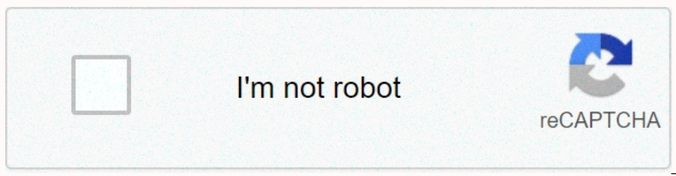

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Xdr tb treatment guidelines rntcp

(PDF icon – 421k) Common Drug Resistant Tuberculosis (XDR TB) What is CommonLy Drug Resistant Tuberculosis (XDR TB)? Common drug-resistant Tuberculosis (XDR TB) is a rare form of isoniazid and rifampin, plus any fluoroquinolone and at least three injectable second-line drugs (i.e., amikacin, canamicin or capreomycin) resistant multiila-resistant tuberculosis (MDR TB). MDR TB causes at least an organism resistant to isoniazid and rifampin, the two most powerful tuberculosis drugs. How does XDR TB spread? The disease-sensitive tuberculosis and XDR TB are spread in the same way. Tuberculosis bacteria are put in the air when a person with tuberculosis disease coughs or coughs of throats, sneezes, shouts or sings. These bacteria can swim in the air for several hours, depending on the environment. People who breathe air containing this tuberculosis bacteria can become infected. Why is XDR TB very serious because XDR TB is resistant to the most powerful tuberculosis drugs, the remaining treatment options are less effective, have more side effects, and are more expensive, since tuberculosis is not spread by shaking someone's hand kissing bed linen or toilet brushes by touching food or drink. XDR TB hiv infection or weakening the immune system is a particular concern for people with other conditions. They are more likely to develop tuberculosis after becoming infected, and have a higher risk of death if tuberculosis develops. Who is the risk of getting XDR TB? Drug-resistant Tuberculosis (MDR or XDR) is more common in people: Do not take tuberculosis medications regularly do not take tuberculosis drugs again as prescribed by the doctor Improve tuberculosis disease, In the past, after taking tuberculosis medication, I spent time with someone known to have drug-resistant tuberculosis from some parts of the world where drug-inspicing tuberculosis is common, how can I prevent myself from getting TB disease? Avoid long periods of close contact with known tuberculosis patients in crowded, closed environments such as clinics, hospitals, prisons or homeless prisons. Can tuberculosis vaccine (BCG) help prevent XDR TB? The tuberculosis vaccine is called Bacille Calmette-Guérin (BCG) and is used in many countries to prevent severe forms of tuberculosis in children. However, BCG is generally not recommended in the United States because it prevents the most common forms of tuberculosis and has limited effectiveness in preventing tuberculosis in adults. The effect of BCG on XDR TB will most likely be similar to its effect on drug-sensitive Tuberculosis. If there is drug-sensitive tuberculosis, how can I prevent taking drug-resistant tuberculosis? The most important thing is to continue taking all tuberculosis drugs exactly as a prescription. No dose should be missed and treatment should not be stopped early. If you are having trouble taking medication or have any side effects, you should tell the health care agency. If you plan to travel, contact your healthcare provider and make sure you have enough medicine to stay away for a while. Make. Can XDR TB be treated and treated? Yes, in some cases. Some Tuberculosis control programs have shown that treatment is possible for about 30% to 50% of those affected. Successful results largely depend on the degree of drug resistance, severity of the disease, whether the patient's immune system will weaken and its commitment to treatment. What are the symptoms of XDR Tuberculosis? General symptoms of tuberculosis include feelings of illness or weakness, weight loss, fever and night sweats. Symptoms of tuberculosis disease of the lungs can also include coughing, chest pain, and blood cough. In other parts of the body, the conditions of tuberculosis disease depend on the affected area. If you have these symptoms, you should contact your doctor or the local health department. What should I do if I'm standing next to someone with XDR TB? If you think you are exposed to someone with XDR TB disease, you should contact your doctor or the local health department to take a TB skin test or blood test for a tuberculosis infection. When you spend time with this person, you have to tell the doctor or the nurse. You should also tell the doctor or nurse where the person with XDR Tuberculosis is treated. It will be important to know about the treatment of this person. If the test is positive for tuberculosis infection, special follow-up is required. How long does it take to find out if you have XDR TB? If the tuberculosis bacterium is found in phlegm (phlegm), the diagnosis of tuberculosis can be made within a day or two, but this finding will not distinguish between drug-sensitive tuberculosis and drug-resistant tuberculosis. To determine drug predisposition, bacteria need to be grown and tested in a special laboratory. The final diagnosis for tuberculosis, and especially for XDR Tuberculosis, can last from 6 to 16 weeks. Is XDR TB a problem in the United States? Because XDR TB is rare in the U.S., the risk of acquiring XDR TB in the United States seems to be low. However, tuberculosis can spread easily. As long as XDR TB exists, the risk to people in the United States is not zero and the U.S. public health system threat address is required. How many XDR TB cases have been reported in the United States? 63 XDR TB cases were reported in the United States between 1993 and 2011** *National Tuberculosis Surveillance System (NTSS) 1993-2011. Is it safe to travel to countries where XDR TB cases were reported? Although MDR and XDR TB occur globally, they are still rare. HIV-infected travelers are at great risk in contact with a person who has MDR or XDR TB. All passengers should avoid high risk settings where there are no infection control measures. Documented places where transmission occurs include crowded hospitals, prisons, homeless shelters, and other environments with vulnerable people who come into contact with people with tuberculosis. What can healthcare providers do to prevent XDR TB? Health providers can help prevent MDR and XDR TB by following the recommended treatment guidelines, rapidly diagnosing cases of tuberculosis, patients' response to treatment and make sure the treatment is complete. Providers must also ensure that infection control procedures are properly implemented to prevent exposure to tuberculosis in hospitals or health settings where tuberculosis patients are likely to be seen. Why do there seem to be more XDR TB cases than in the past? In 2006, the CDC, the World Health Organization (WHO) and other global leaders in TB reported the results of a survey on drug-resistant Tuberculosis conducted by 25 reference laboratories, including the Global Snational TB Reference Laboratory Network, the National TB Surveillance System in the United States, the South Korean national reference laboratory, and the national MDR TB