**Manage TB**
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**National Institute for Research in Tuberculosis, Chennai**

**Lecture - 33**
**Treatment of Drug Sensitive Pulmonary Tuberculosis**

Welcome to this module of Treatment of Drug Sensitive Pulmonary Tuberculosis. I am Dr. Sridhar, Professor of Thoracic Medicine, Government Stanley Medical College and Superintendent, Government Hospital of Thoracic Medicine, Tambaram Sanatorium.

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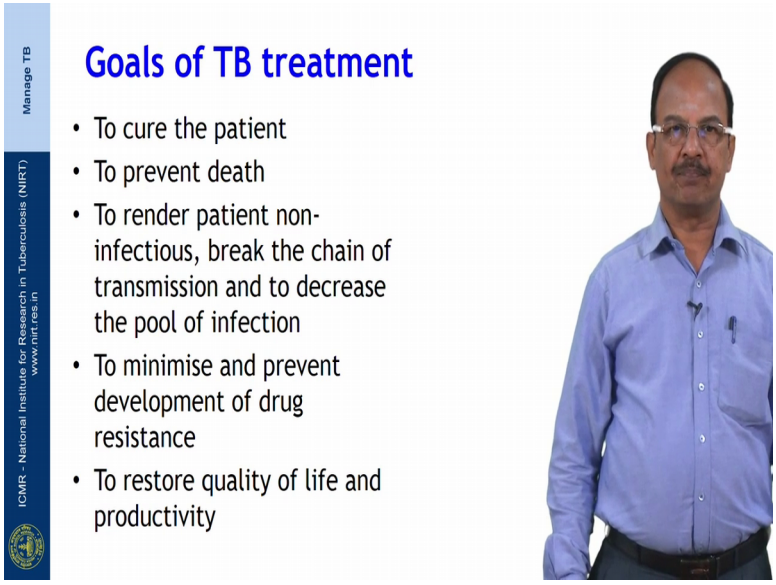


Let us see what are the goals of TB treatment, we are aiming at. We want to queue the patient who are affected by permanent tuberculosis. We want to prevent a death among patients affected with pulmonary tuberculosis.

We want to render patients non-infectious, to break the chain of transmission, which happens within the society, and decrease the pool of infection within the society; to minimize and prevent development of drug resistance and to restore quality of life and productivity.

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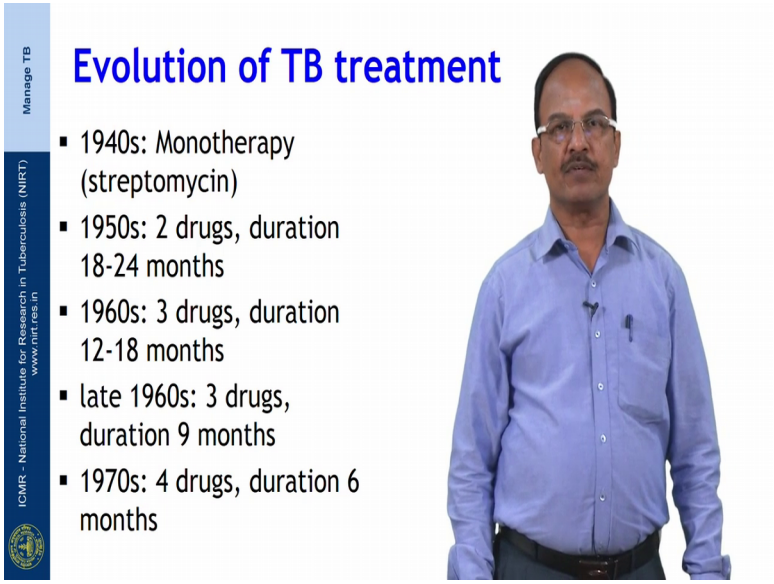


Let us see how the treatment of tuberculosis has evolved over years. 1940s, we saw the monotherapy with streptomycin. 1950s, we had access to 2 drugs and the duration of treatment was 18 to 24 months. In the 1960s, we had access to 3 drugs with a duration of 12 to 18 months.

And in late 1960s, we had 3 drugs with the duration spanning for 9 months with an intensive phase and a continuation phase. And during 1970s, we saw 4 drugs were available the treatment duration was reduced to 6 months based on the trials.

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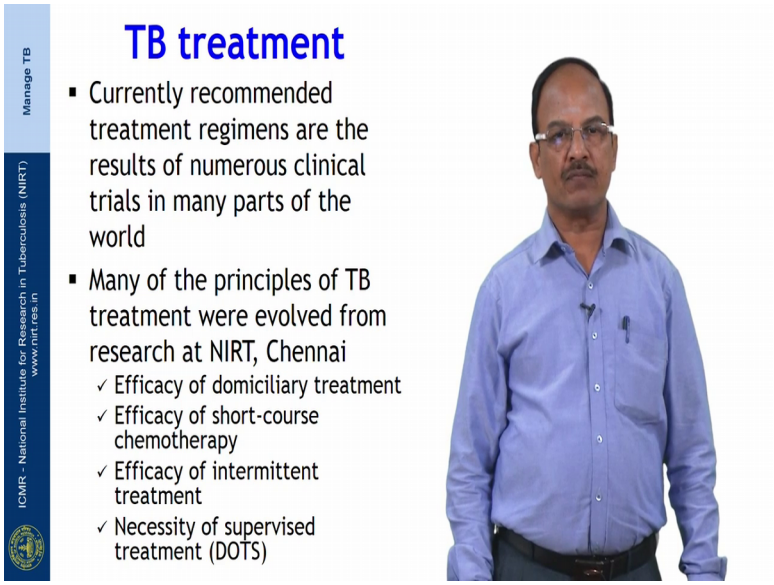

And as far as the TB treatment goes the currently recommended treatment regimens or the results of numerous clinical trials, which has been conducted in many parts of the world. And many of the principles of TB treatment were evolved from research at NIRT, Chennai.

