

Table of contents

Summary	4
Abbreviations	7
GENERAL INTRODUCTION	9
CHAPTER 1: EPIDEMIOLOGY	11
1. INTRODUCTION	11
2. GLOBAL TUBERCULOSIS EPIDEMIOLOGY	11
2.1. Global incidence	11
2.2. Global mortality	13
2.3. WHO targets and trends	15
2.4. Epidemiology of TB in children	16
3. EPIDEMIOLOGY OF TUBERCULOSIS IN BELGIUM	19
3.1. General epidemiology	19
3.2. Epidemiology in children	21
CHAPTER 2: PATHOGENESIS.....	23
1. NATURAL HISTORY OF TUBERCULOSIS	23
2. NATURAL HISTORY OF TUBERCULOSIS IN CHILDREN.....	27
2.1. Introduction to pediatric TB.....	27
2.2. Time-table of primary tuberculosis in children.....	28
2.3. Age-related risk of developing disease after primary infection.....	30
CHAPTER 3: IMMUNOPATHOGENESIS	34
1. INTRODUCTION	34
2. INNATE DEFENSE MECHANISMS	35
3. ADAPTIVE IMMUNITY.....	45
4. DEFENSE MECHANISMS OF <i>M. TUBERCULOSIS</i>	53
5. IMMATURITY OF THE IMMUNE RESPONSE TO <i>M. TUBERCULOSIS</i> IN NEONATES AND INFANTS.....	59
CHAPTER 4: CLINICAL MANIFESTATIONS AND DIAGNOSIS.....	62
1. CLINICAL MANIFESTATIONS	62
1.1. Introduction	62
1.2. Symptoms and signs suggestive of TB.....	64
1.3. Physical examination in case of suspected TB	66
1.4. Radiological features of intrathoracic TB.....	68
1.5. TB meningitis.....	71
1.6. Perinatal tuberculosis.....	72

2. DIAGNOSTIC TESTS	73
2.1. Laboratory tests.....	74
2.2. Microbiological studies.....	74
2.3. Histopathology	78
2.4. Immune based tests	78
2.5. Systematic approach to diagnosis of intrathoracic TB	91
2.6. Specificities of the diagnostic process in case of suspected perinatal TB.....	91
2.7. Non-tuberculous mycobacteria.....	93
2.8. Unusually severe manifestations of tuberculosis.....	94
2.9. Treatment.....	95
AIMS	99
RESULTS	103
1. “Recurrent Tuberculosis in a Young Child”	105
2. “Identification of <i>Mycobacterium tuberculosis</i> Infection in Infants and Children With Partial Discrimination Between Active Disease and Asymptomatic Infection”	108
3. Comparison FASCIA/in-house IGRA (Supplementary material)	125
4. “Age-stratified T cell responses in children infected with <i>Mycobacterium tuberculosis</i> ”	130
5. Supplementary data: Age-related production of IL-17 by CD4+ T lymphocytes in response to HBHA.....	142
6. SUPPLEMENTARY DATA: Cytokine and chemokine concentrations secreted by PBMC stimulated with mycobacterial antigens	144
GENERAL DISCUSSION	167
CONCLUSIONS AND PERSPECTIVES	187
CONCLUSIONS	189
PERSPECTIVES.....	193
APPENDICES.....	195
Appendix A	197
Appendix B.....	206
Citations.....	209
Figures	225
Tables.....	226