patient record in Latvia. The findings showed that 20% of M. tuberculosis isolations were resistant to MDR and 2% were resistant to many additional tuberculosis drugs. This highly resistant form of tuberculosis has been detected in every region of the world where there is laboratory capacity to identify it. In a 2006 report, the highly resistant form of tuberculosis was commonly called drug-resistant Tuberculosis (XDR TB). Since then, we have improved laboratory capacity and XDR TB reporting capabilities to test for more countries XDR TB. These factors contributed to a marked increase in drug-resistant tuberculosis due to better diagnosis and better reporting. What is the CDC doing to prevent XDR TB from becoming a bigger problem? The CDC collaborates with other federal agencies and international partners to raise awareness and develop tuberculosis prevention strategies worldwide: strengthening tuberculosis services for people living with HIV/AIDS; Guidance preparation and epidemic investigation responses; Improving access to tuberculosis drugs; Routine surveillance (including drug predisposition) and conducting periodic surveys; Perform new, rapid diagnostic tests; Developing and promoting national and international tuberculosis testing standards; Execution of program evaluation (e.g. National TB Indicators Project [NTIP]); Improving the capacity of healthcare providers to diagnose and treat tuberculosis; Re-enalering of the Federal Tuberculosis Task Force; Provide assistance to increase tuberculosis program capacity in the U.S. and abroad; and the development of education, risk and media communication (Web and print-based) to help the public awareness and preparation for tuberculosis prevention and control issues. Additional Information CDC. Comprehensive Drug Resistant Tuberculosis Information CDC. TB Questions and Answers About CDC. Tuberculosis: General Information CDC. Multidlith Resistant Tuberculosis CDC. Tuberculosis Information for International Travelers CDC. Comprehensive Drug Resistant Tuberculosis – United States, 1993-2006 This section provides guidance on multidler-resistant and widely drug-resistant tuberculosis (M/XDR-TB) treatment strategies with an emphasis on regimen design. Mono- and drug-resistant tuberculosis treatment is discussed in Chapter 6. The strategies described in this section are largely 2011, updating guidelines for programic management of drug-resistant tuberculosis, which undergoes systematic review and analysis of evidence for best treatment practice (1). Access to quality-guaranteed DST is an important component of tuberculosis treatment. It is critical that drug-resistant tuberculosis programs are familiar with the prevalence of drug resistance in new patients, as well as in different retreatment case groups (failure in a new patient using a primary care anti-TB regimen, failure with primary care anti-Tuberculosis drugs in a previously treated patient, relapse, return after loss of follow-up, and others). This data is usually obtained from an analysis of a country's drug resilience surveillance (DRS) data. In addition, it is essential to determine how often and how often second-line anti-TB drugs are used in

a particular area offered by a programmed strategy. Some second-line anti-TB drugs may have rarely been used and will most likely be effective in drug-resistant tuberculosis treatment regimens, others may have been widely used, and therefore, drug-resistant TB patients have a high probability of ineffectiveness in a large proportion. It is accepted that some drug-resistant tuberculosis programs may have to design strategies based on limited data, as the full assessment of treatment for many patients cannot wait until DRS and other information is available. In such cases, the program can follow the basic principles set out in this section on how an effective regimen is designed and continue to gather the necessary information to design the most appropriate treatment strategy. The following are descriptions of the terms often used to describe treatment strategies. Standardized treatment: DRS data from representative patient populations is used to base regimen design on the absence of individual DST. All patients in a defined group or category receive the same regimen (see Section 4 for risk groups for MDR-TB). Suspect MDR-TB should be confirmed by DST when possible. Individualized treatment: Each regimen is designed according to the patient's past history of tuberculosis treatment and individual DST results. Tuberculosis programs often use a combination of standardized and individualized approaches. However, in cases where DST is not available or is limited to only one or two primary drug, programs most commonly use a fully standardized approach. These strategies are discussed in more detail in Section 5.9, which discusses the use of these strategies in program conditions. This Handbook uses the term empirical to refer to the initiation of treatment before a definitive diagnosis of drug-resistant tuberculosis is determined. Empirical regimens can be used for both standard and individualized treatment strategies. For example, empirical XDR regimen, XDR-TB diagnosis it first means the use of a regimen designed to treat XDR-TB. Classes of anti-TB drugs have traditionally been divided into primary and second-line anti-TB drugs. is reserved. Pyrazinamide, ethambutol and streptomycin are the primary primary anti-TB drugs. While this classification is used in this document, it also use a system that divides drugs into five different groups. The five-group system is based on activity, usage experience, safety and drug class. Different groups are shown in Table 5.1. Not all drugs in the same group are of the same class of drugs or have the same effectiveness or safety. For more information, see individual descriptions of each group in this section. Individual detailed drug information for all anti-TB drugs is given in Section 3.Group 1 drug information pages: First line oral agents. Group 1 anti-TB drugs, to the strongest and best tones, should be used if there is good laboratory evidence and clinical history suggesting that a drug from this group is effective. For patients with resistant but high concentration-sensitive strains in low concentrations of isoniazid, the use of high-dose isoniazid can have some benefit (isoniazid is considered a Group when used in this way 5, see below). New rifamycins like rifabutin, rifampisin has very high cross resistance. It is added to routine MDR regimens (hepatotoxide or other serious side effects) unless there is a reasonable clinical contraindication for the use of pyrazinamide. DST pirazinamide is not reliable, and therefore a regimen is considered an acceptable application to use pirazinamide even when a laboratory result shows resistance. Ethambutol is not added to routine MDR regimens, however, it can be added if the criteria for being a possible effective drug are met (see Section 5.7 for