offered or in other cases where the TB has been diagnosed.

But these cases belong to the category of either they are DRTB contacts, they are previously treated TB cases, they are TB HIV cases or they are not responds to the TB treatment that is the fall of sputum positives. And sometimes the new TB patients which are in the higher scale of the PMDT implementation they can also be offered CB-NAAT upfront.

Once the CB-NAAT report is available we have either rifresistance tuberculosis or we can have rifsensitive tuberculosis and whenever there is a mismatch between the CB-NAAT and the LPA the repeat CB-NAAT is to be done. So, after the RIF resistance TB cases is diagnosed then we do the second line LPA test and is second line LPA test shows fluoroquinolones and or second line rejectible sensitive. Then we can further do the resistance pattern against injectables that is kanamycin and capreomycin and (Refer Time: 15:05) and in case the FQS and the SLI's are sensitive they may be offered short

MDRTB regimen; however, in case you find resistance to the fluoroquinolones or second injectable resistance then DST guided treatment is to be offered to them.

On the other hand, suppose it is found to be rifsensitive tuberculosis on CB-NAAT examination then we do the LPA. If LPA tells us it is h resistance they are offered treatment for INH resistance cases and in case h is sensitive they are given standardized treatment for the new smear positive cases in the country.

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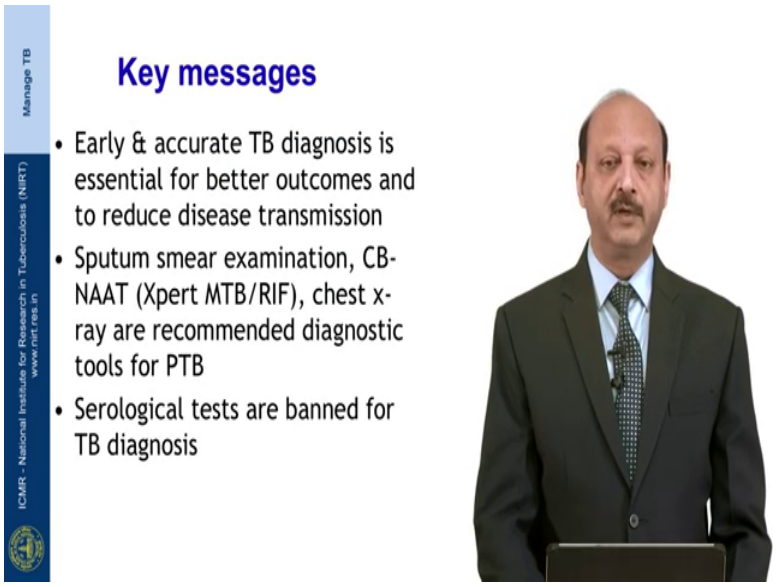

So, dear friends the key messages for diagnostic algorithm for tuberculosis are been must keep in mind that early and accurate TB diagnosis is essential for better outcomes and to reduce disease transmission in the community. Sputum smear examinations, the CB-NAAT that is expert MTB RIF and chest X-ray are recommended diagnostic tools for pulmonary tuberculosis and serological tests are banned for TB diagnosis.

Thank you very much.