Manage TB
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Lecture - 23
Approach to diagnosis of Extra-pulmonary TB

Dear friend's very good morning. In this session we are going to talk about approach to diagnosis of extra pulmonary tuberculosis. I am Dr. Rupak Singla; I am heading a department of TB and respiratory diseases at the National Institute of TB and Respiratory Diseases, New Delhi.

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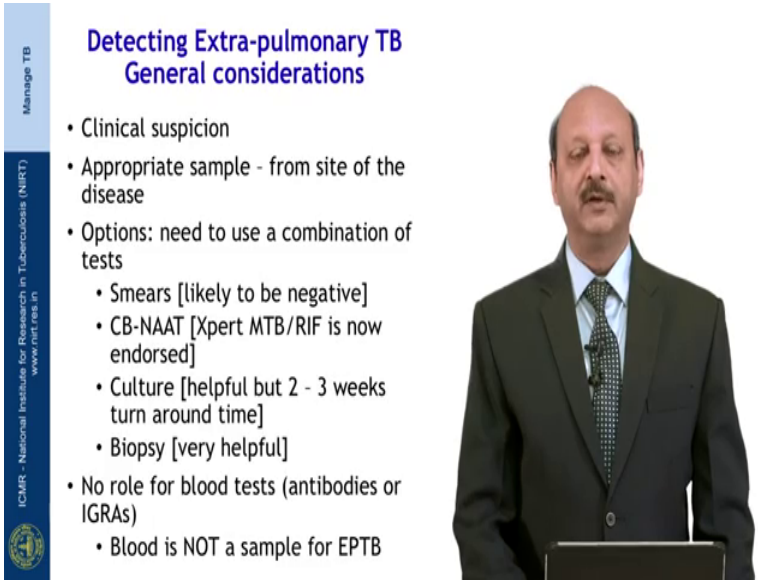

You see whenever we think of extra pulmonary tuberculosis the diagnosis is always the challenge. First is the look for the clinical symptoms which will depend on the site of involvement like for pleural tuberculosis we may have pain chest and disnea, for senior tuberculosis patient may have headache, vomiting, for bone tuberculosis they may have local pains in the bones or the joint.

So, accordingly we suspect extra pulmonary tuberculosis and then the next step is to obtain a (Refer Time: 01:00) specimen from the site of the disease and if the sample is available then we should submit these specimen to smear which unfortunately a likely to be negative in majority of cases. This CB-NAAT examination that is Xpert MTB RIF, it is now endorsed for the diagnosis of EPTB.

Then cultures are helpful, but they take 2 to 3 weeks and biopsy is also very helpful, but we need to remember that there is no role of blood test, antibodies, or IGRAs for diagnosis of EPTB and blood is not a sample for EPTB.

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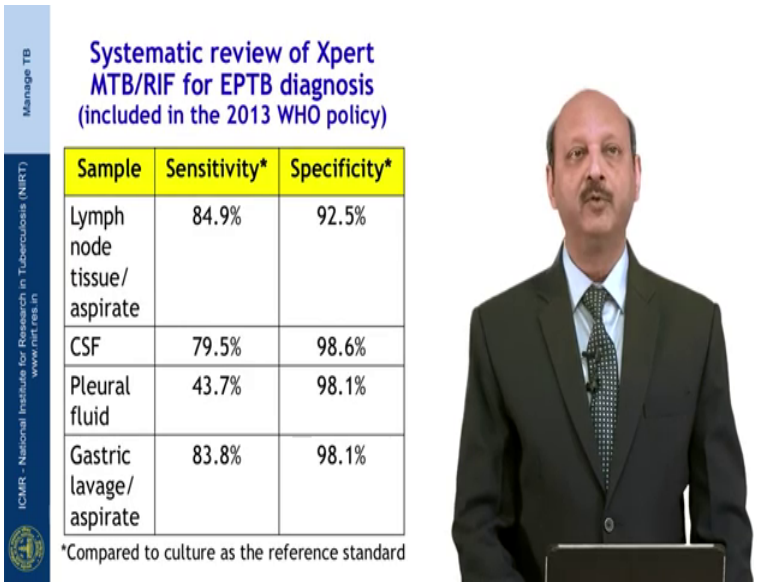

The systematic review for Xpert MTB included in the WHO 2013 guidelines wherein it was compared to the culture as the reference method, it showed that for lymph node tissue or aspirate the sensitive was almost 85 percent with the specificity of 92.5 percent, for CSF the sensitivity was 79.5 percent with the specificity of 98.6 percent, for pleural fluid the sensitive was found to be low just to the tune of 44 percent with the high specificity of 98 percent and for gastric lavage or aspirate in children it was the sensitive was 83.8 percent and with the high specificity of 98 percent.

So, for pleural TB the sensitivity of gene Xpert is low.