criteria for a possible effective drug). Due to testing difficulties, ethambutol has never been considered an important drug in an MDR regimen, it has already been found susceptible to strain. Group 2: Injectable anti-Tuberculosis drugs. All patients should be given a second-line Group 2 injectable agent at the intensive stage of MDR-TB treatment unless resistance is documented or highly suspected. It can be used as the first option if it meets all the possible criteria of canamicin, amikasin or capreomycin. Given the high rates of streptomycin resistance in patients with MDR-TB (more than 50% in some countries) and streptomycin, which is widely used as a primary care agent in many countries, is usually not used in MDR regimens, even if DST predisposes to it. Kanamisin and amikasin capreomycin have lower costs, streptomycin has less toxicity and have been widely used in the treatment of drug-resistant tuberculosis worldwide. The structure of the amikasin and canamisin is very similar, and there is a high frequency of cross resistance between them. Amikacin has a lower minimum Concentration and two (2) can be the most effective, however, clinical comparison is lacking. If rrs gene mutation is present, there may be cross resistance with capreomycin amikasin/canamisin, but the clinical consequences of this are not well understood. Limited evidence suggests that capreomy has less autotoxia than aminoglycosites (3). If isolated is resistant to both streptomyx and canami, or if DRS data shows high resistance rates to amikasin and canami, capreomysin is recommended as injective. In cases where the second step is resistant to all injectable drugs (amikasin, canamicin and capreomycin), streptomycin should be considered, as there is little cross resistance between streptomycin and other injectable agents, with the exception of streptomycin. All Group 2 drugs are given intramuscularly - most often in the deepening of the gluteal muscle upper outer dial. In addition, Group 2 drugs can be given intravenously, but should be given gradually (60-minute period) using this method. Full dosing instructions are given in Section 3. Given the pain caused by intramuscular injection of the canamicin, some programs prefer to install a catheter for daily delivery of the drug (since it is not possible to rotate a standard intravenous catheter for a long time, a central line usually placed peripherally is required. However, standard peripheral IV catheters can be used to give patients short breaks from intra-muscular injections). This method of birth is generally considered better by the patient but comes with additional costs and requires a expertise that is not ready in all environments. There is limited experience in the delivery of injectable drugs through nebulisors for tuberculosis control, and at this stage no recommendations can be made about this delivery mechanism. Group 3: Fluoroquinolones. Fluoroquinolones are often the most effective anti-TB drugs in an MDR-TB regimen. Guidelines for programic management of drug-resistant tuberculosis There are two important recommendations for the use of fluoroquinolone in the 2011 update (1). Fluoroquinolone should be used in the treatment of patients with MDR-TB (strong advice, very low quality evidence). In the treatment of patients with MDR-TB, later generation fluoroquinolone should be used instead of the previous generation fluoroquinolone (conditional recommendation, very low quality evidence). In meta-analysis of MDR-TB therapy (1,2,4), fluoroquinolones were significantly associated with treatment, and its effect was more pronounced in later generation fluoroquinolones. In the analysis, the next generation of quinolones were moksifloxacin and levofloxacin, ofloxacin was compared. However, the second generation of ofloxacin is considered fluoroquinolone, the third generation of levofloxacin, and the fourth generation of myoxyfloxacin and gatifloxacin is considered fluoroquinolones (5). Analysis didn't do one moxifloxacin (fourth generation) against levofloxsasin (third generation). Levofloxacin is the l-isomeria and more active component of racemic ofloxacin (consists of racemic = dextrorotatory and levorotatory forms). Levofoxacin ofloksasin can be considered to have about twice the activity against tuberculosis. In one study, levofloxacin has a better edebrain resistance to ofloxacin-resistant strains than ofloxacin resistance and gives some evidence that levofloxacin can overcome ofloxacin resistance (6). In theory, poor activity of ofloxine can lead to fluoroquinolone resistance faster. There is little reason for programs to choose ofloksasin in standard regimens, and in the future ofloksasin is likely to be eliminated as a choice for tuberculosis regimens. Ciprofloxacin has weaker edema against tuberculosis than other fluoroquinolones and is not recommended as an anti-TB drug (7). Gatifloxsin has been associated with serious side effects such as hypoglycemia, hyperglycemia and new onlask diabetes (8). Until more valid data explain the safety profile of gatifloxacin in the treatment of MDR-TB, moxyfloxacin or levofloxacin are the preferred fluoroquinolones. Fluoroquinolones are known to increase the QT range. Prolongation of QT range torsades de pointes predisposition can result in sudden death. There is variability between fluoroquinolones in this effect; however, lying is considered minimal. Additional cardiyak monitoring is required when used with drugs that extend the QT range (see <a0><a1></a1></a0>). More QT elongation of moxifloxasin and gatifloxacin levofloxacin and ofloxacin has more effect (9)Thus, for fluoroquinolones, it is recommended that all MDR-TB patients should be treated using the next generation of fluoroquinolones – levofloxacin or mfloxacin. Group 4: Oral bacteriostatic second-line anti-Tuberculosis drugs. Both ethionamide and prothionamide are proliers that need to be activotered by mycobacterial enzymes. There is no clear advantage of etionamide on protionamide; the effectiveness and side effects look similar. Thus, the term etionamide/prothionamide is used to indicate that both can be used throughout this Manual. In Group 4 drugs, ethionomics/prothionamide performed best in meta-analysis of MDR-TB treatment to update 2011 guidelines (1.4). However, it should be remembered that in tuberculosis bacteria, inhA gene mutation is associated with low-level isoniazid resistance and cross resistance with high-level ethionamide resistance (10). If the InhA gene mutation is present, etionamide/prothionamide can still be included in an MDR regimen, but probably should not count as an effective second-line anti-TB drug. Cyxerine and/or para-aminocylic acid (PAS) should be included in MDR regimens. Both PAS and cyxerine show cross-resistance to other anti-TB drugs. Since its combination And PAS usually causes gastrointestinal side effects and a high insidy of hypothyroidism, these agents are often used only together when