

شبكة المعلومات الجامعية





شبكة المعلومات الجامعية

جامعة عين شمس

التوثيق الالكتروني والميكروفيلم

قسم

نقسم بالله العظيم أن المادة التي تم توثيقها وتسجيلها على هذه الأفلام قد أعدت دون أية تغيرات



يجب أن

تحفظ هذه الأفلام بعيدا عن الغبار المنافلام بعيدا عن الغبار المنافلام بعيدا عن الغبار المنافلام من ٢٠-٠٤% مئوية ورطوية نسبية من ٢٠-٤٠ مئوية ورطوية نسبية من ٢٠-١٥ be Kept away from Dust in Dry Cool place of 15-25- c and relative humidity 20-40%





شبكة المعلومات الجامعية التوثيق الالكتروني والميكروفيلم



بعض الوثائق الاصلبة تالفة



بالرسالة صفحات لم ترد بالاصل

Tanta University
Faculty of Medicine
Department of Chest
Diseases



Drug Resistance in Tuberculosis with Special Reference to the Present Status in Egypt

An Essay

Submitted to Faculty of Medicine, Tanta University, in Partial Fulfillment of the Requirements of Master Degree in Chest Diseases & Tuberculosis

® 616,995

⊘alia Gizzat Gil Obharang

M.B.B.Ch

Supervisors

Prof. Fawzy Abo El-Naga El-Emery

Prof. of Chest Diseases, Faculty of Medicine, Tanta University

Dr. Amgad Abdel Raouf Farhat Dr. Ayman Hassan Abdel Zaher

Assist. Prof. of Chest Diseases, Faculty of Medicine, Tanta University

Lecturer of Chest Diseases, Faculty of Medicine Tanta University

ر م^ی ۱

Faculty of Medicine Tanta University 2007 المراج ال

رب أوزعنى أن أشكر نعمتك التى أنعمت على وعلى والرى وأن أعمل صالحاً ترضه وأوخلنى برحمتك فى عباوك الصالحين

وَرِي وَ وَلِينِي وَالْعَالِمِينَ الْمُعَالِمِينَ الْمُعَالِمِينَ الْمُعَالِمِينَ الْمُعَالِمِينَ الْمُعَالِم المُعْلِمِينَ عَلَيْهِ مَعْلِمُونَ الْمُعَالِمِينَ الْمُعَالِمِينَ الْمُعَالِمِينَ الْمُعَالِمِينَ (١٩) سورة النمل من الأمة (١٩) University. She provided me with an ideal and inspiring research environment and provided me with sympathy, valuable advice, continuous encouragement and help.



Drug-resistance in Tuberculosis is a phenomenon that is threatening the stabilization of global Tuberculosis (TB) control. It is a worldwide problem, being present virtually in all countries that were surveyed. According to current World Health Organization and the International Union Against Tuberculosis and Lung Disease estimates, the median prevalence of MDR-TB has been 1.1% in newly diagnosed patients. The proportion, however, is considerably higher (median prevalence: 7%) in patients who have previously received anti-TB treatment. While host genetic factors may contribute to the development of drug resistance, incomplete and inadequate treatment is the most important factor leading to its development, suggesting that it is often a man made tragedy. Efficiently run TB control programs based on a policy of directly observed treatment, short course (DOTS), are essential for preventing the emergence of drug resistance in TB. The management is a challenge that should be undertaken by experienced clinicians at centers equipped with reliable laboratory services for mycobacterial cultures and in vitro sensitivity testing as it requires prolonged use of costly second-line drugs with a significant potential for toxicity. The judicious use of drugs; supervised standardized treatment; focused clinical, radiological, and bacteriologic follow-up; and surgery at the appropriate juncture are key factors in the successful management of these patients. With newer effective second line anti-TB drugs, innovative approaches such as DOTS-Plus are showing promise for the management of patients with drug resistant TB under program conditions.

Key words: MDR-TB, PCR, DOTS-Plus, XDR.

- C. C. C.

かんけいけん

ontents

100 TO 10

Page

Introduction	1
Aim of the work	4
Review of literature	
Chapter I: Background on drug resistant Tuberculosis	5
Chapter II: Potential causes of drug resistance	24
Chapter III: Molecular basis of antimicrobial resistance in Tuberculosis	32
Chapter IV: Diagnosis of drug resistance in Tuberculosis	39
Chapter V : Treatment strategies for drug resistance in Tuberculosis	56
Chapter VI: Extensively drug resistant Tuberculosis	118
Chapter VII: Surveillance of drug resistance in TB	125
Chapter IIX: The status of drug resistance in Tuberculosis in Egypt	147
Summary & conclusions	165
Recommendations	167
References	168
Protocol	
Arabic summary	

