Manage TB
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Lecture – 56
Management of Latent TB Infection (Session 1)

Welcome to the session on Management of Latent TB Infection. I am Doctor Banu Rekha; scientists at the National Institute for Research in TB. We will deal this topic in two sessions; the first session will be on the importance of latent TB infection and how to diagnose, the subsequent session will be on the management of latent TB infection through preventive therapy.

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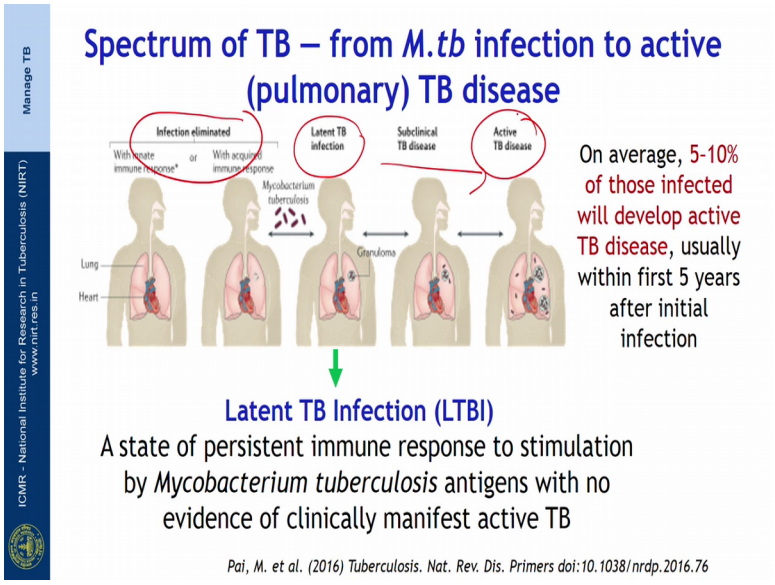

So, before going into the specifics of latent TB infection; it is important to recollect the spectrum of TB from MTB infection to active pulmonary disease.

This has been dealt in detail in the section on pathogenesis; just to refresh your memory on that. After exposure to MTB the infection can be eliminated with innate immune response or with acquired immune response. If the bacteria is not eliminated; they persist in acquire sent or the latent TB stage; known as the latent TB infection.

So, what is latent TB infection? Latent TB infection is a state of persistent immune response to stimulation by mycobacterium tuberculosis antigens with no evidence of

clinically manifest active TB disease, if the individual with latent TB infection has a good host immunity; then there would be no reactivation of this infection.

However on an average 5 to 10 of those infected will developed active TB disease usually within 5 years after initial infection. So, latent TB infection will progress to active TB disease.

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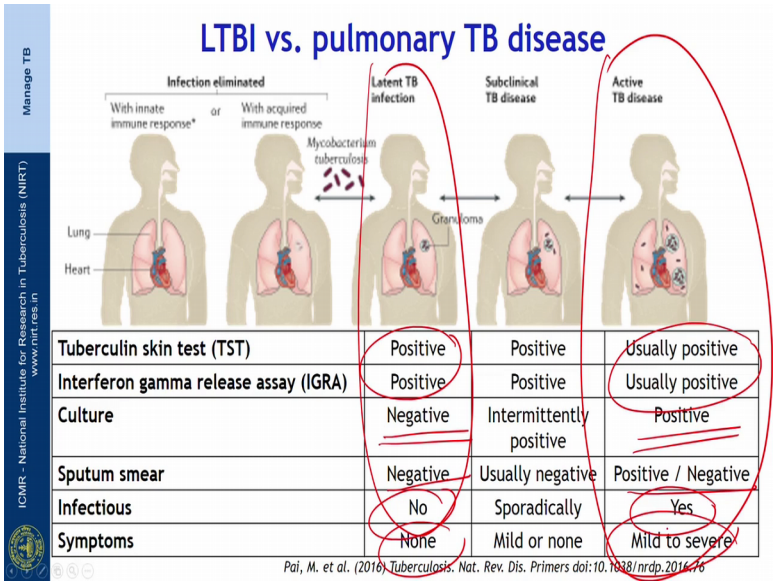

The main difference between latent TB infection and active TB disease; if you can concentrate on these 2 aspects, the first thing is the tuberculin skin test or the interferon gamma release assay which are which are used to detect the latent TB infection would be positive in case of LTBI and the they are usually positive in case of active TB disease, but maybe negative due to energy due to the disease itself or due to co-existing immune compromised conditions especially HIV.