three Group 4 agents are required. It is not known whether terizidone (containing two cyclolyers) two molecules of cyclosis at the time of writing this article was equally effective. Medications from drugs in Group 4 can be started at a low dose, rising from three to 10 days (known as dose-ramping) (11) to reduce the frequency or severity of side effects. Group 5. Group 5 drugs are not recommended by Who for routine use in the treatment of MDR-TB. Although all have shown at least some activity in in vitro or animal models, the quality of their effectiveness and safety evidence in humans for the treatment of drug-resistant Tuberculosis varies. Most of these drugs, with the exception of bedaquiline and delamanid, are not registered to make their use off-label for the treatment of MDR-TB. 6 In some cases the drugs are quite expensive and require intravenous application (imepenem and meropenem). However, they remain options in cases where it is impossible to design adequate regimens with drugs from Group 1-4. If a condition requires the use of Group 5 drugs, most often experts will recommend using two to three drugs from the group, given limited effectiveness knowledge. Below is information that can help choose which Group 5 drugs to use when indicated, and (for full drug information, see Section 3 – Individual Drug Prescribing Information). Bedaquiline – See App app app app appr to Apprel 4 for the definition of bedaquiline, which includes indicators and safety monitoring requirements. Linezolid - Linezolid in vitro and has shown good activity in animal studies. There are also off-label use cases in M/XDR-TB; recently shown to improve results in XDR-TB (12,13) Group 5 is considered one of the most effective drugs against tuberculosis and is usually an important drug in XDR treatment regimens (see also XDR). Chapter 5.15 and Box 5.4). It has numerous serious side effects such as myelosupression (anemia, leukemia, thrombocytopenia and pancytopenia), peripheral neuropathy and lactic acidosis. The drug usually needs to be stopped when serious side effects occur (in some cases the side effects can be managed by reducing the dose (usually 600 mg daily 300 mg daily). while dosing 300 mg is not known if it is effective as a low dosing or if resistance will lead to a higher chance of amplification, although some clinical experts have found that dosing due to anemia quite often coincides with culture conversion, which increases the chances of keeping the drug in the treatment regimen. Clophasemine – There is a significant part of the experience with clophasymine in the treatment of MDR-TB (14-16), included in regimens of 9-12 months and with very good results (17). However, the effectiveness of toiletosis belonging to tuberculosis remains unclear. Clofazimine is usually added For XDR-TB. Depending on side effects, skin pigmentation occurs between 75% and 100% of patients within a few weeks; after treatment, it can take inverse months to years. Amoxiccilin / klavulanate – Generally, beta-lactam antibiotics are not considered very useful drugs against tuberculosis, but the addition of a beta-lactama inhibitor activates them into vitro against tuberculosis. In vivo has evidence of bactérisidal activity (18). While amoxiccilin/klavulanate is probably a relatively weak anti-TB drug, it is often involved in regimens because it is available, inexpensive and with several side effects. Imipenem/cilastin and meropenem. Beta-lactam-carbapenem belonging to the class of imipenem and meropenem drug, given only intravenously. Due to cost and dosing difficulty, it is usually not used in resource-restricted settings. A similar drug - Meropenem - is preferred for use in children and adults with central nervous system disease, as there are fewer relationships with seizures. Given that impenemine is rapidly deteriorating by renal proximal tubule dipeptidases, the dipeptidase inhibitor is marketed in combination with cytoatin. Conversely, meropenem is stable for renal dipeptidases and does not require silastatin (19). Since these antibiotics are in the beta-lactam class it is likely to benefit from the addition of imipenem/silastin and meropenem clavulanate to 125 mg every 8-12 hours. Klavulanate had a pretty good result on mpenem in a study of xdr-tb patients (13). (Klavulanate is not ready alone and give some amoxicin/clavulanate as a 500 mg/125 mg oral tablet). High dose isoniazid. Many experts believe that high doses of isoniazid can be used against low doses of resistant but high dose resistant strains (20) (0.2% of mcg/ml resistant bacillus>1 but susceptible to izoniazid in 1 mcg/ml), whereas isoniazid is not recommended for high dose resistance (>1% bacilli resistant mcg/mlisyon). Some experts give 900 mg (21) three times a week, while others give 16-20 mg/kg/day (22) High doses also do not have good data on the safety of onyakitin and may be associated with higher rates of peripheral neuropathy, hepatitis and other unpredictable side effects. Experts also recommend that you do not use isoniazid if the strain has been documented to be a CATG gene mutation. The KatG mutation can be detected in line catalyd tests available today. Thioacetazone. Alhowever, thioacetazone is a drug with known edemosis against TB, it is not well established in the treatment of drug-resistant Tuberculosis, since Group 5 is placed. In general, there is a weak bacteriostatic drug, cross resistance with thioacetazone etionamide (23) and iyoniazid (24,25). Thioacetazone is contraindiced in HIV-infected individuals (26) due to a serious risk of Stevens-Johnson Syndrome and a negative reaction that can result in death. The drug is also not toned down in people of good Asian descent. For for these reasons, this drug is rarely added as a Group 5 drug. Until more information is learned about its role in MDR-TB treatment, most experts recommend that drug-resistant tuberculosis programs should not include thioasettaz relation, especially if the HIV status is unknown. You're a claritromia. Clarithromymia is included in Group 5, but its activity against M. tuberculosis is unclear. Some studies suggest that clarithromycin may have a synergy effect with oral primary care agents (27.28) but no synergy data with second-line drugs. Most experts consider his claritromia a very weak anti-TB drug and think it has no role in the treatment of MDR-TB. There is a standard code for writing tuberculosis treatment regimens. Each anti-TB drug has an acronym (shown in Table 5.1 and in the list of abbreviations given in front of this book). The drug-resistant tuberculosis regimen consists of two stages: the first stage is the period when the injectable agent is used, and the second is after stopping. These two stages are usually separated by a backslash (/). The number before each stage represents the phase time in the month, and this number is the minimum time that the phase should last. The number in the subseging after a letter (e.g. 3) is