

# Contents

---

|                                                                |           |
|----------------------------------------------------------------|-----------|
| <b>Foreword</b>                                                | <b>ix</b> |
| <b>Acknowledgements</b>                                        | <b>xi</b> |
| <b>1 Basic Principles</b>                                      | <b>1</b>  |
| 1.1 Definitions                                                | 1         |
| 1.2 Notation                                                   | 2         |
| 1.3 Equivalence of Tracer and Tracee                           | 3         |
| 1.4 The Kinetics of Protein Turnover                           | 3         |
| 1.5 References                                                 | 6         |
| <b>2 Models and Their Analysis</b>                             | <b>7</b>  |
| 2.1 Models                                                     | 7         |
| 2.2 Compartmental Analysis                                     | 8         |
| 2.3 Stochastic Analysis                                        | 14        |
| 2.4 References                                                 | 17        |
| <b>3 Free Amino Acids: Their Pools, Kinetics and Transport</b> | <b>20</b> |
| 3.1 Amino Acid Pools                                           | 20        |
| 3.2 Nutritional Effects on the Free Amino Acid Pools           | 24        |
| 3.3 Kinetics of Free Amino Acids                               | 25        |
| 3.4 Amino Acid Transport Across Cell Membranes                 | 27        |
| 3.5 Conclusion                                                 | 29        |
| 3.6 References                                                 | 30        |
| <b>4 Metabolism of Some Amino Acids</b>                        | <b>33</b> |
| 4.1 Leucine                                                    | 33        |
| 4.2 Glycine                                                    | 35        |
| 4.3 Alanine                                                    | 38        |
| 4.4 Glutamine                                                  | 40        |
| 4.5 Glutamic acid                                              | 43        |
| 4.6 Phenylalanine                                              | 44        |
| 4.7 Arginine                                                   | 45        |

---

|          |                                                                                           |            |
|----------|-------------------------------------------------------------------------------------------|------------|
| 4.8      | Methionine                                                                                | 46         |
| 4.9      | References                                                                                | 47         |
| <b>5</b> | <b>The Precursor Problem</b>                                                              | <b>54</b>  |
| 5.1      | Transfer-RNA as the Precursor for Synthesis                                               | 54         |
| 5.2      | A 'Reciprocal' Metabolite as Precursor                                                    | 55         |
| 5.3      | A Rapidly Synthesized Protein as Precursor                                                | 59         |
| 5.4      | Conclusion                                                                                | 60         |
| 5.5      | References                                                                                | 61         |
| <b>6</b> | <b>Precursor Method: Whole Body Protein Turnover Measured by the Precursor Method</b>     | <b>64</b>  |
| 6.1      | Background                                                                                | 64         |
| 6.2      | Outline of the Method                                                                     | 65         |
| 6.3      | Variability of Whole Body Synthesis Rates in Healthy Adults by the Precursor Method       | 65         |
| 6.4      | Sites of Administration and of Sampling                                                   | 66         |
| 6.5      | Priming                                                                                   | 68         |
| 6.6      | The First-pass Effect                                                                     | 69         |
| 6.7      | Recycling                                                                                 | 71         |
| 6.8      | Regional Turnover                                                                         | 73         |
| 6.9      | Measurement of Protein Turnover with Amino Acids other than Leucine                       | 76         |
| 6.10     | Conclusion                                                                                | 79         |
| 6.11     | References                                                                                | 80         |
| <b>7</b> | <b>Measurement of Whole Body Protein Turnover by the End-product Method</b>               | <b>87</b>  |
| 7.1      | History                                                                                   | 87         |
| 7.2      | Theory                                                                                    | 88         |
| 7.3      | Alternative End-products (EP)                                                             | 89         |
| 7.4      | Measurement of Flux with a Single End-product                                             | 90         |
| 7.5      | Behaviour of Different Amino Acids in the End-product Method: Choice of Glycine           | 92         |
| 7.6      | Comparisons of Different Protocols                                                        | 94         |
| 7.7      | Summary of Measurements of Protein Synthesis in Normal Adults by the End-product Method   | 94         |
| 7.8      | Variability                                                                               | 95         |
| 7.9      | Comparison of Synthesis Rates Measured by the End-product and Precursor Methods           | 96         |
| 7.10     | Comparison of Oxidation Rates by the Two Methods                                          | 97         |
| 7.11     | The Flux Ratio                                                                            | 98         |
| 7.12     | Kinetics Findings by the End-product Method                                               | 100        |
| 7.13     | Conclusion                                                                                | 100        |
| 7.14     | References                                                                                | 102        |
| <b>8</b> | <b>Amino Acid Oxidation and Urea Metabolism</b>                                           | <b>106</b> |
| 8.1      | Amino Acid Oxidation                                                                      | 106        |
| 8.2      | Metabolism of Urea                                                                        | 109        |
| 8.3      | References                                                                                | 116        |
| <b>9</b> | <b>The Effects of Food and Hormones on Protein Turnover in the Whole Body and Regions</b> | <b>120</b> |
| 9.1      | The Immediate Effects of Food                                                             | 120        |
| 9.2      | The Effects of Hormones on Protein Turnover in the Whole Body, Limb or Splanchnic Region  | 130        |
| 9.3      | References                                                                                | 135        |