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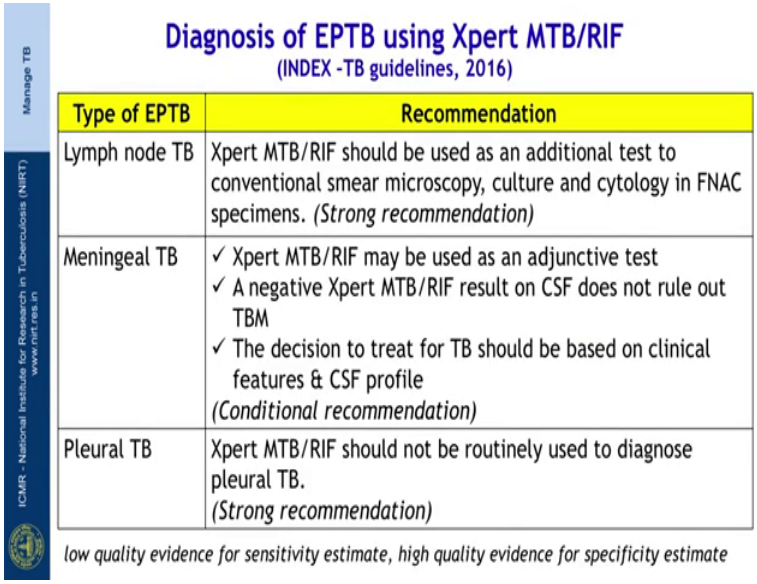

Now, the diagnosis of EPTB using MTB RIF as mentioned in our Indian index TB guidelines 2016 are for lymph node tuberculosis the Xpert MTB should be used as an additional test to conventional smear microscopy, culture and cytology in a FNAC specimens there is a strong recommendation for that.

For meningeal tuberculosis Xpert MTB RIF may be used as an adjunctive test; however, a negative Xpert MTB RIF result on the CSF does not rule out TB meningitis and the decision to treat for tuberculosis should be based on clinical features and CSF profile, it is a conditional recommendation.

For pleural tuberculosis, the Xpert MTB RIF as you mentioned earlier should not be used routinely to diagnose pleural tuberculosis there is a strong recommendation for that.

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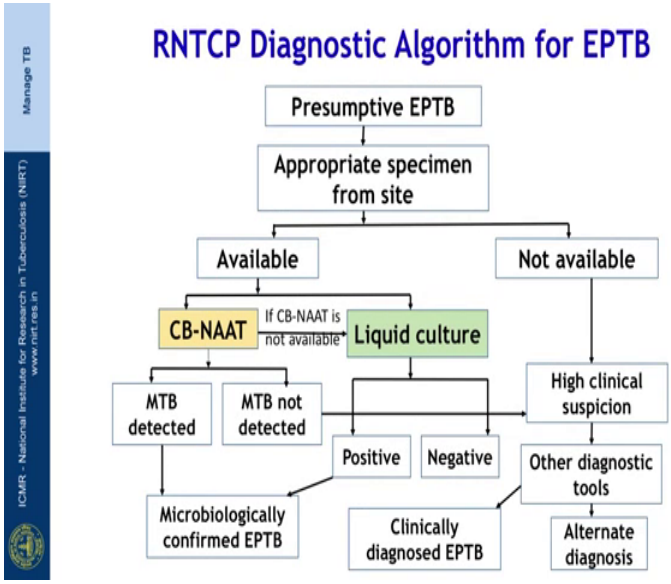

Looking at the diagnostic algorithm for EPTB as per our national TB control program, first all we aspect EPTB based on the symptoms and science, we try to obtained appropriate specimen, we can have either the specimen is available or not available. In case is specimen is available we subjected to CB-NAAT, in case CB-NAAT is not available we also subjected to the liquid culture and based on this if the CB-NAAT shows MTB detected or the liquid culture shows it is positive we label the patient as microbiologically confirmed extra pulmonary tuberculosis.

However, the CB-NAAT it shows MTB not detected liquid culture is negative and there is high clinical suspicious then we subject the patient to other diagnostic test. In case the (Refer Time: 03:58) tuberculosis we level the patient as clinically diagnosed EPTB or this test may tell us an alternative diagnosis for the patient.

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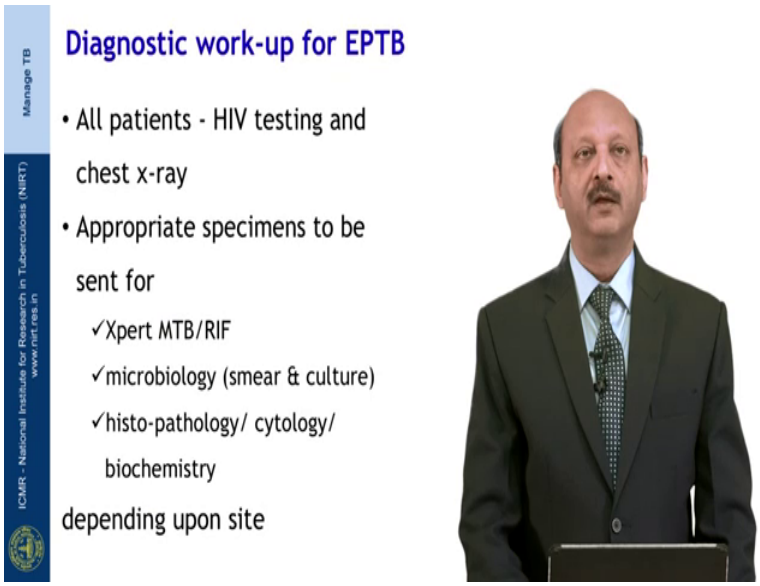