the number of drug doses per week. If there are no numbers in the subseging, the treatment is daily (injectables are usually given 5-6 days a week). Drugs in higher groups are first prescribed by others in descending group order. EXAMPLES Box 5.1.EXAMPLES OF STANDARD DRUG CODES USED TO IDENTIFY DRUG REGIMENS. The initial stage of 8Km6-Lfx7-Eto7-Cs7-Z7/12Lfx7-Eto7-Cs7-Z7 consists of five drugs and lasts eight months in most patients (see Chapter 5.9). Six days a week and all of the canamisin is given (more...) See Section 3 for a full discussion about the use of DST in programclady management of drug-resistant tuberculosis. Countries have diverse access to reliable mycobacterial laboratories, and many do not have regular local access to DST. Not being able to perform routine DST in all patients should not be an obstacle for patients with MDR regimens. Fully standardized regimens using second-line anti-TB drugs have been shown to be feasible and cost-effective in the treatment of drug-resistant tuberculosis (29-31). The reliability and clinical value of DST of some primary and second-line anti-TB drugs has not been fully determined (see DST cannot 100% precisely estimate the effectiveness or ineffectiveness of a drug (32). DST for ethambutol, streptomysin, pynapynamide, Group 4 and 5 drugs has problems with accuracy and repeatability in most environments. Therefore, current WHO guidelines dst results caution against baseing individual regimens of these drugs. DST isoniazid, rifampisin, fluoroquinolones, and second-line injectable agents are considered accurate and repeatable; When DST results come from a quality-assured laboratory, individual regimens may be based on. In countries with reliable DST available, the Xpert MTB/RIF test can be introduced quickly and used as the first diagnostic tool for MDR-TB (see Section 4 for more information about using Xpert as a test for MDR-TB). While strategies can be designed as a single DST mechanism with Xpert MTB/RIF, even based on the history of TB treatment to identify mdr-TB, every effort must be made to improve the laboratory capacity of the ATB program to gain access to the traditional phenotypic DST and/or secondary molecular DST method (see Section 3). This section describes how to design and manage an MDR regime. Applies to standard and individualized regimes. The WHO's interim policy on the use of delamanid will be published in late 2014 and should be taken into account when designing an MDR-TB treatment regimen. The basic principles included in the treatment of MDR-TB are as follows (recommendations for the 2011 update of the Guidelines for programic management of drug-resistant tuberculosis have been included and, if any, indicated) (1). Early MDR-TB detection and rapid initiation of an effective treatment are important factors in achieving successful results. The intense stage of MDR-TB treatment should consist of at least four second-line anti-TB drugs (including an injectable anti-TB drug) and pyrazinamide (conditional recommendation, very low-quality evidence) that are likely to be effective (1). Where there is unething evidence about the effectiveness of a particular drug, this drug may still be part of the regimen, however, it should not depend on success. MDR regimens should include at least pyrazinamide, fluoroquinolone, an injectable anti-TB drug, ethamide (or prothionamide) and cycloserine or PAS (para-aminosalycylic acid) if cycloserine is unavailable (conditional advice, very low quality evidence)(1). It should be assessed that drugs in the regimen are most likely effective. An anti-TB drug is considered likely to be effective:-The drug has not been used in a regimen that fails to treat individual patents;-DST shows that the patient is susceptible to the drug made on the strain (for DST isoniazid, rifampisin, Groups 2 and 3 drugs are considered reliable; For all other drugs, DST is not reliable enough for individual patient management);-There is no known resistance to high cross-resistance drugs (See Section 3, Table 3.2);-Close contact known for resistance to medication;–Drug resistance surveys show that drug resistance is rare in patients with a similar history of Tuberculosis. This last criterion is related to the absence of DST or for drugs for which individual DST is not reliable. Note: It is not always possible to identify information in all five criteria. Therefore, clinical judgment is usually necessary about whether it is most likely necessary to effectively count a drug. There are cases when more than five drugs are used. These conditions are is unlikely or unsym suspected for a drug. This is a relatively common condition XDR-TB treatment (see Section 5.15). Medications known to have a strong use contraindication of the patient due to drug-drug interactions, high-level toxicity, co-morbidities, severe allergies or other adversity reaction drugs and/or pregnancy should not be used. Fluoroquinolone should be used (strong advice, very low quality evidence) (1). Instead of the previous generation fluoroquinolone, the later generation fluoroquinolone should be used (conditional recommendation, very low-quality evidence) (1). Etionomide (or protionamide) should be used in the treatment of patients with MDR-TB (strong advice, very poor quality evidence) (1). This recommendation meets the criteria for the probability of effective use of recommended drugs and assumes that there is no contraindication in its use (for example, serious side effects). The intensive phase (i.e. the first part of treatment using a group 2 injectable agent) lasts at least eight months in total, but the duration can be changed according to the patient's response to the treatment (1). The most appropriate intensive stage time following the culture transformation associated with treatment success cannot be directly removed from the analysis used in 2011 to review WHO programmed management of drug-resistant Tuberculosis guidelines. Some clinical experts may prefer to continue at least four months before the culture transformation of the dense universe (see intensive phase Length Part 5.9). The total duration of treatment for MDR-TB in the majority of previously untreated patients is expected to be at least 20 months (1). Some clinical experts may prefer that the total treatment be at least 12 months past the point at which the culture turns negative, and some may prefer not to give less than 20 months in total (see Section 5.10 on the duration of treatment). Each dose is given under directly observed treatment centered on the patient throughout the treatment. A treatment card is marked for each observed dose (see <a0><a1></a1></a0>). Chapter 4 – Forms for drug-resistant tuberculosis programs). DOT can be performed at facility-based or community-based levels, considering that social support is an important component of care and treatment presentation (see <a0><a1></a1></a0>). Chapters 12 and 18). Any side effects of medications should