21 Disorders of Sulfur Amino Acid Metabolism

Generoso Andria, Brian Fowler, Gianfranco Sebastio

21.1 Homocystinuria due to Cystathione β-Synthase Deficiency – 275
21.1.1 Clinical Presentation – 275
21.1.2 Metabolic Derangement – 276
21.1.3 Genetics – 276
21.1.4 Diagnostic Tests – 277
21.1.5 Treatment and Prognosis – 277

21.2 Methionine S-Adenosyltransferase Deficiency – 278
21.2.1 Clinical Presentation – 278
21.2.2 Metabolic Derangement – 278
21.2.3 Genetics – 279
21.2.4 Diagnostic Tests – 279
21.2.5 Treatment and Prognosis – 279

21.3 Glycine N-Methyltransferase Deficiency – 279
21.3.1 Clinical Presentation – 279
21.3.2 Metabolic Derangement – 279
21.3.3 Genetics – 279
21.3.4 Diagnostic Tests – 279
21.3.5 Treatment and Prognosis – 279

21.4 S-Adenosylhomocysteine Hydrolase Deficiency – 279
21.4.1 Clinical Presentation – 279
21.4.2 Metabolic Derangement – 279
21.4.3 Genetics – 280
21.4.4 Diagnostic Tests – 280
21.4.5 Treatment and Prognosis – 280

21.5 γ-Cystathionase Deficiency – 280
21.5.1 Clinical Presentation – 280
21.5.2 Metabolic Derangement – 280
21.5.3 Genetics – 280
21.5.4 Diagnostic Tests – 280
21.5.5 Treatment and Prognosis – 280

21.6 Isolated Sulfite Oxidase Deficiency – 280
21.6.1 Clinical Presentation – 280
21.6.2 Metabolic Derangement – 280
21.6.3 Genetics – 281
21.6.4 Diagnostic Tests – 281
21.6.5 Treatment and Prognosis – 281

References – 281
Metabolism of the Sulfur-Containing Amino Acids

Methionine, homocysteine and cysteine are linked by the methylation cycle (Fig. 21.1, left part) and the trans-sulfuration pathway (Fig. 21.1, right part). Conversion of methionine into homocysteine proceeds via methionine S-adenosyltransferase (enzyme 4). This yields S-adenosylmethionine, the methyl-group donor in a wide range of transmethylation reactions, a quantitatively important one of which is glycine N-methyltransferase (enzyme 5). These reactions also produce S-adenosylhomocysteine, which is cleaved to adenosine and homocysteine by S-adenosylhomocysteine hydrolase (enzyme 6). Depending on a number of factors, about 50% of available homocysteine is recycled into methionine. This involves methyl transfer from either 5-methyl-tetrahydrofolate (THF), catalyzed by cobalamin-requiring 5-methyl THF-homocysteine methyltransferase (enzyme 2), or betaine, catalyzed by betaine-homocysteine methyltransferase (enzyme 3). Homocysteine can also be condensed with serine to form cystathionine via a reaction catalyzed by pyridoxal-phosphate-requiring cystathionine β-synthase (enzyme 1). Cystathionine is cleaved to cysteine and α-ketobutyrate by another pyridoxal-phosphate-dependent enzyme, γ-cystathionase (enzyme 7). The last step of the trans-sulfuration pathway converts sulfite to sulfate and is catalyzed by sulfite oxidase (enzyme 8), which requires a molybdenum cofactor.

- Fig. 21.1. Metabolism of the sulfur-containing amino acids. 1, cystathionine β-synthase; 2, 5-methyltetrahydrofolate-homocysteine methyltransferase; 3, betaine-homocysteine methyltransferase; 4, methionine S-adenosyltransferase; 5, glycine N-methyltransferase; 6, S-adenosylhomocysteine hydrolase; 7, γ-cystathionase; 8, sulfite oxidase.