The culture for MTB is negative in case of latent TB infection, while it is positive in case of active pulmonary TB disease. This sputam smear is negative, while in disease it can be positive or negative. Latent TB infection is non-infectious while the active TB disease is infectious. The symptoms the respiratory symptoms are not present in case of latent TB infection, while the symptoms may be mild to severe in case of active TB disease.

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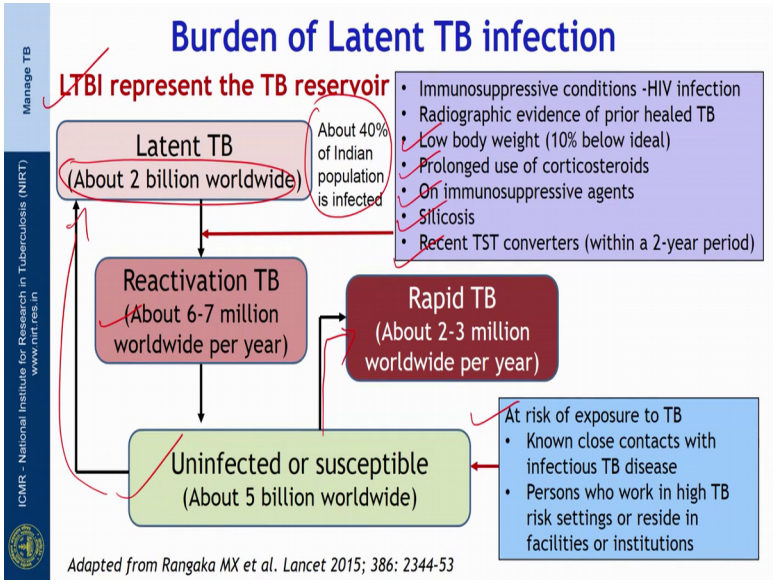

So, why is it important to know about latent TB infection? latent TB infection represents the reservoir of future TB cases.

So, this slide shows the dynamics of for tuberculosis transmission; it is estimated that about 2 billion people worldwide have latent TB infection about 40 percent of Indian population are infected, of them about 6 to 7 million people worldwide develop TB each year. And this is due to reactivation of latent TB infection; which is facilitated by immunosuppressive conditions like HIV infection or there is radiographic evidence of prior heal TB, low body weight; that is less than 10 percent below the ideal weight, prolonged use of corticosteroids or on immunosuppressive agents, silicosis or re recent tuberculin skin test converters that is within a 2 year period.

So, those who have a reactivation TB or active TB then proceed to infect the new hosts who are uninfected or susceptible and they in turn can develop rapid TB; that is about 2 to 3 million worldwide per year develop rapid TB or they would go and join into the pool of latent TB infection. Those at risk of exposure to TB include no close contacts with infectious TB disease and persons who work in high TB re settings or reside in facilities or institutions.