be managed promptly and adequately to alleviate pain, minimize the risk of interruption of treatment, and prevent morbidity and mortality due to serious side effects (see Antiretroviral therapy (ART) is recommended for all patients with HIV and drug-resistant tuberculosis as early as possible (within the first eight weeks) after the initiation of anti-TB therapy, regardless of the number of CD4 cells (strong advice) (1). The dose of the drug is usually determined by age and weight. The recommended weight-based dosing scheme is shown in Appeasing 2. Dosing of paediatric cases is defined in Chapter 7 and Annex. ethambutol and fluoroquinolones should be given once a day. Depending on patient tolerance, dosing once a day is also used for Group 4 oral second-line anti-TB drugs, however, etionamide/protionamide, cycloserine and PAS are given in divided doses throughout the day to reduce traditional side effects. All anti-TB drugs can be started in full dose. However, if tolerance is a problem, cycloserine, ethionamide and PAS dosing can be gradually increased over a two-week period (11). Injectable drugs can be prescribed five to seven days a week, depending on the availability of a medical person skilled to make intra-muscular injections. Injectable anti-TB drugs should be given once a day, that is, do not divide the dose during the day. If side effects are problematic in a patient, the injectable agent can be given three times a week, preferably only after culture transformation (11). When possible, oral drugs should be given seven days a week under direct observation. Some programs recommend whether all drugs are given six days a week, but it is not known if this is equal to seven days a week. Oral drugs should not be given five days a week (only the injectable agent is allowed to be on the program five days a week, see above). Pyrazinamide can be used for all treatment. Many drug-resistant tuberculosis patients have chronically inflamed lungs that theoretically produce the acidic environment in which neuroanamid is more effective. Alternatively, in patients who do well, piazinamide can be stopped with injectable medication if the patient can continue with at least three possible effective drugs. In MDR treatment strategies, which initially enroll patients according to their strains, which are rifampisindirening on their own, izoniazid can be included in the MDR regimen up to DST to determine whether the isoniasis should continue and be needed. Patients with MDR-TB should first be treated using ambulatuar care instead of hospitalization (conditional recommendation, very low quality evidence) based care models (1,33). Empirically standardized regimens usually need to be adjusted based on patient clinical history, when additional history or DST results are made available. Individual regimens are designed based on infected strain DST, tuberculosis treatment and contact deposit patient's history. Figure 5.1 explains the steps to create a regimen for the treatment of drug-resistant tuberculosis. Treatment strategies for drug-resistant tuberculosis may vary depending on access to DST and drugs, drug-resistant tuberculosis rates, HIV prevalence, technical capacity and financial resources. Tuberculosis programs may need to adjust the strategy to meet specific conditions and local context. Representative DST survey data for different types of patients – new, relapse, retreatment after follow-up loss, first or retreatment failure with primary anti-TB therapy, and failure of treatment with second-line anti-TB drugs – are important when making choices in treatment strategies. Standardized With four effective second-line anti-TB drugs plus pyraznamide will treat the vast majority of patients, it may be required to use more than four second-line drugs plus pyrazinamide to cover all possible resistance patterns. When using an empirically standardized regimen, Tuberculosis programs are strongly encouraged to order drugs from groups and classes that are not routinely involved in the standard regimen. For example, a program that uses an empirical standardized regimen that does not contain PAS will still need PAS if: (i) patients who are intolerant of one of the basic drugs; (ii) pregnant patients with drug-resistant tuberculosis and unable to take all medications of the standard regimen; (iii) as part of a regimen in which the standard MDR treatment regimen fails or is in regimens for XDR-TB. All programs are encouraged to have regimens designed to treat XDR-TB when the standardIzed MDR regimen fails. In MDR treatment strategies, which initially enroll patients according to their strains, which are rifampisindirening on their own, isoniazid can be included in the standard regimen up to DST to determine whether it should continue. Even if the resistance of mono-or poly-rifampisin is relatively common, isoniazid can be added to the regimen. However, in cases where mono or poly-rifampisin resistance is extremely rare (only 1% or 2% of all rifampisin resistance), it makes sense to leave out the isoniasis of the empirical standard MDR treatment regimen; if patients are found to be susceptible to strain, they can be added later. Box 5.2 provides three examples for designing an MDR treatment regimen. The first example is to design a standardized regime based on drug resistance survey data, while the second example shows designing a regimen based on individual DST. The regime design for XDR-TB is described in Section 5.15.EXAMPLES STANDARD AND PERSONAL REGIMENT DESIGN. EXAMPLE 1: A standardized MDR regimen based on drug resistance survey data with low resistance to second-line anti-TB drugs. Survey data from 200 consecutive registered patients (more...) Some programs or clinicians may prefer to use shorter (for example). 9-12 months) MDR-TB treatment regimen is the treatment regimen consisting of a combination of later generation fluoroquinolones (moxifloxacin or gatifloxacin), klofazimin, ethambutol and pynanamide during the treatment period supported by protiyomyd, canamisin and high-dose isoniazid at an intense stage. Evidence for these short regimes comes from limited observational studies. Until May 2014, only one study of a series of patients using a short regimen in Bangladesh had yet to be published in a peer-reviewed journal (17). The ongoing randomized clinical trial assesses the effectiveness and safety of a shorter regimen in the treatment of MDR-TB treatment and results should be given around 2017 (51). Those who choose to use shorter regimes are In the treatment of xdr-tb, and in patients who already harbor bacillus resistant to second-line drugs, it is likely to achieve additional resistance. Therefore such regimens should not be taken into account for the treatment of XDR-TB, among patients with second-line injector or any fluoroquinolone resistance, or for patients who have previously been exposed to second-line anti-TB drugs for more than a month. Combined off-label use of