Proving the efficacy of domiciliary treatment, proving the efficacy of short-course chemotherapy, proving the efficacy of intermittent treatment, and proving the efficacy of DOTS, where in which the treatment was (Refer Time: 02:05) administered under supervision.

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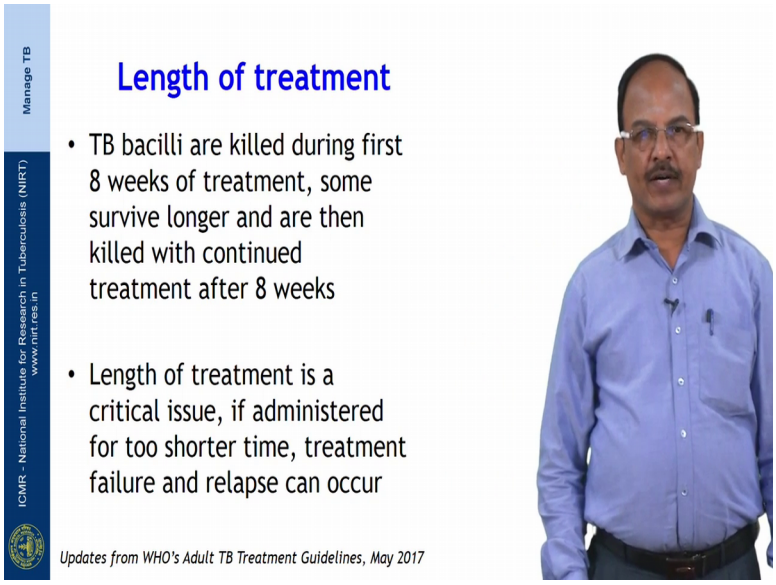


And as far as length of treatment is concerned, TB bacilli are killed during the first 8 weeks of treatment, when we are administering back to seidel drugs as a combination with 3 or 4 drugs, and some survived longer, and or then killed with continuation treatment which happens after the end of intensive phase.

Length of treatment is a critical issue, if administered for too shorter time, treatment failure and relapses can occur.

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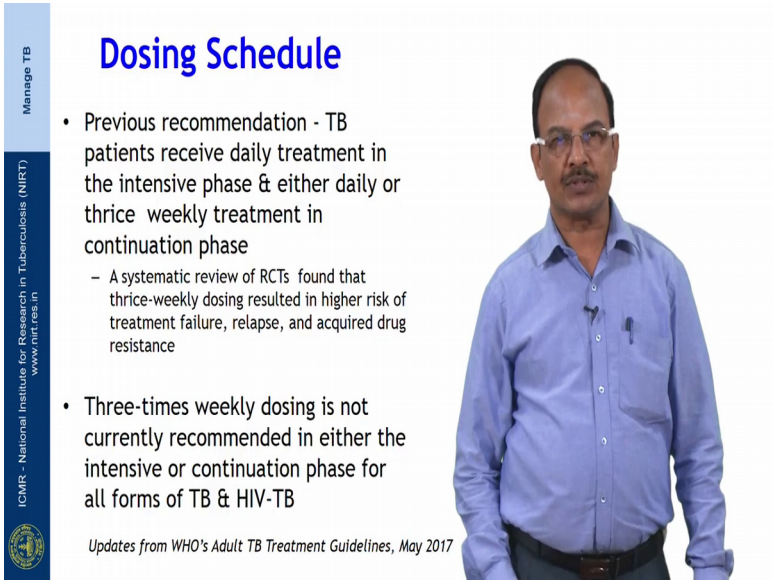


We have to find out what is the ideal dosing schedule also. Previous recommendation was TB patients receive daily treatment in the intensive phase, and either daily or thrice-weekly treatment in the continuation phase, this was based on systematic review by RCTs.

Three-times weekly dosing is not currently recommended by the WHO, either in the intensive phase or in the continuation phase as per the latest recommendation, which was published in 2017 may.

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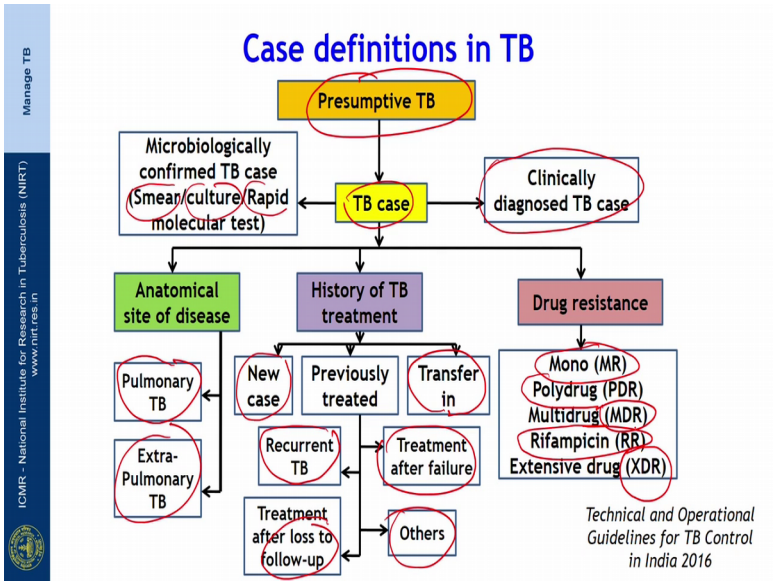

Let us see the case definitions in TB. The terminology presumptive TB is used, now which was used earlier as suspect TB. This presumptive TB patients who are identified or subjected to either smear microscopy or sputum culture or sputum is subjected for rapid molecular tests. Through which we identify and confirm a cases as confirmed tuberculosis case. Sometimes a smear may be negative radiologically or by other clinical means, we may consider a patient as clinically diagnosed with tuberculosis case.