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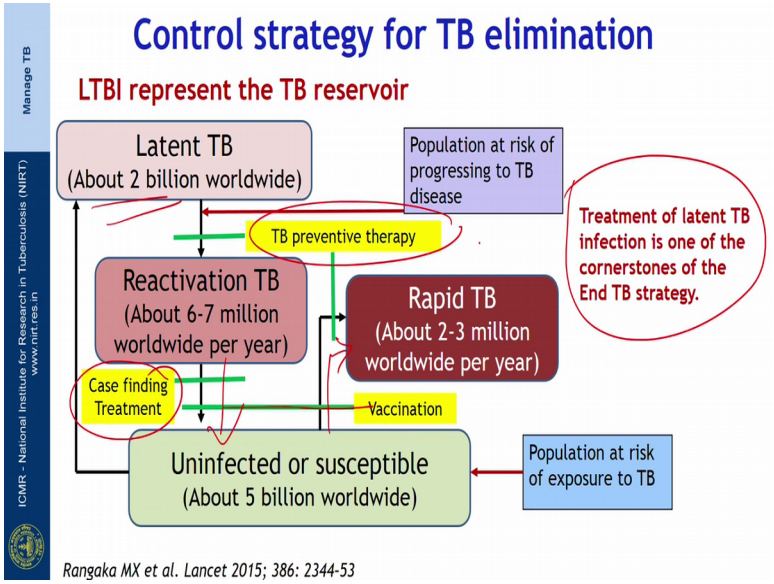

So, what are the main important control strategies for TB elimination? So, addressing latent TB infection is very important for TB elimination and treatment of latent TB infection is one of the cornerstones of MTB strategy.

In order to prevent the latent TB infected to breakdown to active TB disease TB preventive therapy can be used and those who have reactivation or active TB disease to prevent them infecting the susceptible or the uninfected, early case detection and appropriate treatment is very important. And those that are susceptible for them to prevent them from progressing to rapid TB disease vaccination is very important strategy and preventive therapy also helps in their breakdown.

So, with this now we come to know about the importance of latent TB infection; since they are there is a while for subsequent TB cases in our community.

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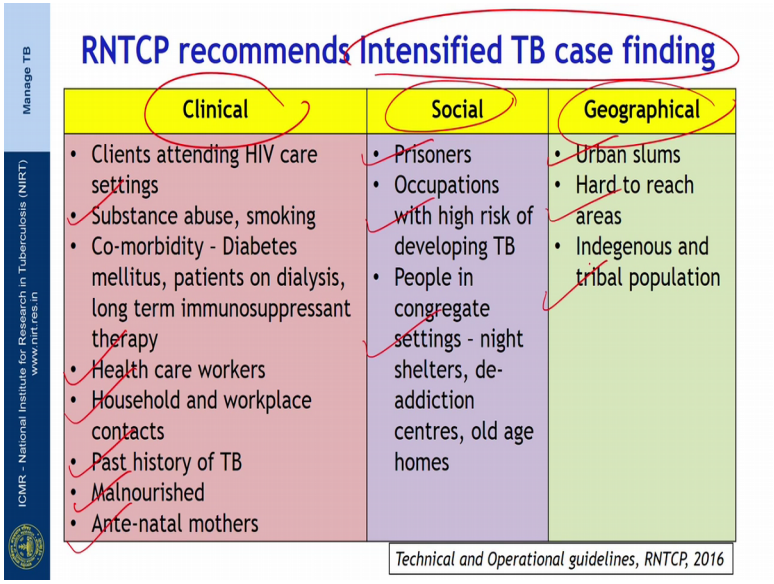

The revised national TB control program of India recommends intensive TB case finding. So, they are recommending intensive TB case finding in those groups who are vulnerable to TB; known as the high risk groups for TB either because of their clinical condition which include clients attending HIV care settings, those with substance abuse or smoking, those with co morbidity especially diabetes, mellitus and patients on dialysis non long term immunosuppressant therapy, healthcare workers who are at high risk, household and workplace contacts of TB patients, those with past history of tuberculosis, those malnourished and ante-natal mothers attending the clinics.

They may be persons who are vulnerable to TB due to sociological reasons which include prisoners, occupations with high risk of developing TB, people in congregate settings like night shelters d addiction centers and old age homes and because of the geographical scenario like urban slums, hard to reach areas indigenous and tribal population. These are referred to as vulnerable groups or address groups for TB and intensified TB case finding is important for early diagnosis of TB in these groups of patients.