clophase and other drugs (e.g. fluoroquinolones) that extend the QTc range in the ECG in these regimens is active pharmacoviglylans (see active pharmacoviglylans (see Fluoroquinolones) to ensure proper oversight management of safety issues. Longer treatment regimens for MDR-TB represent the standard of care that is more common and used for much longer (52); it has also shown that they produce good results in some countries and that the adversity drug reactions associated with them are well documented (53). It is therefore mandatory for clinicians and/or NTPs to maintain an informed process of care with patients under the supervision of the national or local ethics committee before starting treatment. Some programs may choose to register patient cohorts to treatment with shorter regimens as part of observational studies aimed at producing evidence about its safety and effectiveness to inform local and global policy. The commitment to the international standards of good clinical practice, including proper independent monitoring, should be implemented by the relevant program managers of these observational studies (54). The time of the MDR-TB patient on injectable anti-TB drugs is called the intensive stage of treatment. An intensive eight-month stage is recommended for most patients in the treatment of patients with MDR-TB, which can be changed according to the patient's response to treatment (conditional recommendation, very low quality evidence) (1). The main indicator of the response to treatment is dissemination and culture-transformation (defined in Section 2), however, the overall clinical picture (weight gain, resolution or improvement of respiratory symptoms and/or lesions in pulmonary images) can also be considered when deciding whether an injectable agent should continue for more than eight months. In a meta-analysis (1) conducted in the preparation of WHO guidelines for programmed management of drug-resistant tuberculosis, it is important to start taking into account that injectable stages have no benefits of more than eight months, and for those who have not generally turned into culture by the eighth month, the failure of treatment should be taken into account. In terms of smear and culture-transformation, expert opinion is that the intensive phase should continue for at least four months of transformation; however, there is little evidence and the most appropriate time-by-pass conversion has not been determined. The optimal duration of the injective phase was also not determined in patients with minimal disease; they can decide individually that such patients can eat a dense stage for less than 8 months, provided they convert for at least four months. Intermittent treatment with the injectable agent (three times a week) can also be considered when it is injectable for a long time and toxicity becomes a greater risk for the patient (11). This is based on expert opinion, as there are direct comparisons of three times a week against daily doses. If the patient is on the empirical regimen of more than four second-line anti-TB drugs, some oral second-line anti-TB drugs, in addition to the injectable agent, can be accepted for suspension at the end of the intense phase. This is usually done when DST results predispose to at least four second-line agents, drugs are still considered effective, and the patient has been a good response to treatment. Usually, pyrazinamide is continued for all treatment, especially if there is extensive parankimal lung damage. However, there is no data on the most appropriate duration of the use of pyronamide in the treatment of MDR-TB. If the patient has minimal disease, some clinicians stop pirazinamid with the injectable agent at the end of the dense phase. In any case, the patient should at least continue with the second-most powerful second-line anti-TB drug, which is determined to be effective against the infected strain of the patient with tuberculosis. In the treatment of new patients diagnosed with MDR-TB (i.e. previously untreated for MDR-TB), a total of 20 months of treatment is recommended for most patients, and the duration can be changed according to the patient's response to treatment (conditional recommendation, very low quality delameti) (1). The main method used to evaluate the response to treatment is through dissemination and culture-transformation (defined in Section 2); however, clinical symptoms and radiography can also be considered as to whether the treatment is longer than 20 months. It has not been determined if the total duration of treatment will be in the past transformation. Some clinicians and programs can choose to treat conversions that have passed at least twelve months (but total at least 20 months). In the meta-analysis carried out in the preparation of the WHO Guide, programic management of drug-resistant tuberculosis (1) showed that the total duration of treatment in patients previously treated with the MDR regimen was more than 24 months, but the number of patients observed was relatively small. Therefore, patients who have previously been treated for MDR-TB (and usually XDR-TB patients) usually receive treatment for at least 24 months in most programmes. Extrapulmonary drug-resistant Tuberculosis is treated with the same strategy and duration as pulmonary drug-resistant Tuberculosis; an exception is central nervous system involvement. If the patient has symptoms suggesting central nervous system involvement and With drug-resistant Tuberculosis, then you should use drugs that have sufficient penetration into the central nervous system of the regime. Ioniazid, pynanamide, protionamide/etionamide and cyclocene, all have good penetration into the cerebrine fluid, while the canamisin, amikasin and streptomisin only do so in the presence of meningeal inflammation. In addition, penetration of capreomycin is less studied and not well determined. PAS and ethambutol are bad or have no penetration. Fluoroquinolones have variable cerebrine fluid penetration, with better penetration of moxifloxacin based on animal studies. There is no data on central nervous system penetration of klophazimine or clarithromymia. Linezolid is believed to penetrate the central nervous system and is used to treat meningitis (35). Imipenem has good central nervous system penetration, but children treated with meningitis imipenem had high seizure rates (meningitis cases and meropenem preferred for children) (11,36,37). The most common surgical procedure in patients with pulmonary drug-resistant tuberculosis is resection surgery (taking part or all of the lung). Large case series analysis has proven that resection surgery is effective and safe under appropriate surgical conditions (38). It is considered to assist chemotherapy and seems to be beneficial for patients when skilled thoracic surgeons and excellent postoperative care are available (39). It is not indicated in patients with intense bilateral disease. The case