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The 2011 update of the World Health Organization guidelines for the programmatic management of drug-resistant tuberculosis

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Introduction: The production of guidelines for the programmatic management of drug-resistant tuberculosis fit into the mandate of the World Health Organization (WHO) to provide technical support to countries to reinforce care of drug resistant tuberculosis patients.

Methods: WHO commissioned systematic reviews of evidence, including meta-analysis and modeling studies, to summarize evidence on priority questions regarding case finding, treatment regimens for multidrug-resistant TB (MDR-TB), monitoring of response to MDR-TB treatment and models of care. The quality of evidence assembled varied from low to very low. A multidisciplinary expert panel used the GRADE approach to develop recommendations based on best available evidence.

Findings: The recommendations encourage the wider use of rapid drug-susceptibility testing with molecular techniques to detect rifampicin resistance and treat patients adequately. The use of culture remains important for the early detection of failure during MDR-TB treatment. The guidelines provide recommendations about the early use of anti-retroviral agents for TB patients with HIV who are on second-line TB drug regimens. Systems that primarily employ ambulatory models of care to manage MDR-TB patients are recommended over others based mainly on hospitalization.

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Conclusion: Practitioners and decision makers involved in MDR-TB care should be guided in their work by these updated recommendations. Additional research is necessary to improve the quality of existent evidence, particularly on regimen composition and duration of treatment.

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Treatment outcomes for multidrug-resistant tuberculosis (MDR-TB) patients in Africa

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Introduction: As countries in Africa scale up their treatment of multidrug-resistant tuberculosis (MDR-TB) patients, it is important to monitor the results of treatment efforts.
Methods: In 2010, as part of its global TB surveillance activities, the World Health Organization gathered information on treatment outcome cohorts of MDR-TB patients starting treatment in 2007. The delay allowed programmes time to recover data for patients whose treatment commonly lasts two years or more.
Results: Seventeen of the 46 countries in the African region reported treatment outcomes for an aggregate of 4523 MDR-TB cases, mostly from South Africa (3815). Thirteen of these countries had notified a total of 8234 MDR cases in 2007 (4 countries had no data), and outcome cohorts varied in size between 20% and >100% of cases originally notified. Outcome reports were incomplete with five national cohorts having no information on >20% of the patients treated. Treatment success ranged between countries from 14% to 100% of patients (median: 60%) and deaths from 0% to 57% (median: 14%). Defaults were more frequently reported (12 countries; median 9%) than failures (5 countries; median 0%).
Conclusions: Coverage and success in the African cohorts are comparable with other regions in the world. Reports on enrolment of MDR-TB patients on treatment and their outcomes are incomplete in many countries even when compared to original MDR notifications by the countries. This is a result of low capacity for scaling up care and ineffective reporting. Treatment success for MDR-TB patients remains low as a result of a high risk of dying, of failed treatment or of interruption of prescribed treatment.

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Increasing TB drug resistance in Moldova during the 2006-2010

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Background: The emergence of drug-resistance (DR) hampers tuberculosis (TB) control. The level of primary DR, particularly multidrug resistance (MDR) is one of the main causes of ineffective treatment of new TB cases. The aim of the study was to estimate the trends of TB DR in Moldova during the last 5 years.
Materials and methods: Retrospectively analysis of 11,193 pts cards of drug sensitivity tests performed in the National TB Reference Laboratory and three Regional TB Reference Laboratories during 2006-2010. DST was performed on L-J media using absolute concentration method and on liquid media (MGIT960) in laboratories with controlled quality (concordance with reference laboratory >95%). The last two years were implement the Hain method for rapid diagnosis of MDR TB.
Results: From all examined patients, 5241 (47,2%) were new TB cases tested before treatment. The level of primary DR has been increased from 42,9% to 49,5 during the 5-years period. MDR TB also increased (19,4% and 25,6% respectively). The level of secondary DR also has been increased from 70,5% to 80,2% and MDR TB from 51% and 65% respectively. The concordance of DST results between L-J, MGIT and molecular method consist 96%.
Conclusion: At the current stage DR TB is a serious problem for the Moldova, bringing serious public health and economic consequences. The high level of MDR TB reflects the failure of TB control programs in the previous years. The low rate treatment success leads to the increase of DR and the worsening of epidemiological situation with regard to TB control. Non-compliance of patients to treatment regimes is the most serious and still one of the major problems facing control TB in country and the most determinant of develop DR TB.

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Drug-resistant tuberculosis in Belarus: Results of the first representative survey

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Introduction: Drug-resistant tuberculosis (TB) is a public health threat in all