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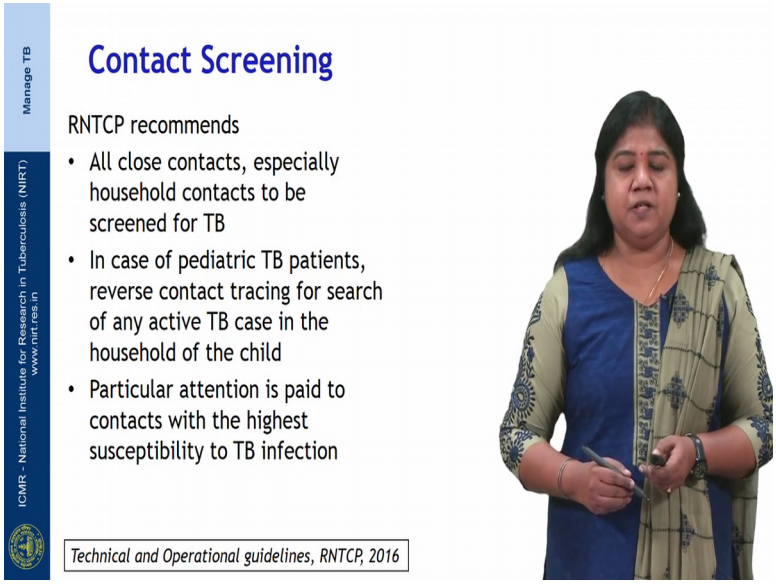

So, contact screening RNTCP recommends that all household contacts especially household contacts to be screened for TB for early detection of TB disease.

In case of periodic TB patients; reverse contact tracing is very important since this will help us to search for any active TB case in the household of the child. Particular attention is paid to contacts with highest susceptibility of to TB infection which includes HIV, diabetes, malnutrition, smoking, alcohol intake etcetera.

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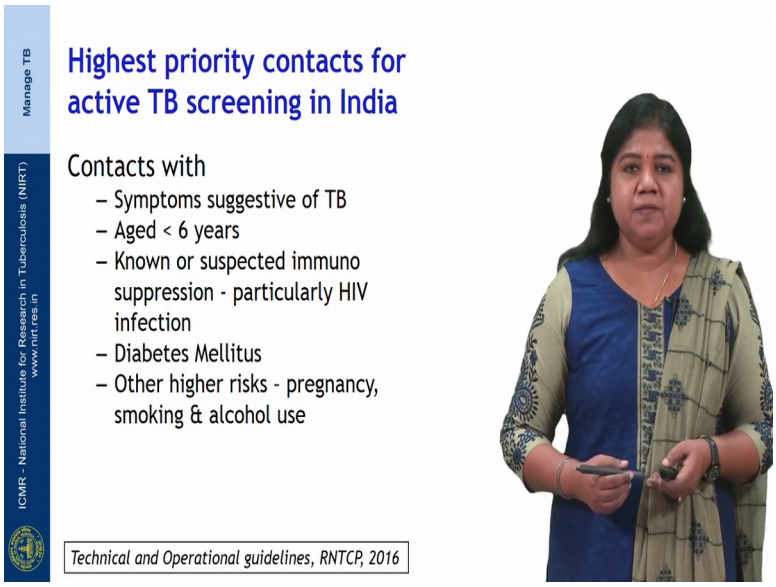

The highest priority contacts for active TB screening in India include; contacts with symptoms suggestive of TB, those aged less than 6 years known or suspected immune suppression particularly HIV infection, those with diabetes mellitus and either higher risk which include pregnancy, smoking and alcohol use and contacts of patients with drug resistant tuberculosis.