For all cases of EPTB we need to be remember that they should be subjected for HIV testing and chest x-ray which very commonly for the each and forget to get it done. Then depending on the side the appropriate specimen should be sent for Xpert MTB RIF, the microbiologically smear and culture and histo-pathology, cytology, biochemistry, this will see in the subsequent slides.

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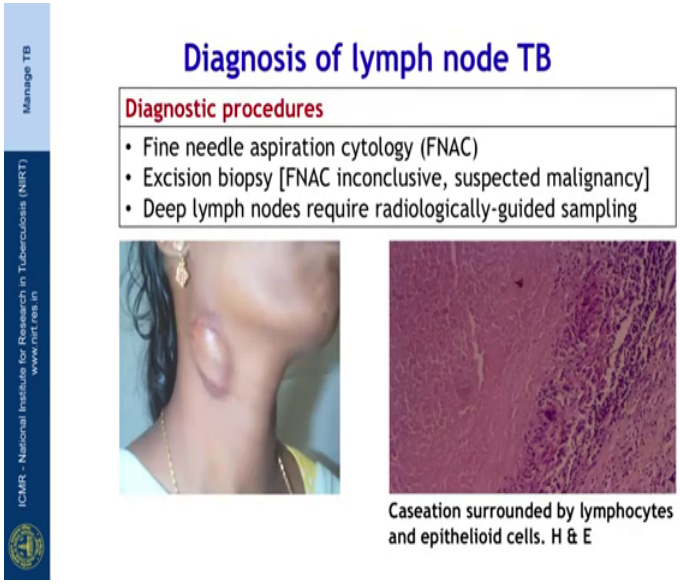

Coming to the lymph node tuberculosis, the FNAC that is fine needle aspiration cytology should be done and this simple should be sent for Xpert MTB RIF, smear, culture and

cytology. If the FNAC is inconclusive and especially when we are thinking malignancy excision biopsy should be done.

For malignant lymph nodes we can do baroscopic guided that is the trans vocal needle aspiration or (Refer Time: 04:55) sound and we can have the specimen and that can be sent to the appropriate investigations as we just discussed just now and there may be deep settled lymph nodes which may require radiologically-guided sampling.

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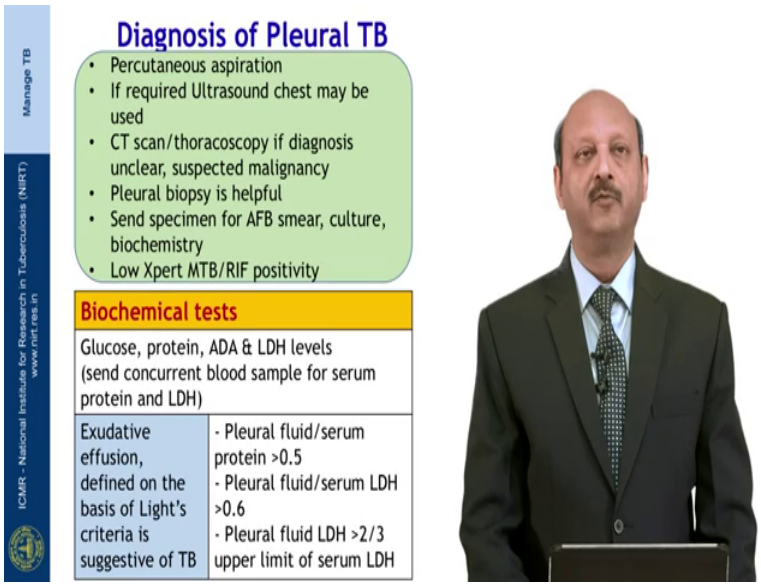

For pleural tuberculosis simplest backside method is the percutaneous aspiration and this specimen can be sent for AFB smear, culture and biochemistry. Xpert MTB is sensitivity is low so, it may not be sent for that. If required ultrasound chest can be done, if the diagnosis still uncertain then we can take the help of CT scan or thoracoscopy and the pleural biopsy is usually helpful in cases of pleural effusion and the biochemical test which should be done in cases of pleural effusions are the glucose, protein, ADA and LDH levels and also simultaneously we should do the blood, proteins and LDH.

And the life studied they have been defined that if any one of the three that is pleural fluid to serum protein ratio more than 0.5, pleural fluid to serum LDH ratio more than 0.6 or the pleural fluid LDH stood more than two-third of the upper limit of normal fluid pleural LDH, they all indicate exudative effusion which again goes in favor of tuberculosis.