countries of the former Soviet Union. In Belarus the magnitude of the problem has been unknown, given that no representative, quality-assured data exist.
Objective: To investigate frequencies of 1st and 2nd-line anti-TB drug resistance in Minsk City, and to explore risk factors for multidrug-resistant (MDR) TB.
Methods: Between November 2009 and August 2010 all new and previously treated patients with smear- or culture-positive TB presenting to all TB units in Minsk City were invited to take part in the study. Drug susceptibility testing (DST) for 1st-line drugs was conducted on all isolates; DST for selected 2nd-line drugs was conducted on MDR-TB isolates. External quality assessment of DST was performed at the Stockholm Supranational Reference Laboratory.
Results: 156 new and 67 previously treated TB patients were enrolled in the study. MDR-TB was found in 35.3% (95%CI: 30.8-40.0) of new patients and 76.1% (95%CI: 65.9-84.1) of those previously treated. Extensively drug resistant (XDR) TB was found in 15 of the 106 MDR-TB patients (14.2%; 95%CI: 8.1-22.3). History of previous treatment was found to be an independent predictor of MDR-TB (OR: 5.9; 95%CI: 2.9-12.0) and XDR-TB (OR: 11.1; 95%CI: 2.8-62.9). Patients under 35 years old had a 2.0 times higher odds of MDR-TB than those 35 and older (95%CI: 1.0-4.2). No association was found between MDR-TB and sex.
Conclusions: Very high frequencies of MDR-TB and XDR-TB are documented in Minsk City. These results greatly contribute to the understanding of the burden in urban areas of Belarus and will be complemented by findings of a nationwide survey currently underway.

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First second line anti-tuberculosis drug resistance survey in Romania

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Introduction: It's estimated that Romania notifies about 800 MDR-TB cases yearly. The first XDR-TB case has been reported in 2006.
Aim and objectives: To assess the second line anti-TB drugs resistance among MDR-TB patients and provide recommendations for MDR-TB case management at country level.
Methods: The survey included all MDR-TB patients diagnosed countrywide from October 1st 2009 to January 31st 2010. Indirect proportion method on Lowenstein Jensen media has been used to test susceptibility to Izoniazid, Rifampicin, Kanamycin and Ofloxacin in four reference laboratories. Both clinicians and laboratory specialists have been trained before the start of the survey. Quality assurance for each laboratoty was performed before and durring the survey.
Results: The results were assessed for 756 MDR-TB cases. Of them, 394 (52.1%) show resistance to only INH and RMP, 211 (27.9%) to INH, RMP, KM and 66 (8.7%) to INH, RMP, OFX. XDR-TB has been observed in 85 cases (11.2%). Any resistance to KM was almost double than any resistance to OFX (296 and 151 respectively). In 28% of subjects no DST was performed before the survey. The most frequent MDR-TB cases were chronics (285-37.7%), followed by relapses (191-25.3%), new cases (101-13.4%), retreatments after failure (92-12.2%) and retreatments after default (80-10.6%). In 7 cases (0.9%) the category by treatment history was unknown. Out of 388 HIV tested MDR-TB patients 10 (2.6%) were positive.
Conclusions: The XDR-TB rate among MDR-TB cases in Romania is 11.2%. In order to early detect drug-resistant cases it's necessary to test all strains from retreated TB cases and from new cases with high risk for MDR.

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Successful treatment of multidrug-resistant tuberculosis through a binational consortium

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Background: Multidrug resistant tuberculosis (MDR-TB) is expensive to diagnose and treat, and requires a high degree of expertise by the laboratory and medical team, resources that may be scarce in regions with the highest rates of MDR-TB. Baja California, a Mexican state that shares the international border with California, United State of America (USA) has the highest rate of tuberculosis in the country.
Methods: A binational consortium constituted by USA and Mexico partners started a program dedicated to the diagnosis and treatment of MDR-TB in the region. All regimens were individualized according to drug susceptibility tests with a mean of 5.38 drugs used per regimen. Strict directly observed therapy was enforced in every case.Funding from USAID, Rotary International and private donors has augmented existing program funds
Results: From June 2006 through December 2010 forty patients started treatment. The lapse between their initial diagnosis and the referral to the program was 43.6 months; they had received 2.15 treatment regimens in the past. Their strains were resistant to 4.15 drugs; 2 patients (5.1%) had an XDR-TB strain.
All patients converted their culture on treatment, on average after 4.0 months.

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Nineteen patients (47.5%) have been discharged as cured (mean follow-up after discharge 6.8 months), 3 patients died (7.5%) and one patient abandoned (2.5%).
Conclusions: Highly resistant cases can be cured under a well organized, outpatient program. In this consortium the USA partner introduced program elements that have been gradually integrated into the state TB program. After 5 years, the consortium continues to fine-tune sustainable interventions and provides quality control.

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Tuberculosis in household contacts of multidrug-resistant tuberculosis patients

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Setting: The burden of tuberculosis disease amongst household contacts of multidrug-resistant tuberculosis patients is poorly understood and might represent a target for transmission-interrupting interventions.
Design: This retrospective cohort study conducted in Lima from June to September 2008, estimated the incidence of tuberculosis disease among household contacts of multidrug-resistant tuberculosis patients in 358 households.
Results: 108 (5%) of 2112 household contacts in 80 households (22% of households) developed tuberculosis disease during the study, equating to an incidence rate of 2360 per 100,000 contact follow-up years for each of the first 3 years after exposure. Drug susceptibility tests were available on 50 diseased contacts of whom 36 (80%) had multidrug-resistant tuberculosis. Forty-two pairs of index-contact drug susceptibility tests were available amongst which the contact had an identical or less resistant phenotype than the index case in 27 pairs. Multivariate clustered Cox regression demonstrated that contacts with a previous history of tuberculosis disease (Hazard Ratio 15.0, P<0.001) and with associated (non-HIV) comorbidities (Hazard Ratio 7.8, P<0.001) were significantly more likely to develop tuberculosis.
Conclusion: The high percentage of diseased household contacts highlights an opportunity for household level interventions to prevent transmission, whether or not these subsequent cases were all attributable to the index case.

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