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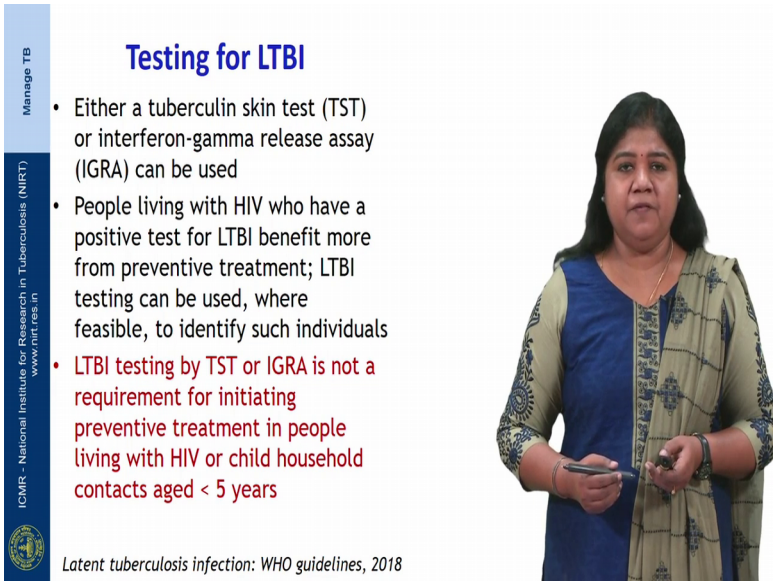

So, how do we test for latent TB infection? The WHO had showed 2018 guidelines on programmatic management of latent TB infection recommends for testing for LTBI either a tuberculin skin test or an interferon gamma release assay which is IGRA can be used. People with HIV who have a positive test for LTBI will benefit more from preventive treatment and LTBI testing can be used where feasible to identify just identify such individuals.

The LTBI testing for by TST or IGRA is not a requirement for initiating preventive therapy in people living with HIV or child household contacts aged less than 5 years.

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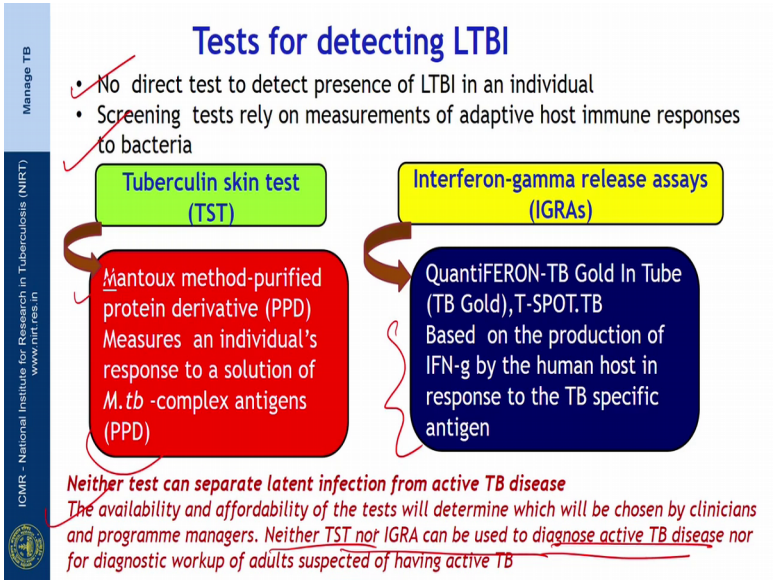

So, what are the tests for dictating latent TB infection? There is no direct test to detect presence of LTBI in an individual the screening test relied basically on measurements of adaptive and host immune responses to bacteria. So, what tests do we have? It is a tuberculin skin test which is a mantoux method and it uses the purified protein derivative; this measures an individual's response to a solution of MTB complex antigens which is the PPD. The other test that we have is the interferon gamma release assay which is a quantifier on TB gold in tube or the TB gold test or T-spot TB test.

This sub this works in the principle which is based on the production of interferon gamma by the human host in response to the TB specific antigen; however, it must be borne in mind that neither tests can separate latent infection from active TB disease. The availability and affordability of the test will determine which will be chosen by the clinician and programmatic program managers; neither TST nor IGRA can be used to diagnose active TB disease. So this is very important nor for diagnostic workup of adult suspected of having active tuberculosis.