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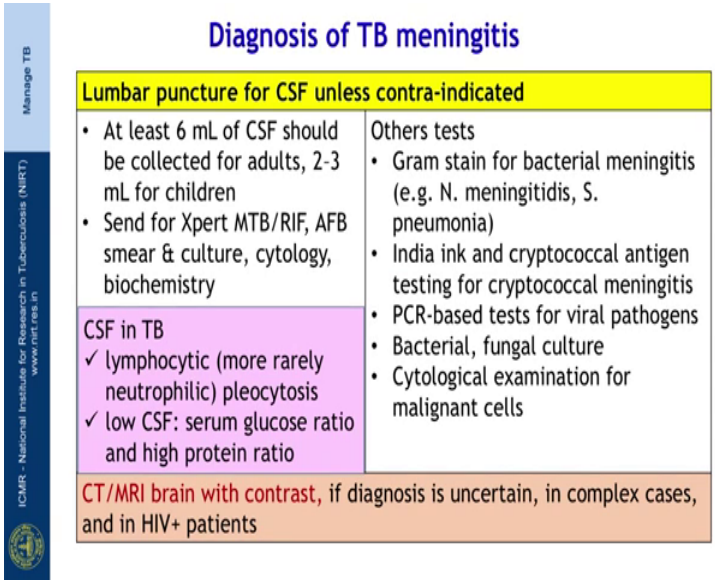

But tubercular meningitis lumbar puncture should also always we done unless there is a contra indication for the same. At least 6 mL of CSF should be obtained in adults and we should try to have 2 to 3 mL of CSF in children and this specimen should be send for Xpert test, AFB smear, culture, cytology and biochemistry. In cases of tuberculosis CSF usually shows lymphocytosis although rarely it may shows neutrophilic to be there. In the low CSF serum glucose ratio and high protein ratio it indicates tuberculosis.

Depending on the clinical condition in mind other test should be done like gram stain for bacterial meningitis like in case of neisseria meningitides or streptococcus pneumonia. The India ink and cryptococcal antigen testing for cryptococcal meningitis and HIV patients whenever we are suspect them, then PCR-based tests for viral pathogens, then cytological examination for malignant cells in case meningitidis in mind. If diagnosis is uncertain and in complex cases an HIV positive patients, the CT MRI brain with contrast can also be helpful.

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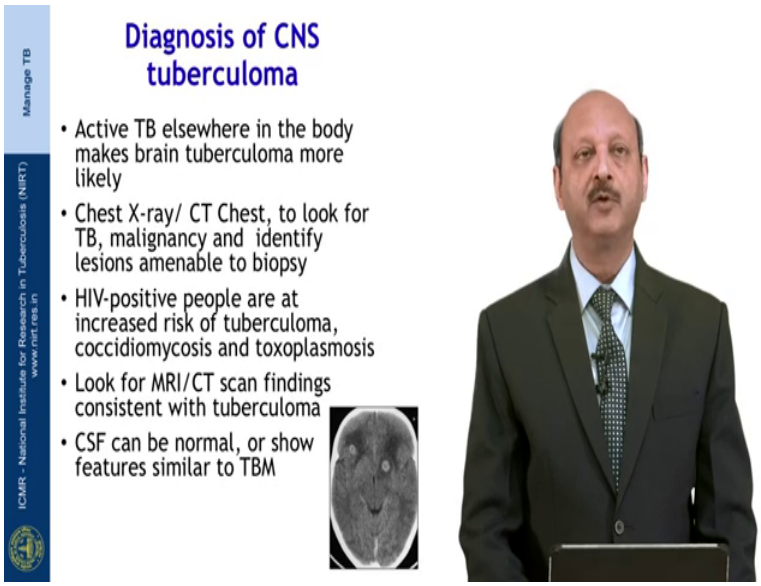

For CNS tuberculoma active tuberculosis elsewhere in the body makes the brain tuberculomas more likely. Chest x-ray CT scan of the chest should be done, it can help in looking for TB elsewhere they can also help in looking for malignancy and other lesion which are amenable to biopsy.

And HIV positive patients they are at increased risk of tuberculomas coccidiomycosis and toxoplasmosis and there CT finding sometime confused at each other. Then we should look for MRI CT scan findings which are consistent with tuberculosis and we need to remember that CSF can be normal or show features similar to the tubercular meningitis.