Anatomical site wise they may labeled as a case of either pulmonary TB or extra permanent TB vocalized-noise]. And based on the history of previous treatment, if there is no previous treatment history, then the patient will be labeled as a case of new pulmonary case or extra-pulmonary case. If there has been a previous treatment history this TB has happened after the previous treatment that will be labeled as a case of recurrent TB, and if the patient was lost during treatment, he will be considered as a case of loss to follow up.

And those patients who failed with the earlier regimen will be labeled as a case of treatment after failure, and some of the patients may belong to other groups. Then some of the patients may be diagnosed elsewhere, and transferred to our facility for treatment they be labeled as a case of transferring. As far as drug resistance is concerned, if there is resistance to only one direct except rifampicin, this group will be labeled as mono drug resistance.

If they have resistance to only rifampicin or rifampicin resistance is identified by molecular diagnostic that will be labeled as a case of RR or rifampicin resistance. When there is resistance to more drugs except a combination of INH and refampicin they will be labeled as a case of poly drug resistance, if there is a resistance to INH, and resistance INH, and refampicin with or without progressed into other drugs, they will be labeled as a case of MDR TB.

And when they have extensive drug resistance that is resistance to most of the drugs which are available, they will be labeled as a case of extensively drug resistant tuberculosis.

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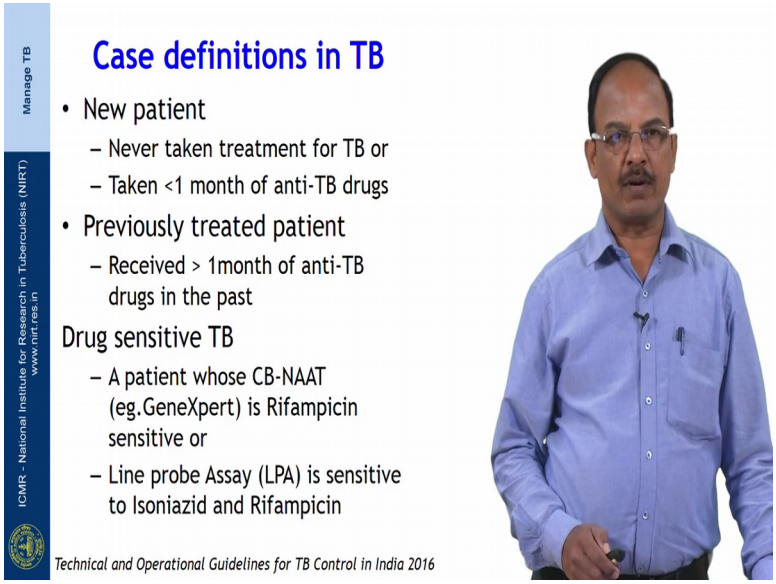


Let us discuss the case definition so what we use in tuberculosis. A patient will be labeled as a case of new patient, if they have never taken treatment for tuberculosis, or if they have taken treatment for less than 4 weeks.

A patient who had previous treatment received more than 1 month of treatment will be labeled as a case of previously treated patient. Drug sensitive TB is labeled, when a patient CB-NAAT says that the sensitive rifampicin or is line probe assay says is sensitive to isoniazid and rifampicin.

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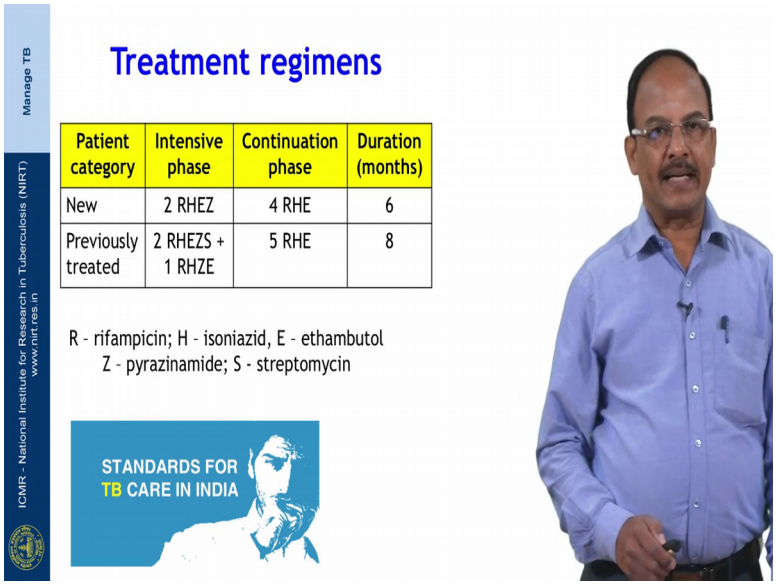

What are the drug regimens currently recommended for drug sensitive tuberculosis, both pulmonary and extra pulmonary for all new patients, who never had treatment or had treatment less than 4 weeks, they will have 6 months of total duration of treatment with the 2 months of intensive phase with the continuation phase of 4 months, we will have 4 drugs administered during the intensive phase.

