

Table of contents

Acknowledgments	1
Preface	3
Introduction	5
Summary – the role of specific interventions	9
1. Chemotherapy	15
Essential drugs	15
Isoniazid	17
Rifampicin	26
Pyrazinamide	35
Ethambutol	37
Streptomycin	41
Thioacetazone	45
Fixed-dose combinations	49
Principal prerequisites for an efficacious anti-tuberculosis drug	50
Early bactericidal activity	51
Sterilizing activity	52
Ability to prevent emergence of resistance to the companion drug	53
Emergence of anti-tuberculosis drug resistance	54
Effective or functional monotherapy	55
Monotherapy during sterilization of special populations	56
Differences in bactericidal activity	57
Sub-inhibitory concentrations	57
Differences in post-antibiotic effect (lag phase)	59
Clinical trials in the treatment of pulmonary tuberculosis	59
Streptomycin monotherapy	61
Streptomycin plus para-aminosalicylic acid	61
Streptomycin plus para-aminosalicylic acid plus isoniazid	62
Isoniazid plus ethambutol	64
Isoniazid plus thioacetazone	65
Isoniazid plus rifampicin	66

4. Preventive chemotherapy	127
Prevention of disease in tuberculin skin test reactors	128
Prevention of disease in persons with risk factors	130
Recently acquired infection	130
Infection with the human immunodeficiency virus	131
Spontaneously healed tuberculosis with fibrotic residuals	134
Silicosis	135
Renal failure	135
Prevention of disease following cessation of preventive chemotherapy	136
Prevention of disease with different durations of treatment	136
Prevention of disease with alternatives to isoniazid	138
Rifampicin and rifampicin combinations in comparison to placebo	140
Rifampicin and rifampicin combinations in comparison to isoniazid	141
Effectiveness of preventive chemotherapy	143
Indications and recommendations for the use of preventive chemotherapy	145
Appendix 1 – Adjunctive treatment	147
Adjunctive therapy with corticosteroids	147
Pulmonary tuberculosis	147
Extrapulmonary tuberculosis	148
Tuberculosis of serous membranes	148
Pleural tuberculosis	148
Pericardial tuberculosis	148
Peritoneal tuberculosis	149
Meningeal tuberculosis	149
Corticosteroid treatment in other forms of tuberculosis	150
The role of surgery in the chemotherapy era	150
Surgical treatment in respiratory tract tuberculosis	151
Tuberculous pyopneumothorax	151
Pleural tuberculosis	152
Surgical treatment in tuberculosis of the spine	152
Appendix 2 – Active agents other than essential drugs and drug classes (second-line drugs)	153
Aminoglycosides (other than streptomycin)	153
Amikacin	153
Kanamycin	154
Capreomycin	154
Cycloserine	155

Para-aminosalicylic acid	156
Quinolones	158
Rifamycins other than rifampicin	158
Rifabutin	158
Rifapentine	160
Thioamides	161
Drugs and drug classes with potential activity against <i>M. tuberculosis</i>	
under investigation and development	161
Acetamides	162
Amoxicillin plus clavulanic acid	162
Clarithromycin	163
Fullerene derivatives	163
Nitroimidazopyrans	163
Oxazolidinones	164
Paromomycin	164
Phenothiazines	164
Tuberactinomycin	165
Appendix 3 – Current vaccine development strategies	167
Immunotherapy with <i>M. vaccae</i>	167
Vaccination with saprophytic (environmental) mycobacteria	168
Auxotrophs	168
DNA vaccines	168
Recombinants	169
Subunits	169
References	171