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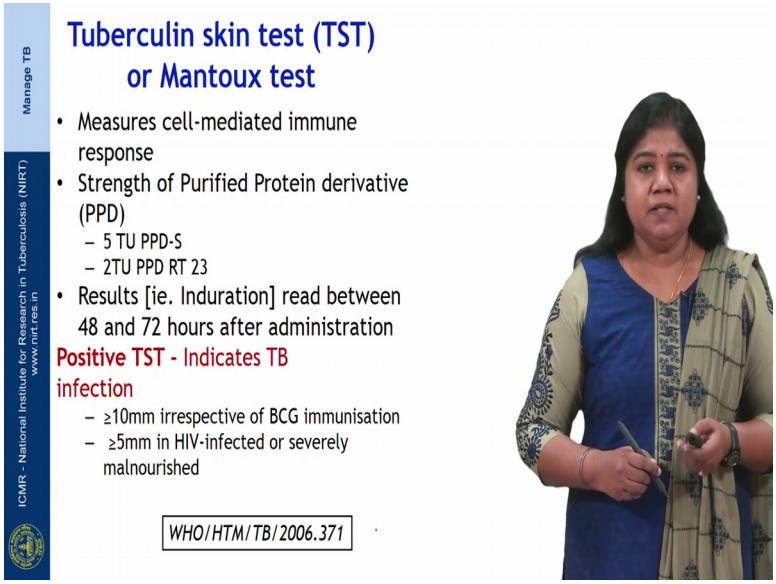

The mantoux test or the tuberculin skin test measures the T cell mediated immune response. The strength of the purified protein derivative use can be 5 TU PPD-S or 2 TU PPD RT 23 the results in the form of in duration is read between 48 and 72 hours after administration.

A positive test indicates TB infection and this positivity is more than or equal to 10 millimeter a respective of BCG immunization. Here the millimeter refers to the in duration and more than 5 or equal to 5 millimeter and HIV infected are severely malnourished.

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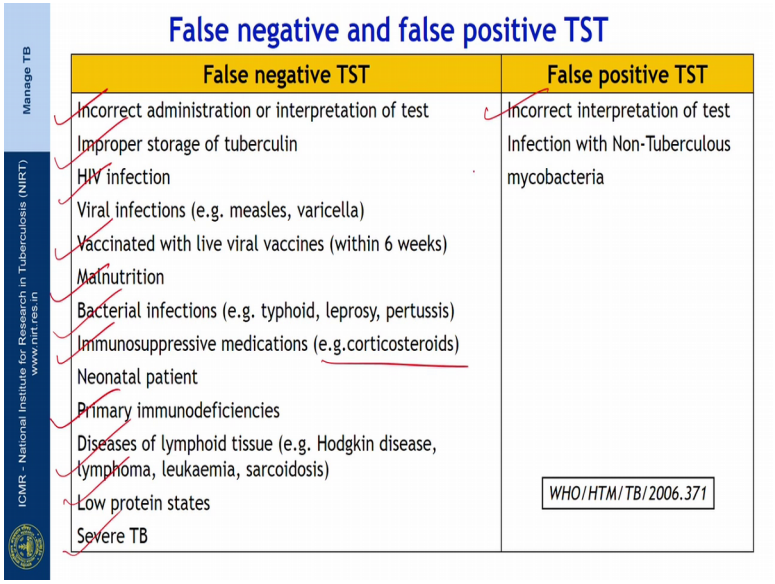

They are instances where there are false positive and false negative TST. The false negative TST can be due to incorrect administration or interpretation of test, improper storage of tuberculin HIV or viral infections vaccinated with viral vaccines within 6 weeks, malnutrition, bacterial or bacterial infections on with the patient is on immunosuppressive medications; example corticosteroids, primary immune deficiencies diseases of lymphoid tissue, low protein states and severe TB.

The false positive TST can be due to incorrect interpretation of the test and infection with not non-tuberculosis mycobacteria.

