

# CONTENTS

|  |           |
|--|-----------|
| <b>1. Introduction . . . . .</b>   | <b>9</b>  |
| 1.1. Perinatal distress . . . . .  | 10        |
| 1.2. Late consequences of perinatal distress . . . . .   | 12        |
| 1.3. Incidence of perinatal morbidity . . . . .  | 13        |
| 1.4. Recent measures for decreasing the danger of perinatal distress and of its consequences . . . . . | 16        |
| 1.5. Aim and design of the study . . . . .   | 19        |
| 1.6. Brain development — the relevance of the animal model to human problems .                         | 20        |
| 1.7. Pyritinol, pharmacological and clinical review . . . . .  | 22        |
| <b>2. Experiments in Rats . . . . .</b>  | <b>26</b> |
| 2.1. Nutritional distress in developing rats — experimental procedure . . . . .                        | 27        |
| 2.2. Body, brain and muscle growth . . . . .   | 28        |
| 2.3. Behaviour . . . . .   | 31        |
| 2.4. Learning ability . . . . .  | 35        |
| 2.5. CNS excitability . . . . .  | 38        |
| 2.6. Biochemical and metabolic studies . . . . .   | 42        |
| 2.7. Pyritinol treatment in adult rats protein-malnourished in early life . . . . .                    | 47        |
| 2.8. Discussion and conclusions . . . . .  | 48        |
| <b>3. Clinical Study (perinatological part) . . . . .</b>  | <b>52</b> |
| 3.1. Principles of selecting newborns for the study . . . . .  | 54        |
| 3.2. General characteristics of the treated and control group . . . . .                                | 56        |
| 3.3. Prenatal history of both groups . . . . .   | 58        |
| 3.4. Intranatal conditions of both groups . . . . .  | 61        |
| 3.5. Postnatal conditions of both groups . . . . .   | 65        |
| 3.6. Clinical disorders of the newborns during the intensive care period . . . . .                     | 69        |
| 3.7. Biochemical disturbances of the newborns . . . . .  | 74        |
| 3.8. Essential treatment of both groups . . . . .  | 77        |
| 3.9. Schedule of pyritinol treatment . . . . .   | 80        |

|   |     |
|---|-----|
| <b>4. Clinical Study (neurological part)</b>  | 81  |
| 4.1. Principles of neurological evaluation  | 83  |
| 4.2. Neurological evaluation of both groups in the 1st trimenon                       | 84  |
| 4.3. Neurological evaluation of both groups in the 2nd trimenon                       | 87  |
| 4.4. Neurological evaluation of both groups in the 3rd trimenon                       | 89  |
| 4.5. Neurological evaluation of both groups at the end of the 1st year                | 91  |
| 4.6. Final results in both groups   | 92  |
| 4.7. Rehabilitation and other therapy in both groups                                  | 95  |
| 4.8. Case histories of six high-risk infants from both groups                         | 96  |
| 4.9. Children with brain damage in whom pyritinol therapy was started at a higher age | 99  |
| 4.10. Discussion of clinical results  | 103 |
| <b>5. General Discussion and Conclusions</b>  | 108 |
| <b>6. Summary</b> (English, German, Spanish)  | 112 |
| <b>7. References</b>  | 118 |