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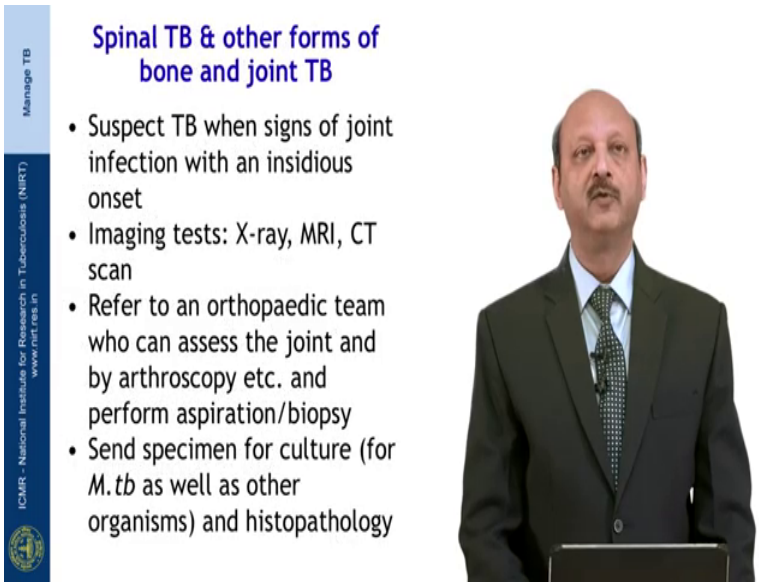

In spinal TB and other forms of bone and joint tuberculosis we should suspect tuberculosis when there are signs of joint infection with an insidious onset. Here the imaging test which can be of used are x-ray, MRI CT scan and we should refer the patient to an orthopaedic team who can assess the joint by arthroscopy etcetera and perform aspiration or biopsy has the case may be and this specimen should be sent for culture for MTB as well as other organisms and histopathology.

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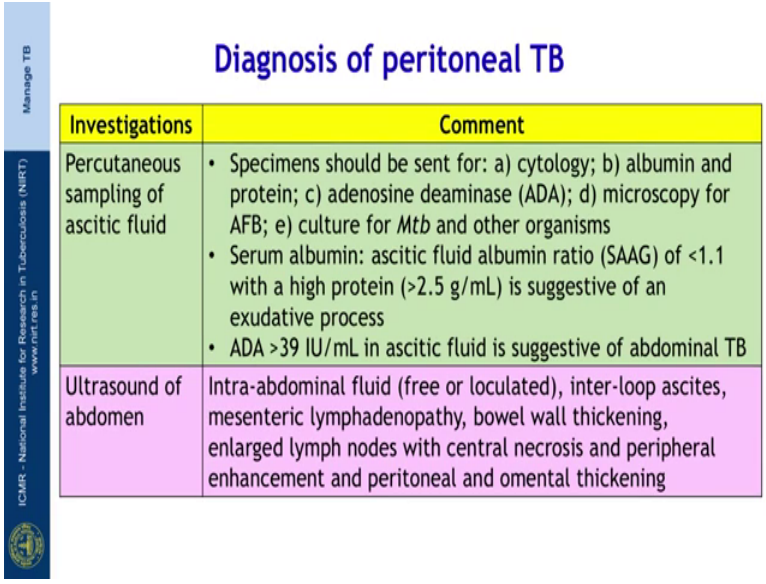

For peritoneal tuberculosis the simplest test is to do percutaneous sampling of the ascitic fluid and this specimen should be sent for cytology, albumin and protein, ADA levels and microscopy for AFB and culture and other organisms. The serum albumin to ascitic fluid ratio if it is less than 1.1 or there is a high protein contained in the peritoneal fluid this is suggestive of an exudative process indicating it could be tuberculosis. Also an ADA level of more than 39 transit units is suggestive of abdomen tuberculosis.

Ultrasound of abdomen may also be done if it is available. It may show finding such as intra abdominal fluid which could be free or loculated, inter loop ascites, mesenteric lymphadenaopathy, enlarged lymph nodes with central necrosis and peripheral enhancement it may show bowel wall thickening and peritoneal and omental thickening.

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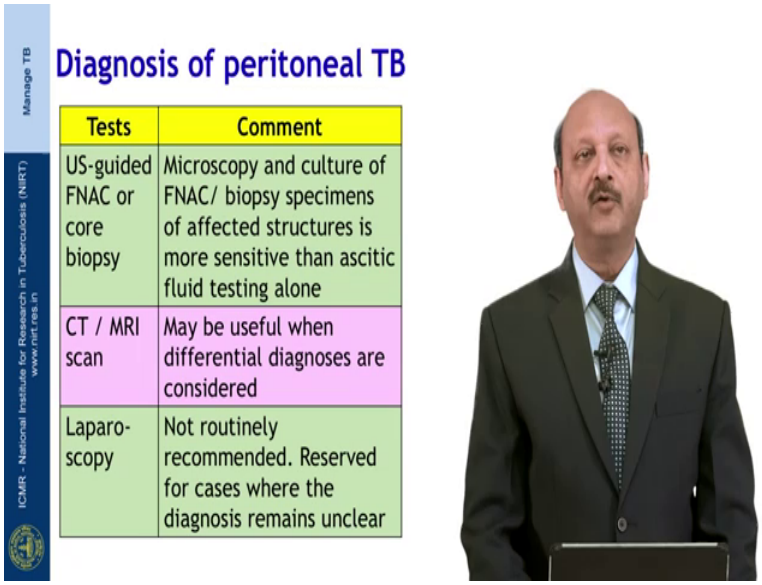

Then ultrasound guided FNAC or the core biopsy can also be done and this sample should be sent for microscopy and culture and also it may be more sensitive when ascetic fluid aspiration is done alone.