R stands for rifampicin, INH stands for H stands for INH, E stands for ethambutol, and Z stands for pyrazinamide, which is administered for 2 months followed by INH rifampicin, and ethambutol for a further period of 4 months.

Those patients who had previous treatment, presenting again with tuberculosis disease, which is confirmed eight back either back to logically or by other means, at the same time is still drug susceptible, will receive the regimen of 8 months duration, where in which the intensive phase will be 3 months with 2 months of INH rifampicin; ethambutol; pyrazinamide and streptomycin and 3rd month, they will receive only INH rifampicin; pyrazinamide; ethambutol.

The continuation phase will continue for 5 months with INH, and refampicin with ethambutol, this is as per the new standards of TB care introduced by in Indian government.

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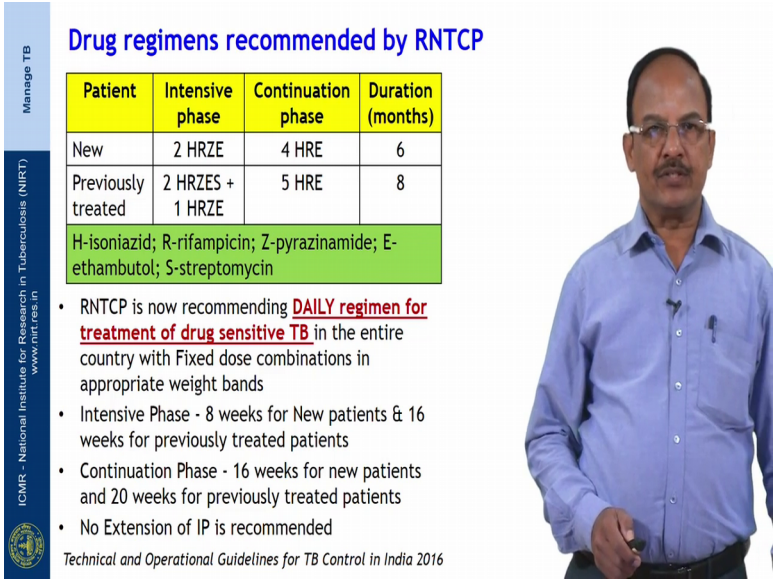

The RNTCP is now recommending daily regimen for treatment of drug sensitive TB in the entire country with fixed those combinations in appropriate weight bands. Intensive phase is 8 weeks for new patients, and 16 weeks for previously treated patients. And continuation phase is 16 weeks for new patients, and 20 weeks for previously treated patients. No extension of intensive phase is recommended in this schedule.

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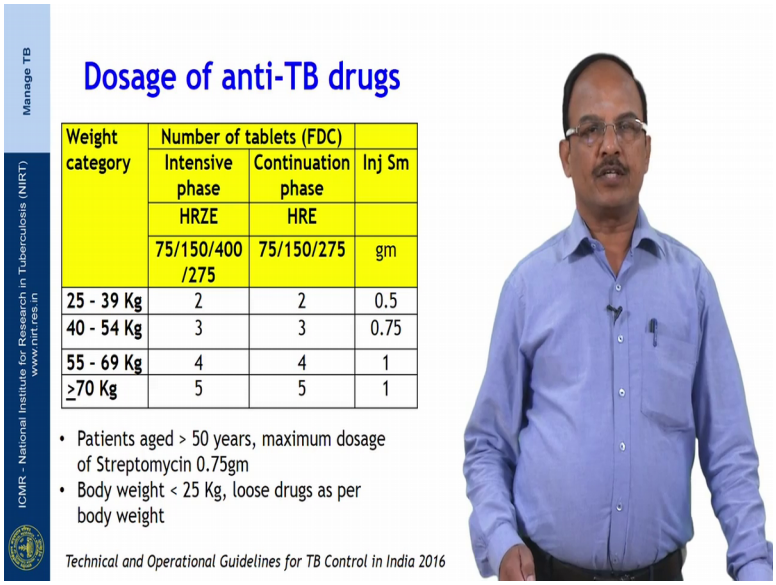


Now, we will see the dosage of anti-TB drugs, which are used in the fix of those combinations. In the intensive phase each pill will have 75 milligrams of INH, 150 milligram of rifampicin, 400 milligram of pyrazinamide, and 275 milligram of ethambutol, if the person is weighing between 25 to 39 kg, they will receive 2 pills. And continuation phase will have the pill with INH 75, rifampicin 150, and ethambutol 275, once again they will receive 2 pills in that.

If there is any requirement for certain medicine in that age, in that weight band, the streptomycin dose will be 0.5. Whereas, if the persons weight band is 40 to 54 kg, the intensive phase, and phase continuation phase will have 3 pills each with the streptomycin dosage of 0.75 gram.

If the patient is in the weight band of 55 to 69 kg, in the intensive phase, they will receive 4 pills, and continuation phase will have 4 pills with streptomycin administered at 1 gram. Whereas, if the weight band is more than 70 kgs, then they have to receive 5

pills in the intensive phase, and in the continuation phase another 5 pills, and the streptomycin dose will remain as one gram.

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These are the fixed dose combination pouches from which the number of pills is administered for the patients.

