

# CONTENTS

1. Introduction	5
2. ANCA testing	6
2.1 Indirect immunofluorescence	6
2.2 Enzyme-linked immunoassay	7
3. Disease associations	7
3.1 Drug-induced vasculitis	7
3.2 Cystic fibrosis	8
3.3 Autoimmune liver diseases	8
3.4 Ulcerative colitis	8
3.5 Autoimmune rheumatic diseases	8
3.6 Infections	9
3.7 ANCA and anti-GBM double positivity	9
3.8 ANCA associated vasculitides	9
3.8.1 Wegener's granulomatosis	9
3.8.2 Microscopic polyangiitis	10
3.8.3 Churg-Strauss syndrome	11
3.8.4 Renal-limited vasculitis	11
4. Disease scoring	11
5. Disease stages	12
6. Diagnostic tools	12
6.1 Own observation – Multiple organ involvement in WG	13
7. Etiology and pathogenesis of AAV	15
7.1 Etiology – environmental factors	15
7.1.1 Own observation – Silica and asbestos exposure in AAV	17
7.2 Etiology – genetic factors	18
7.2.1 Own observation – Two familial cases of AAV	19
7.3 Pathogenesis	21
7.3.1 Own observation – The role of T cells in AAV	22
8. Treatment of ANCA-associated vasculitis	22
8.1 Induction therapy	22
8.1.1 Cyclophosphamide	22
8.1.2 Own observation – the Cyclops trial	23
8.1.3 Methotrexate	24
8.1.4 Plasma exchange	24
8.1.5 Recommendations for induction treatment	24
8.2 Maintenance therapy	25
8.2.1 Azathioprine	25
8.2.2 Mycophenolate	25

8.2.3 Methotrexate .....	25
8.2.4 Trimetoprim-sulfamethoxazole (co-trimoxazole) .....	26
8.2.5 Cyclosporin A .....	26
8.2.6 Recommendations for maintenance therapy .....	26
8.3 Treatment of relapse .....	26
8.4 Other therapeutic approaches .....	27
8.5 New therapeutic approaches .....	27
8.6 Supportive treatment .....	28
9. PR3-ANCA and MPO-ANCA disease – Is there a difference? .....	28
10. Factors involved in relapse of AAV .....	29
11. Outcome of patients with AAV .....	30
11.1 Morbidity and mortality .....	30
11.2 Renal outcome .....	31
11.3 Own observation – long-term outcome of patients with renal AAV .....	32
12. Conclusion .....	33
List of Abbreviations .....	35
Figures .....	37
References .....	39

## ACKNOWLEDGEMENT

I would like to thank to Professor Vladimír Tesař, MD., PhD., FASN for his continuous scientific guidance. Thanks also to Professor Jiřina Bartůňková, MD., PhD. (Institute for Immunology, 2<sup>nd</sup> Medical Faculty), Helena Marečková MD., PhD. (Institute for Immunology and Microbiology, 1<sup>st</sup> Medical Faculty) and all the laboratory technicians from the two institutions for their invaluable help with compiling and reading the immunological data. I would also like to thank Professor Daniela Pelclová MD., PhD. (Occupational Medicine Department, 1<sup>st</sup> Medical Faculty) and all my co-workers from the Nephrology Clinic for their support.