So, in case it is available they should be considered, the CT and MRI scan it may be useful when the differential diagnosis others are considered. Laparoscopy not routinely recommended, but it may be reserved for cases where diagnosis remains unclear after the (Refer Time: 09:55) test.

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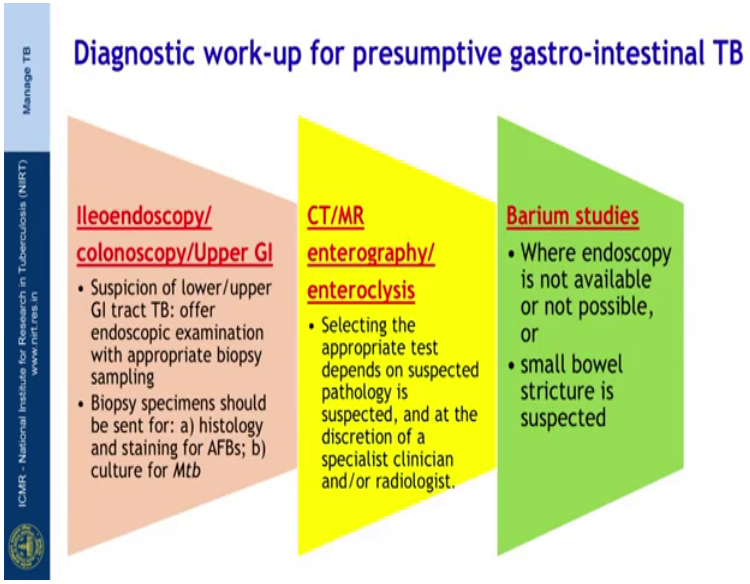

For presumptive gastro intestinal tuberculosis it is really difficult to reach a conclusion of TB of the GI track. Whenever we suspect lower or upper GI tuberculosis we should offer them endoscopic examination and also try to have appropriate biopsy sampling and this biopsy specimen should be sent for histopathology and staining for AFB, smear and culture. In appropriate situations and depending on the choice of (Refer Time: 10:24) inclinations and radiologist 1 can do ct or mr enterography or enteroclysis.

Nowadays, a barium studies are less often done; however, it may be done wherever the endoscopy is not available or not possible or we are thinking of small bowel stricture in these cases barium studies can be considered.

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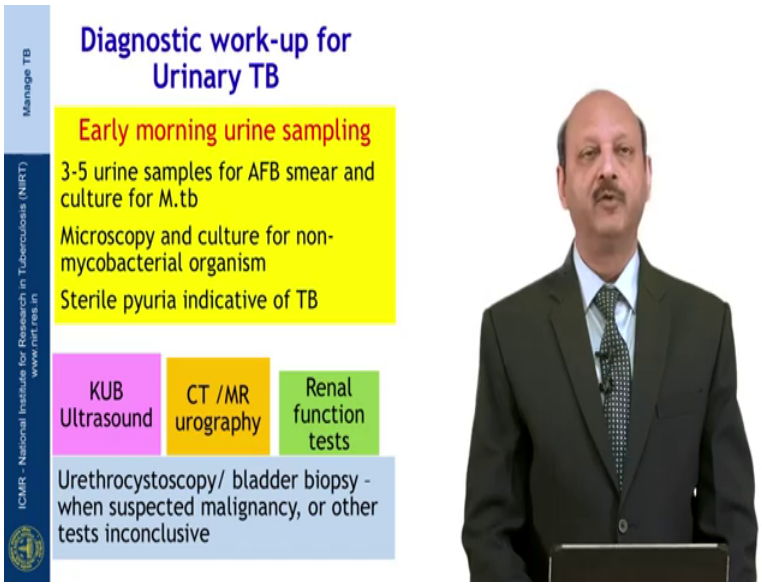

For urinated tuberculosis we should have early morning urine samples, 3 to 5 so, sample should be there and they should be subjected to smear and culture and also the microscopy and culture for non mycobacterial organism should also be done and we need to remember the sterile pyuria is indicative of tuberculosis.

Other tests which can be done are KUB ultrasound, CT MR urography, renal function tests and in cases where we are thinking of malignancy or other tests are inconclusive the test which can be of use are urethrocystoscopy and bladder biopsy.