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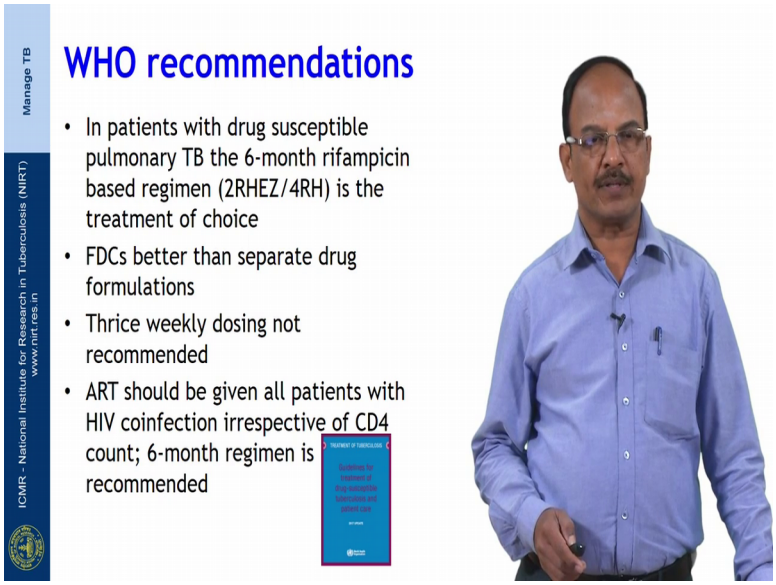


What is the WHO recommendations on all these issues. In patients with drug susceptible pulmonary TB the 6-months rifampicin based regimen is the treatment of choice. Fixed those combination is better than separate drug formulations. And thrice weekly dosing is

not recommended. ART should be given to all patients with HIV infection irrespective of CD4 count; and 6-months regimen is recommended for this group also.

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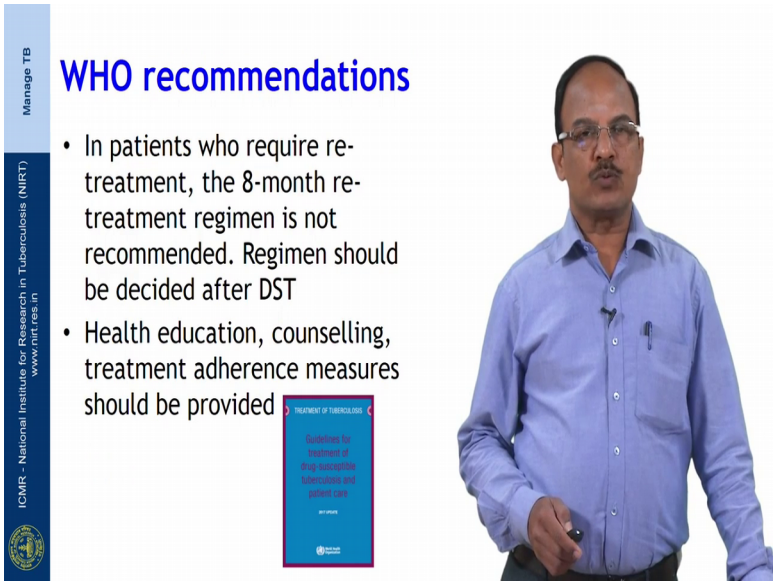


In patients who require re-treatment, the 8-month re-treatment regimen is not recommended. It should be decided after DST. Health education, counseling, treatment adherence measures should be provided.

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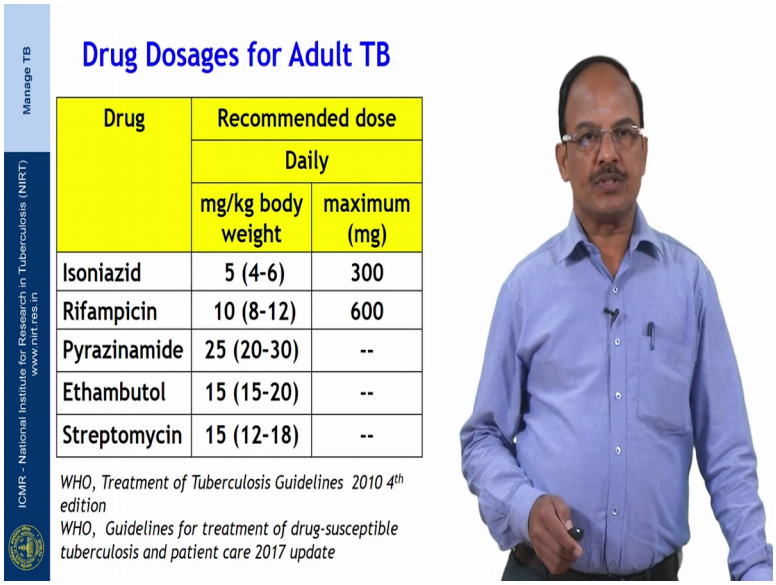


And these are the direct dosages which based on which the FDC is formulated; INH at the dosage of 5 milligram per kilogram body weight, not exceeding 300 milligram.

Rifampicin 10 milligram per kilogram body weight, not exceeding 600 milligram; Pyrazinamide administered at the dose of 25 milligram per kilogram body weight. Ethambutol 15 milligram per kilogram body weight; And streptomycin 15 milligram per kilogram body weight, not exceeding 1 gram.