Laist of Tables

0.00000

5000



NO		Pages
Table (1):	Causes of Inadequate Treatment	25
Table (2):	The perturbations in the individual drug target genes that are responsible for the genesis of anti-TB drug resistance	38
Table (3):	Target groups for drug susceptibility testing	53
Table (4):	Recommended treatment strategies for MDR-TB	56
Table (5):	Alternative method of grouping antituberculosis drugs	58
Table (6):	Some of the Older Drugs and Newer Drugs With Potential as Anti-TB Agents at Various Stages of Development	61
Table (7):	Summary of general principles for designing a regimen	63
Table (8):	Individualized regimen design based on DST for first-line drugs	65
Table (9):	Other Agents Used in the Treatment of MDR-TB	73
Table (10):	Suggested regimens for mono- and poly-drug resistance	77
Table (11):	Paediatric dosing of second-line antituberculosis drugs	82
Table (12):	Adjustment of antituberculosis medication in renal insufficiency	84
Table (13):	WHO recommended collaborative activities for TB/HIV	88
Table (14):	Monitoring during treatment of drug-resistant TB	95
Table (15):	Frequency of common adverse effects among 818 patients	97

	in C. The are	
	in five DR-TB control program sites	
Table (16)	Adverse effects, suspected agent(s) and management	99-
	strategies	101
Table (17)	Commonly used ancillary medication	102
Table (18):	Weight-based dosing of antituberculosis drugs in the	112-
	treatment of drug-resistant TB	113
Table (19):	Comparison of the Principles Underlying DOTS and the	116
	DOTS-Plus Strategies	110
Table (20):	Quality assurance for drug susceptibility testing of	131
	Mycobacterium Tuberculosis in the WHO/IUATLD Super	
:	national Reference Laboratory Network	
Annex (1):	Prevalence (%) of drug resistance among new TB cases, by	132-
	country/geographical setting and WHO region (1999-2002)	134
Annex (2):	Prevalence (%) of resistance to specific drugs among new	135-
	TB cases, by country/geographical setting and WHO region	137
	(1999-2002)	20,
Annex (3):	Prevalence (%) of drug resistance among previously treated	138-
	TB cases, by country/geographical setting and WHO region (1999-2002)	140
Annex (4):	Prevalence (%) of resistance to specific drugs among	141-
	previously treated TB cases, by country/geographical setting	143
	and WHO region (1999-2002)	143
Annex (5):	Prevalence (%) of drug resistance among new TB cases, by	144-
	country/geographical setting and WHO region (1999-2002)	146
	Resistance to each individual drug	148
Table (22):	Incidence of primary drug resistance in Egypt	157

9(9)(9)

Table (23):	Incidence of secondary drug resistance in Egypt	1.50
Table (24):	Incidence of defaulters in Egypt	157
Table (25):	L	158
	L Lgypt	158
Table (26):	Incidence of initial drug resistance in Egypt	158
Table	Case detection	
(27a,b,c):		159-
Table	T	161
_	Treatment outcome	162-
(28a,b,c):	·	164
		164

100 mg

THE PROPERTY OF STREET, STREET

List of Figures

经的

NO		Pages
Fig. (1):	Prevalence of multidrug-resistant tuberculosis among new tuberculosis cases in countries and regions surveyed, 1994–1999	19
Fig. (2):	Locations with the highest prevalence of multidrug-resistant Tuberculosis among new tuberculosis cases ("hot spots").	20
Fig. (3):	Locations with the highest prevalence of combined multidrug-resistant Tuberculosis (among both new and previously treated cases).	20
Fig. (4):	Drug resistance among culture-confirmed Tuberculosis cases (Mycobacterium tuberculosis complex) in the German Central Committee against Tuberculosis study, 1996–2000	21
Fig. (5):	Schematic analysis of the 4 steps involved in development and spread of drug-resistant Tuberculosis	30
Fig. (6):	Mycobactrium tuberculosis bacteria using acid fast Zeihl-Neelsen stain (magnified 1000X)	40
Fig. (7):	Simplified account of the chemical steps involved in the polymerase chain reaction. Two DNA strands are created from one after a single cycle.	46
Fig. (8):	A typical test result obtained in a case of rifampicin resistant tuberculosis. In this case a mutation in the region of the wild type probe S4 with a lack of hybridization of this probe and binding of the mutant probe R4a has occurred.	47

Fig. (9a):	Chest x-ray of patient with MDRTB showing a cavity in the left upper lobe	70
Fig. (9b):	Section of a CT scan showing an isolated thick walled cavity.	70
Fig. (9c):	A chest x-ray of the same patient after left upper lobectomy	70

(6132.60) (6132.60)

A STATE OF

100 mm

variant though thereas the feet to the first