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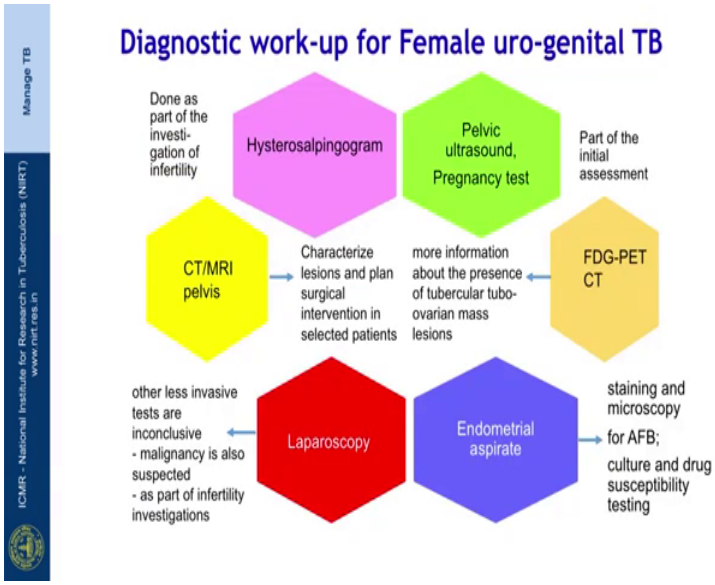

Regarding female uro-genital tuberculosis this is again common in our country, but at the same time difficult to diagnose. As a part of initial assessment or as a part of for infertility the hysterosalpingogram may be done and also the pelvic ultrasound pregnancy test they are commonly used. The CT MRI pelvis it can help in characterizing the lesion wherein even the interventions and biopsy can be done. The FDG-PET CT scan it gives more information about the presence of tubercular tuboovarian masses then this can be of use.

When this other less invasive test are inconclusive and also one has malignancy in mind then the laparoscopy examination should be done and in case we have endometrial aspirate it should be sent for staining for microscopy for AFB smear and culture and also the drug susceptibility tests.

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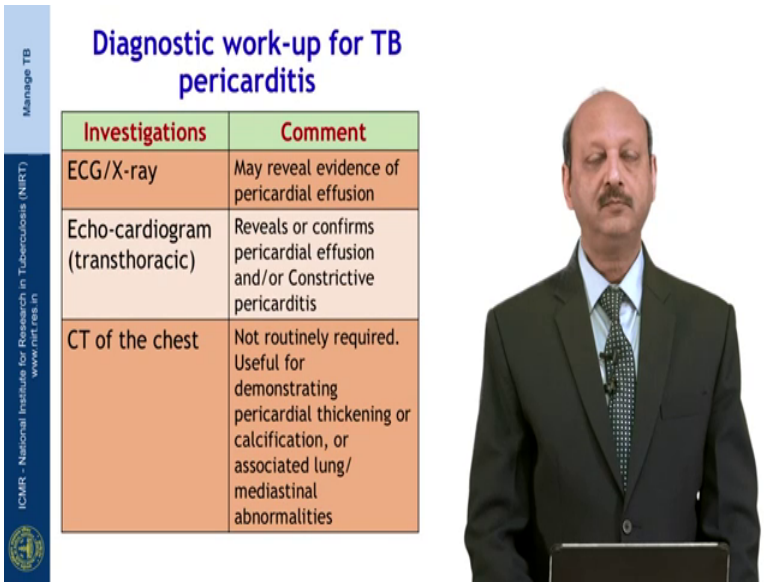

For pericarditis the initial investigations are ECG or X-ray it may help in revealing the pericardial effusion for the first time. Echo-cardiografic test it may reveal or confirm the presence of pericardial effusion and even constrictive pericarditis it is of use. CT scan of the chest for pericardial effusion is not routinely required; however, it may be of useful for demonstrating pericardial thickening, calcification or any associated abnormalities in the lung of mediastinal.

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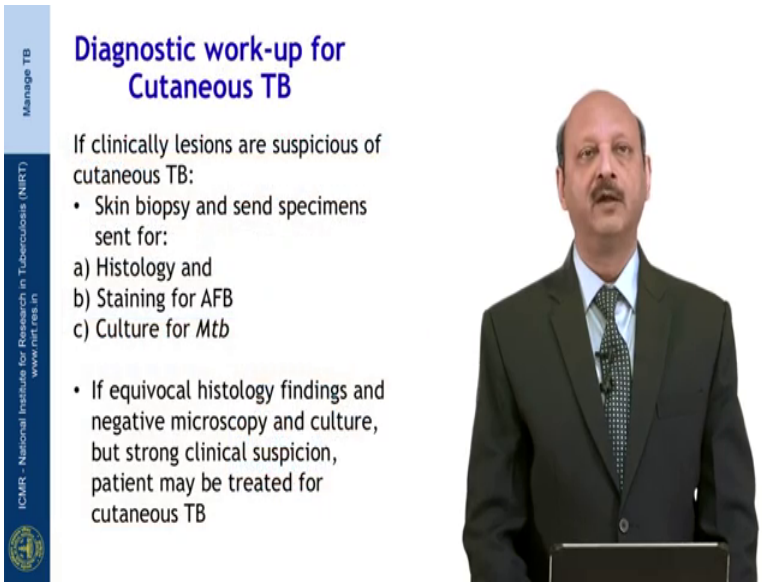

For cutaneous tuberculosis if clinically lesions are suspicious of cutaneous tuberculosis, skin biopsy should be done and sent this specimen for histopathology, staining for AFB smears and culture. And if you equivocal histological findings are there and negative microscopy and culture which is very commonly happens in our clinical practice, but there is a strong clinical suspicion patient may be treated for cutaneous tuberculosis.