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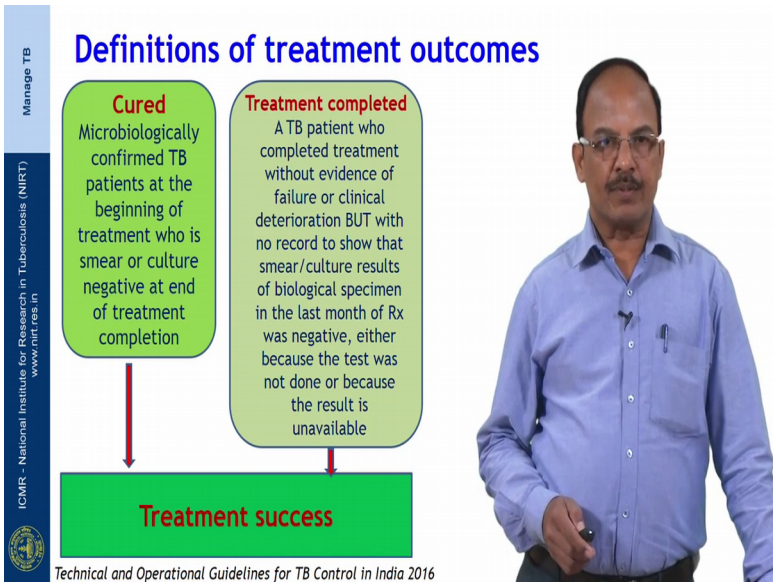


And let us see the definitions of treatment outcomes. We label a person ask cured, when microbiologically confirmed tuberculosis patients at the beginning of treatment, who is smear or culture is negative at the end of treatment completion will be labeled as a case of cured.

Whereas, a tuberculosis patient who are completed treatment at the end of treatment, we do not have the data, microbiological data or otherwise, but complete the of entire duration of treatment will be labeled as treatment completed. Both the groups put together will be labeled as treatment success, as far as treatment outcome is concerned.

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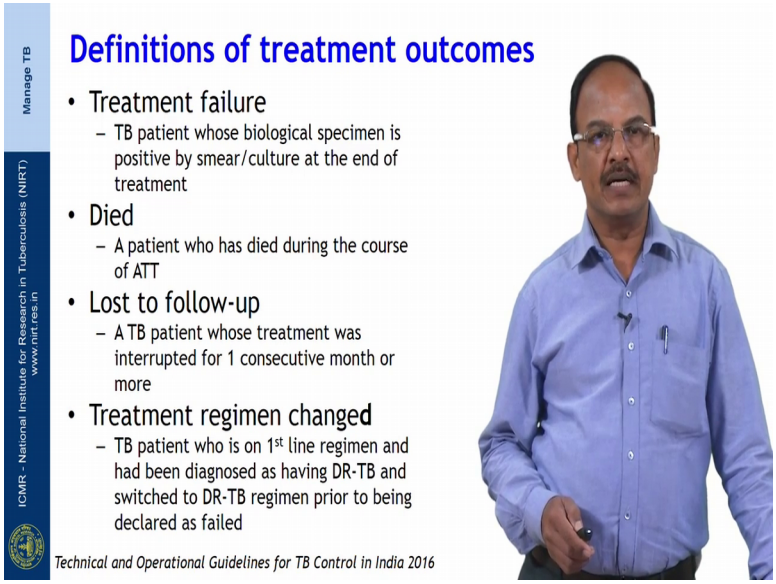


The tuberculosis patients whose biological specimen is positive by smear or culture at the end of treatment will be labeled as a case of treatment failure.

If any patients dies during treatment that outcome will be labeled as died; If the tuberculosis patients whose treatment was interrupted for 1 consecutive month or more will be labeled as a case of loss to follow up and that if by any chance due to drug susceptibility testing showing resistance, the treatment regimen is change that would captured as treatment regimen changed.

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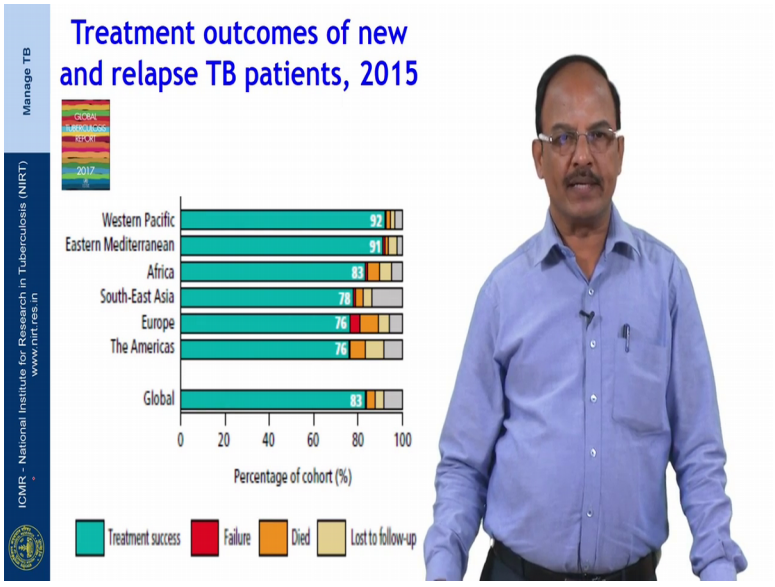

When we see the treatment outcomes of new and relapse TB patients, who were treated during 2015, the range starts between 76 to 92 percent globally.

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The common drug adverse events, which we encounter includes, the pill burden; gastrointestinal symptoms; arthralgia, hepatitis, itching, hypersensitivity, rarely renal failure, thrombocytopenia, and flu syndrome etcetera.