|           |                                                                                            |            |
|-----------|--------------------------------------------------------------------------------------------|------------|
| <b>10</b> | <b>Adaptation to Different Protein Intakes: Protein and Amino Acid Requirements</b>        | <b>142</b> |
| 10.1      | Adaptation                                                                                 | 142        |
| 10.2      | Requirements for Protein and Amino Acids                                                   | 148        |
| 10.3      | References                                                                                 | 156        |
| <b>11</b> | <b>Physiological Determinants of Protein Turnover</b>                                      | <b>160</b> |
| 11.1      | Body Size – the Contribution of Allometry                                                  | 160        |
| 11.2      | Growth and its Cost                                                                        | 165        |
| 11.3      | The Effect of Muscular Activity and Immobility on Protein Turnover                         | 171        |
| 11.4      | Conclusion                                                                                 | 176        |
| 11.5      | References                                                                                 | 176        |
| <b>12</b> | <b>Whole Body Protein Turnover at Different Ages and in Pregnancy and Lactation</b>        | <b>182</b> |
| 12.1      | Premature Infants                                                                          | 182        |
| 12.2      | Neonates                                                                                   | 184        |
| 12.3      | Infants 6 months–2 years                                                                   | 184        |
| 12.4      | Older Children                                                                             | 186        |
| 12.5      | Pregnancy                                                                                  | 186        |
| 12.6      | Lactation                                                                                  | 190        |
| 12.7      | The Elderly                                                                                | 191        |
| 12.8      | References                                                                                 | 194        |
| <b>13</b> | <b>Protein Turnover in Some Pathological States: Malnutrition and Trauma</b>               | <b>200</b> |
| 13.1      | Malnutrition                                                                               | 200        |
| 13.2      | Trauma                                                                                     | 203        |
| 13.3      | References                                                                                 | 207        |
| <b>14</b> | <b>Protein Turnover in Individual Tissues: Methods of Measurement and Relations to RNA</b> | <b>210</b> |
| 14.1      | Methods of Breakdown                                                                       | 210        |
| 14.2      | Measurements of Synthesis                                                                  | 214        |
| 14.3      | RNA Content and Activity                                                                   | 217        |
| 14.4      | References                                                                                 | 219        |
| <b>15</b> | <b>Protein Turnover in Tissues: Effects of Food and Hormones</b>                           | <b>223</b> |
| 15.1      | Synthesis in the Normal State                                                              | 223        |
| 15.2      | The effects of Food on Protein Turnover in Tissues                                         | 227        |
| 15.3      | The Effects of Hormones on Protein Turnover in Tissues                                     | 234        |
| 15.4      | References                                                                                 | 241        |
| <b>16</b> | <b>Plasma Proteins</b>                                                                     | <b>250</b> |
| 16.1      | Albumin                                                                                    | 250        |
| 16.2      | Other Nutrient Transport Proteins                                                          | 258        |
| 16.3      | The Acute-phase Proteins                                                                   | 259        |
| 16.4      | The Immunoglobulins                                                                        | 263        |
| 16.5      | References                                                                                 | 264        |
| <b>17</b> | <b>Collagen Turnover</b>                                                                   | <b>270</b> |
| 17.1      | Collagen Turnover                                                                          | 270        |
| 17.2      | Markers of Synthesis and Breakdown                                                         | 272        |
| 17.3      | References                                                                                 | 273        |

|                                                       |            |
|-------------------------------------------------------|------------|
| <b>18 The Coordination of Synthesis and Breakdown</b> | <b>275</b> |
| 18.1 Synthesis                                        | 275        |
| 18.2 Breakdown                                        | 276        |
| 18.3 Coordination                                     | 281        |
| 18.4 References                                       | 283        |
| <b>Index</b>                                          | <b>287</b> |