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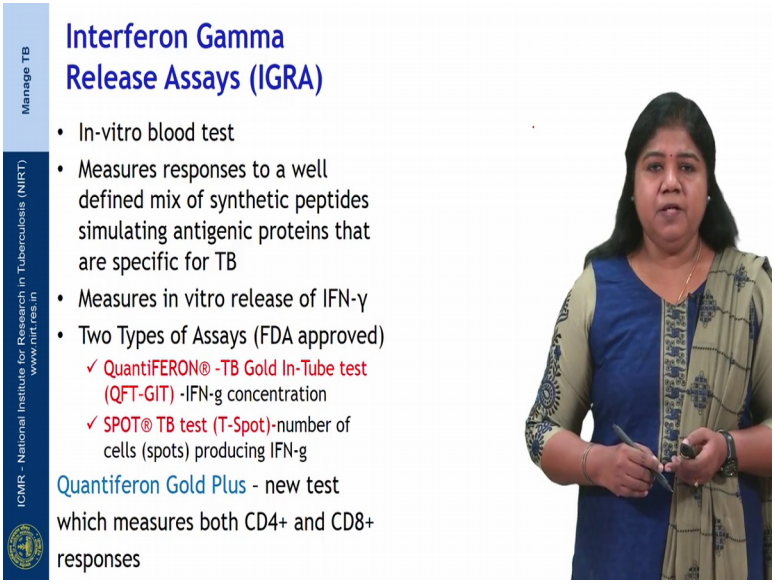

So, what is interferon gamma release assay? It is a in-vitro blood test; it measures responses to a well defined mix of synthetic peptides stimulating antigenic proteins that are specific for tuberculosis these are e sat 6, culture filtrate protein 10 and TB 7.7. This measures in-vitro release of interferon gamma. The 2 types of assays of IGRA are approved by FDA, they are the quantiferon TB gold in tube test this measures the interferon gamma concentration the T-spot TB test with measures the number of cells or sports producing interferon gamma. The quantiferon gold plus is a new test which measures both CD 4 and CD 8 responses.

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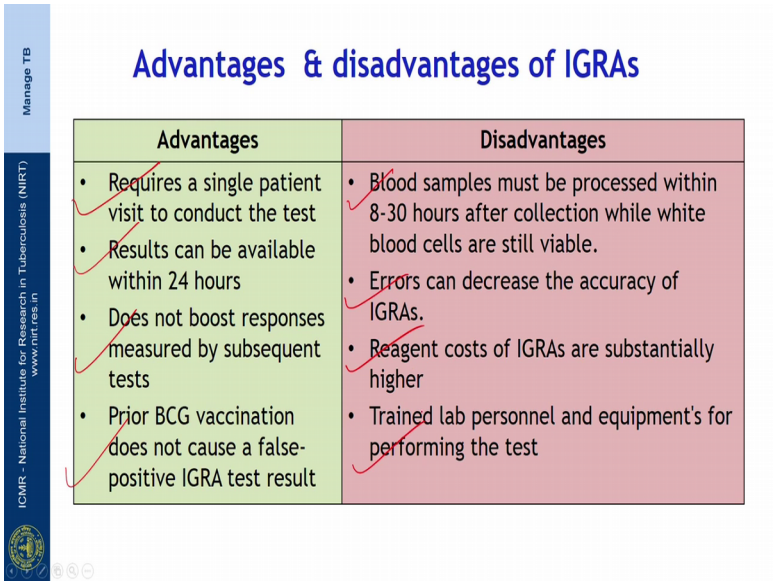

So, what are the advantages and disadvantages of IGRA? The advantages include it has only a single patient visit to conduct the test; it is a blood test; unlike the TST whether a patient has to come twice to read the in duration after a period of 48 to 72 hours. The results are can be available within 24 hours this does not boost immune response is measured by subsequent tests; prior BCG vaccination does not cause false positive IGRA test results unlike the TST.

The disadvantages include that the blood samples must be processed within 8 to 10 hours of the collection, while the white blood cells are still viable. The errors can decrease the accuracy of IGRA, the reagent cause of IGRAs or substantially higher and trained lab personnel and equipments are required for performing the test. So, with this we come to the end of the first session.

Thank you for your attention.