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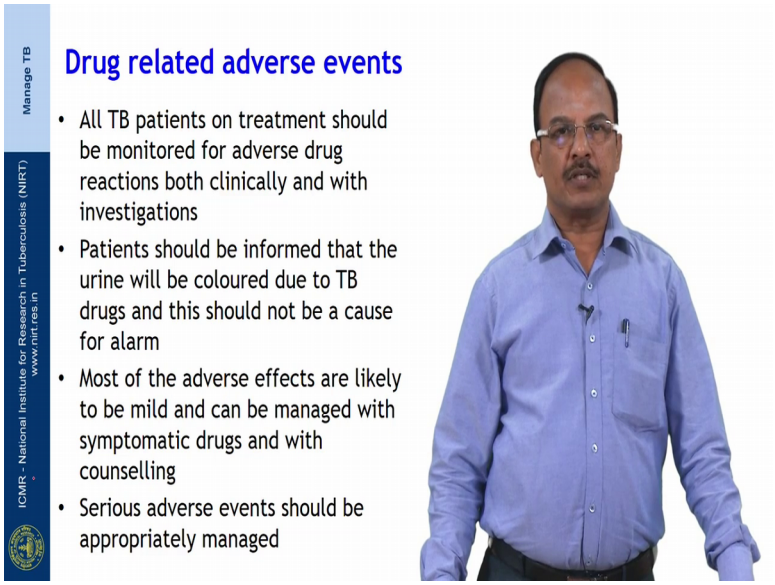


When we see the drug related adverse events. All TB patients on treatment should be monitored for adverse drug reactions both clinically, and with investigations. Patient

should be informed that the urine will be coloured due to TB drugs, and they should not be a cause for alarm. Most of the adverse effects are likely to be mild, and can be managed with symptomatic drugs, and with counseling. All tuberculosis patient on treatment should be monitored for adverse drug reactions.

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What will the treatment support programs that is in researched. Adherence to treatment is the key to relapse free cure. The counseling of patients, and family members will ensure regular treatment. The patients family, especially children should be screened for tuberculosis.

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And initial and frequent follow up counseling of patients and family members is a must. Patients should ideally have nutritional support.

There should be a mechanism to retrieve the patients who are lost to follow up. And that should be a systematic screening of adverse events. Psycho-social support should also be available. And there should be a provision for co-morbidity management like, diabetes and so on.

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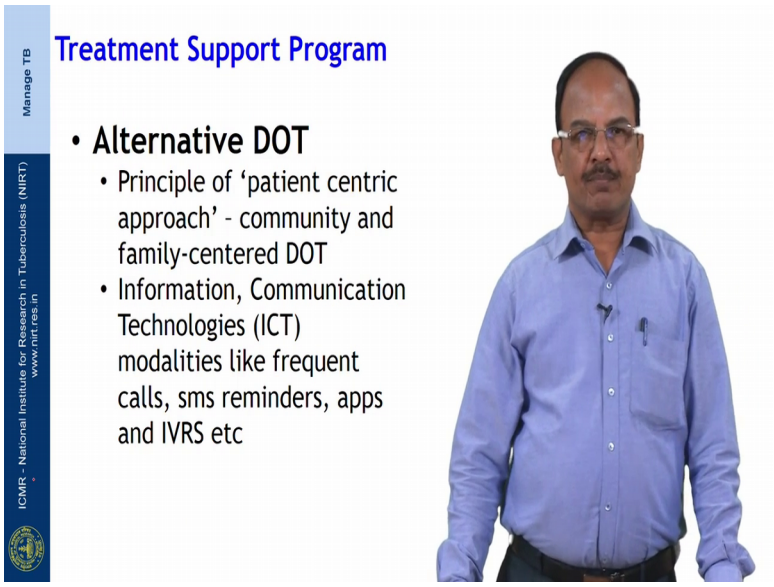

The alternative treatment concept also has to be kept in mind. The principle of 'patient centric approach'-community and family- centered DOTS should be given priority. The information, communication technologies modalities like frequent calls, sms reminders, apps and IVRS etcetera will help us to keep the patience continue with the treatment.

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Compensation to mitigate out of pocket expenditure like for transportation, or for nutritional support can be considered. And incentive for treatment supporters also can be planned. And capacity building and engaging local community like self help groups, patient support groups can also be considered.

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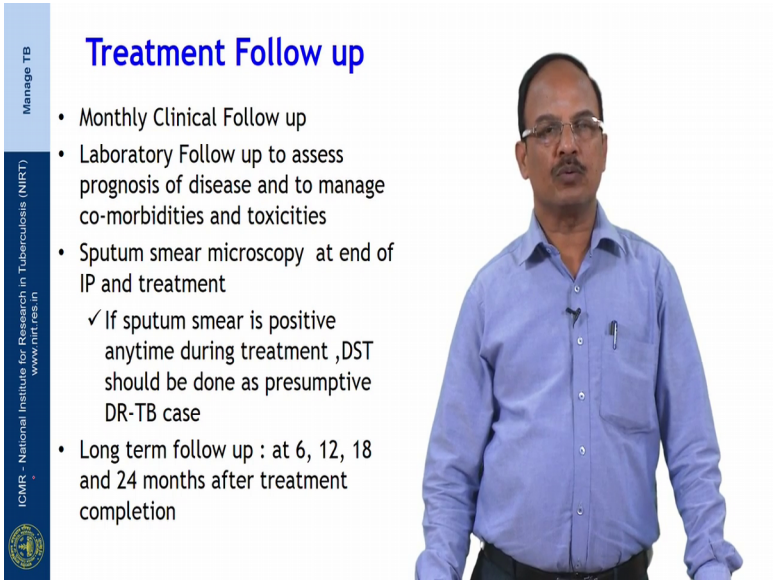


There should be a monthly clinical follow of these patients who are put on treatment. And laboratory follow up to access prognosis of the disease and manage co-morbidities and toxicities should also follow.