series, which shows that surgery is effective, may have a choice bias because very sick patients with accompanying morbidies, elderly patients and those with extensive illnesses are often excluded from surgery. Resection surgery should be timed in such a way that the patient has the best possible chance of treatment with the least morbid. Therefore, when the patient has a lower risk of morbidity and mortality, for example, when the disease is still localized into a lung or a pulmonary lobe, the timing of surgery may be earlier in the course of the disease. In other words, surgery should not be considered a last resort. In general, treatment should be given at least two months ago with resection surgery to reduce bacterial infection in the surrounding lung tissue. Even in successful resection, the intensive phase and total duration of treatment should be guided according to recommendations in Sections 5.9 and 5.10. Special surgical facilities should include strict infection control measures, given that large quantities of infectious substances and aerosols are produced during surgical, mechanical ventilation and postoperative lung hygiene maneuvers. Many programs will have limited access to surgical interventions. General best notations for resection surgery for programs with limited access to surgery include patients who remain smear positive and are resistant to a large number of drug- resistant patients; localized lung disease. Computed tomography, pulmonary function test and pulmonary perfusion/ventilation is recommended as part of pre-surgical work. In programs with lower optimal surgical facilities without trained thoracic surgeons, resection surgery should not be performed as it may increase morbidity or mortality. The role of adjuvant treatments has not been fully determined. However, some auxiliary methods were useful in certain indications (i.e. the use of corticosteroids in certain forms of tuberculosis, such as the central nervous system and pericardialysis), while others showed the potential to improve results (e.g. immunomodulators) (40). In drug-resistant tuberculosis patients, the use of adjuvant of corticosteroids has been shown not to increase mortality while the patient is on an effective regimen. Corticosteroids can be useful in cases such as severe central nervous system or pericardianial involvement. Expert opinion, respiratory failure and military tuberculosis can also help. Prednizone is usually used with a tapering of dosage within a few weeks (21). Corticosteroids can also alleviate symptoms in patients with a flare-up of obstructive pulmonary disease. When a more immediate response is required, injectable corticosteroids are often used initially. Corticosteroids can weaken the body's response to fight tuberculosis and therefore should only be used if it is clearly stated and the patient is on an adequately effective regimen. If corticosteroids are used on an inadequate regimen, this can accelerate the deterioration of the patient. The results from the use of immunonoteraptic interventions have so far been only moderately encouraging. Evidence examined by a specialist group in 2007 has found that immunomodulators have the potential to improve all tuberculosis outcomes, including M/XDR-TB (40). The effectiveness and safety of this treatment should be further evaluated before any recommendations regarding special treatment are made. Drug-resistant tuberculosis treatment (as in all tuberculosis treatment) and care should include integrated nutritional evaluation counseling and support throughout the disease. In addition to causing malnutrition, as in other forms of tuberculosis, drug-resistant tuberculosis can be exacerbated by malnutrition. Without nutritional support, patients can be enmeshed in a vicious circle of malnutrition and disease, especially if they already suffer from border-bound hunger. Second-line anti-TB drugs can also further reduce appetite, making adequate nutrition a bigger problem. Providing free food probably doesn't increase weight gain during treatment, and is thought to improve quality of life but further research is needed (41). Food support can increase treatment sediment in foods, as food insecurity is a major access barrier. Vitamin B6 (pylyoxin) is a high dose of isoniazid or linezolide to all MDR-TB patients taking cycloserine or terizidone and to prevent neurological side effects (See Section 11 for dosage and more information). Vitamins (especially A) and mineral supplements can be given in areas where patients have a high rate of these deficiencies. Multivitamins and minerals (zinc, iron, calcium, etc.) should be dosed for three to four hours outside fluoroquinolones, as this can interfere with the absorption of drugs. Note, no studies have assessed whether vitamin tuberculosis treatment should improve. Vitamins probably do not increase weight gain, and no study can assess their effect on quality of life (41). XDR-TB is estimated to have occurred in approximately 9.6% of MDR-TB patients first identified in 2006 (42). While occurring all over the world, it has been reported as a major problem in some countries (39.42). The likelihood of treatment has proven to be much lower than in other MDR-TB cases, and deaths are higher, especially in hiv-infected patients (39.44-48). There is very limited data on different clinical approaches to XDR-TB, and there is no relationship between success and any specific medications or regimens in the recent review of treatment results of XDR-TB patients; however, the analysis shows that success is highest in XDR-TB patients when at least six drugs are used in the intensive phase and four at the stage of resection (48). A different meta-analysis provides empirical evidence that although DST has shown resistance to a representative fluoroquinolone, the use of advanced generation fluoroquinolones in patients with xdr-tb significantly improves treatment outcomes (47). Although effectiveness and safety data are limited, it is conceivable that regimens designed to treat XDR-TB should be included in the bedilaline (49) (See Appeasing 4). New anti-TB drugs are currently under development and program managers should follow WHO recommendations while they are published and updated by the New Drug Policy Development Task Force's website (50). For more information about compassionate use and early access programs, see <a0> </a0>. TREATMENT MANAGEMENT FOR PATIENTS WITH XDR-TB, DOCUMENTED OR ALMOST CERTAIN. Use pirazinamide and other Group 1 agents that can be effective. Use an injectable agent where strain is sensitive and consider the long-term duration of use (12 months (more...) XDR-TB REGIMEN DESIGN EXAMPLE. EXAMPLE 1. One patient failed the standard regimen of Z-Km-Lfx-Eto-C's and remained phlegm smear positive after eight months of treatment. DST HRZE-S-Km-Cm-Lfx resistance from a sample taken four months ago revealed resistance (more...)

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