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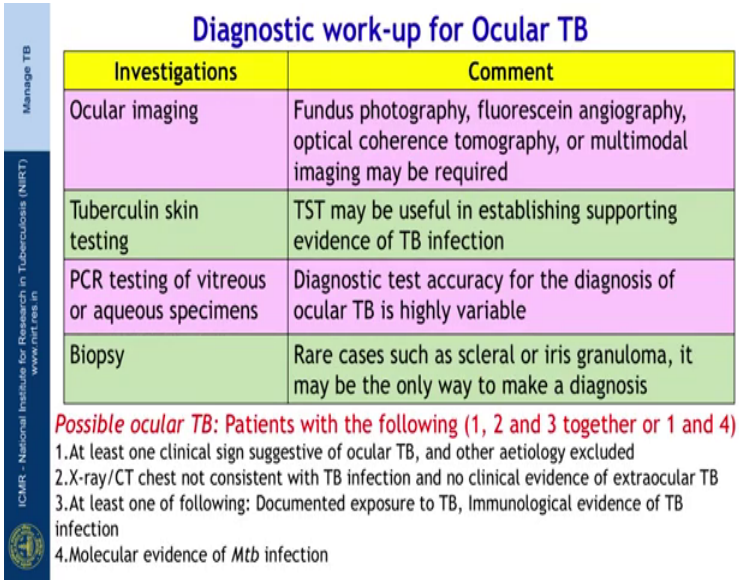

For ocular tuberculosis, nowadays the various investigations are available in higher centers and these include ocular imaging wherein fundus photography, fluorescein

angiography, optical coherence tomography or multimodal imaging techniques may be required. Tuberculin skin test it may be useful in establishing and supporting evidence for TB infection, the PCR testing of the vitreous or the aqueous specimens, the diagnostic accuracy is highly variable. .

So, we need to remember that and biopsy in rare cases such as scleral or iris granuloma, it may be the only way to make a diagnosis and also the there is a possibility of labeling the patient as possible ocular tuberculosis.

This can be done when we have the 1 2 3 given below they are present like 1 is at least 1 clinical sign suggestive of ocular tuberculosis and other aetiology have been excluded, 2 is the x ray of CT scan not consistent with TB infection and no clinical evidence of extra ocular tuberculosis and 3 is at least one of the following that is documented exposure to tuberculosis and immunological evidence of TB infection if all the 3 are there we can label the patient as possible ocular TB or we have one of the first one and the fourth is molecular evidence of MTB infection, that is 1 and 4, then also patient can be labeled as possible ocular tuberculosis.

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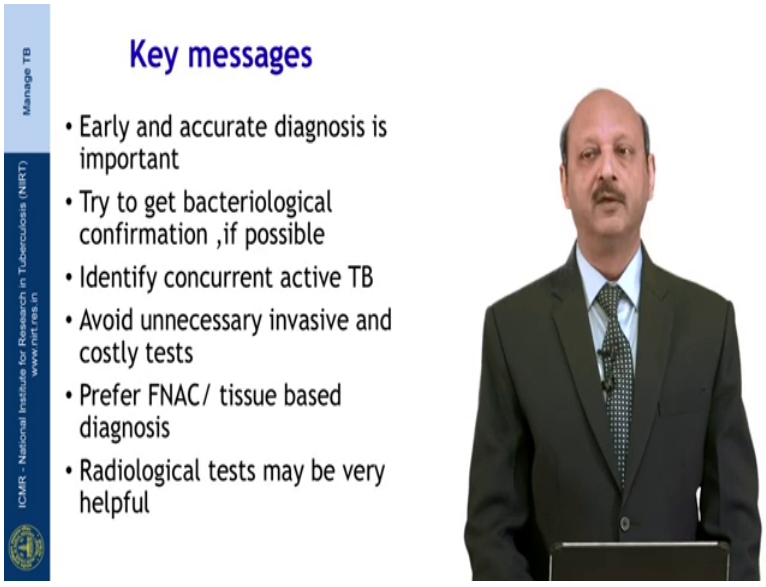

So, dear friends I like to give the key messages that early and accurate diagnosis is important. We should try to get bacteriological confirmation if possible, identify the concurrent active tuberculosis. One should prefer FNAC tissue based diagnosis in all EPTB cases. The radiological tests may be very helpful in extra pulmonary TB cases and

we should avoid unnecessary invasive and costly tests. So, it is the we have to use our experience and the site of the diseases where and where we have to use this test, otherwise some people they tend to use invasive test and costly test right on the day 1 which is not correct.

Thank you.