Sputum smear microscopy at the end of intensive phase is most important to declare the treatment outcome, and if this sputum is positive at any time during treatment, DST should be done as presumptive DR-TB case. Long term follow up includes, doing sputum cultures for those patients who have completed treatment at the 6, 12, 18 and 24 months after treatment to make sure they do not relapse.

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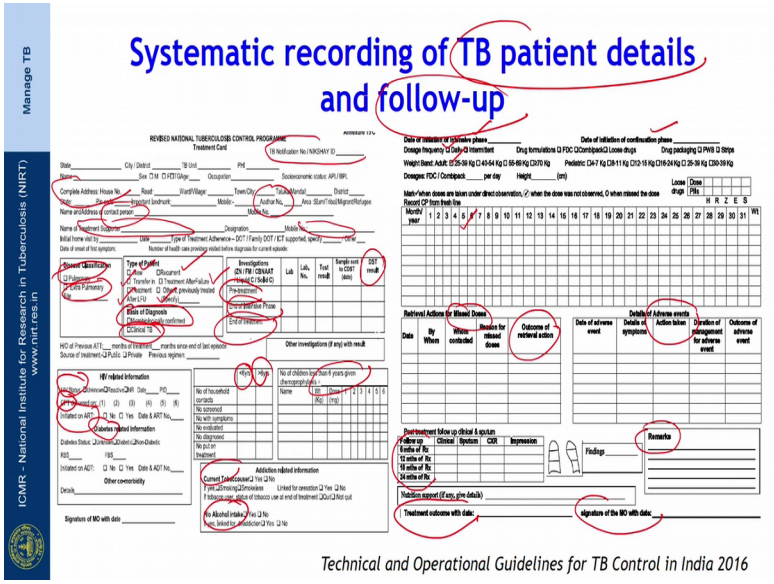


The new treatment called systematically records all the details about the patient, and the follow-up details as well. It captures the TB notification number or nikshay ID, it takes the name, complete address of the individual as well as their Aadhaar number. This will affect the patients to have direct benefit transfer of the support from the government, and name of the contact person also is recorded, and the name of treatment supporter also is recorded, and the mobile number is also captured. And the disease classification goes like this either it is labeled as pulmonary or extra pulmonary.

And the type of patient finds as either new or recurrent or transferring or treatment after failure or treatment after loss of follow up loss to follow up, and others also. The basis of diagnosis also is captured either as microbiologically confirmed or clinical tuberculosis. And all the basic data with regard to microbiological diagnosis, pretreatment, end of IP, and end of treatment also is captured with a lab, which an lab number, test result whether it is sent with cultured DST, and what is the DST result also is captured.

Patients HIV status is recorded, whether the patient received code remarks or preventive therapy also is recorded, when the patient was initiated on ART that is also recorded. If there is a co-morbidity like diabetes that is also captured and children who are having contact with this patients who is sputum positive also is recorded children with less than 6 year and more than 6 years are systematically recorded. And INH prophylaxis therapy is initiated for them, addiction related information is also recorded like current tobacco

use; or whether there is current alcohol use; and counseling is done for these patients to stay away from these addiction habits.

The entire treatment schedule takes both the intensive phase as well as the continuation phase, whether it is a daily regimen that information is also captured, according to the patients weight band the number of pills is recorded, and it is recorded as per the calendar dates in which the treatment is initiated. If the patient is not taking the drugs regularly, they missed a doses also and when they were retrieved that is (Refer Time: 17:08) is also recovered.

And if the patient has any adverse events during the course of anti-TB treatment that also gets recorded; And patients follow up details at the end of 6 months, 12 months post treatment, 18 months post treatment, and 24 months post treatment is also recorded. If there is any remarks there is a separate column and to record that also. Treatment outcome is recorded with the date, and signature of the medical officer also is recorded with the date; if the patient has received any nutritional support that is separately captured here.

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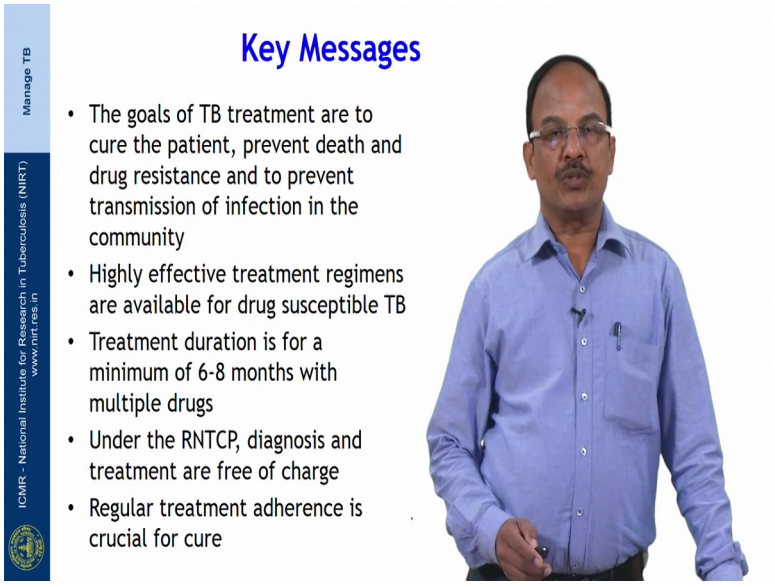


So, the key messages are the goals of TB treatment are to cure the patient, prevent death; and drug resistance; and to prevent transmission of infection in the society. Highly effective treatment regimens are available for drug susceptible TB. Treatment duration is

for a minimum of 6 to 8 months with multiple drugs. Under the RNTCP, diagnosis and treatment are free of charge. Regular treatment adherence is crucial for cure.

Thank you very much.