(e.g., testosterone sulfate), and 20-sulfates are not. The 3-sulfates of 5β-steroids are hydrolyzed very slowly.[2]

Other possible sulfatase activities in the preparation have not been investigated. However, ascorbate 2-sulfate is hydrolyzed only slowly (<1% of the rate for 4-nitrophenyl sulfate), and early work[8] would suggest that any glycosulfatase will be slight.

Sulfate weakly inhibits the arylsulfatase[1,9] and glucosinolate[3] sulfatase activities, and much more powerfully the steroid sulfatase activities,[2] with a K_i of about 0.5 m*M*. The latter inhibition is noncompetitive.[2] Sulfite is a particularly powerful inhibitor.[1,9]

Sulfatases 1 and 2 are firmly bound to phosphocellulose and cannot be eluted from it, even by 0.5 *M* NaCl at pH 9. The bound enzyme is active and could be an economical means of characterizing metabolites of xenobiotics. Thies[3] has adopted the alternative technique of using glucosinolates bound to DEAE–Sephadex in his method of quantitatively determining these compounds in plant extracts. The technique is useful when gas–liquid chromatography is subsequently to be used because the sulfate formed on hydrolysis remains bound to the ion exchanger.

[8] K. S. Dodgson, *Biochem. J.* **78,** 324 (1961).
[9] P. Jarrige, *Bull. Soc. Chim. Biol.* **45,** 761 (1963).

[63] Mammalian Sulfur Amino Acid Metabolism: An Overview

By OWEN W. GRIFFITH

Introduction[1]

Methionine and cysteine, the two sulfur-containing protein amino acids, are metabolized by a variety of reactions and pathways to at least two dozen intermediates and products. Some of these metabolites serve functions that are essential for survival of the organism. Methionine and cysteine have, in addition, important catalytic roles in the active sites of many enzymes. Several of these metabolic processes and catalytic functions exploit unique aspects of sulfur chemistry to accomplish biochemical transformations that would be difficult or impossible to effect in the

[1] Studies from the author's laboratory were supported in part by the National Institutes of Health, Grant AM26912, and an Irma T. Hirsch Career-Scientist award.

absence of the sulfur amino acids. Methionine, for example, is metabolized primarily to *S*-adenosylmethionine (AdoMet), a sulfonium compound mediating most biochemical methylation reactions.[2] It is doubtful if other amino acid derivatives or other " 'onium" compounds could adequately serve this role; quarternary ammonium compounds are too thermodynamically stable to effectively methylate most acceptors, and oxonium compounds (e.g., a hypothetical oxygen analog of AdoMet) lack the kinetic stability to survive *in vivo*.

Cysteine similarly participates in a number of biochemical processes that depend directly on the particular reactivity of thiols. The high nucleophilicity of thiols facilitates the role of cysteine as an active site, covalent catalyst (e.g., in papain[3] and glyceraldehyde-3-phosphate dehydrogenase[4]) and allows the cysteine residue of glutathione to scavenge and detoxify electrophiles during mercapturic acid biosynthesis[5,6] and peroxide reduction.[7] The easy formation but low reactivity of sulfur free radicals permits glutathione to also capture and detoxify the more reactive free radicals of oxygen and carbon.[8] Coenzyme A and acyl carrier protein mediate a variety of acyl transfer reactions involving thioesters of the cysteamine residue (derived from cysteine) of these cofactors; the poor resonance stability of thioesters serves to maintain the high transfer potential of the acyl group.[9] Oxidized derivatives of cysteine have additional metabolic roles. The disulfide bonds of cystine residues stabilize the tertiary structure of proteins, for example. More extensive oxidition of cysteine yields sulfate and taurine, metabolites with important physiological roles in detoxification, bile acid formation, membrane stabilization and neurotransmission.[10]

[2] S. H. Mudd and H. L. Levy, *in* "The Metabolic Basis of Inherited Disease" (J. B. Stanbury, J. B. Wyngaarden, D. S. Fredrickson, J. L. Goldstein, and M. S. Brown, eds.), p. 522. McGraw-Hill, New York, 1983.

[3] A. N. Glazer and E. L. Smith, *in* "The Enzymes" (P. D. Boyer, ed.), 3rd ed., Vol. 3, p. 502. Academic Press, New York, 1971.

[4] J. I. Harris and M. Waters, *in* "The Enzymes" (P. D. Boyer, ed.), 3rd ed., Vol. 13, p. 1. Academic Press, New York, 1976.

[5] S. S. Tate, *in* "Enzymatic Basis of Detoxification" (W. B. Jakoby, ed.), Vol. 2, p. 95. Academic Press, New York, 1980.

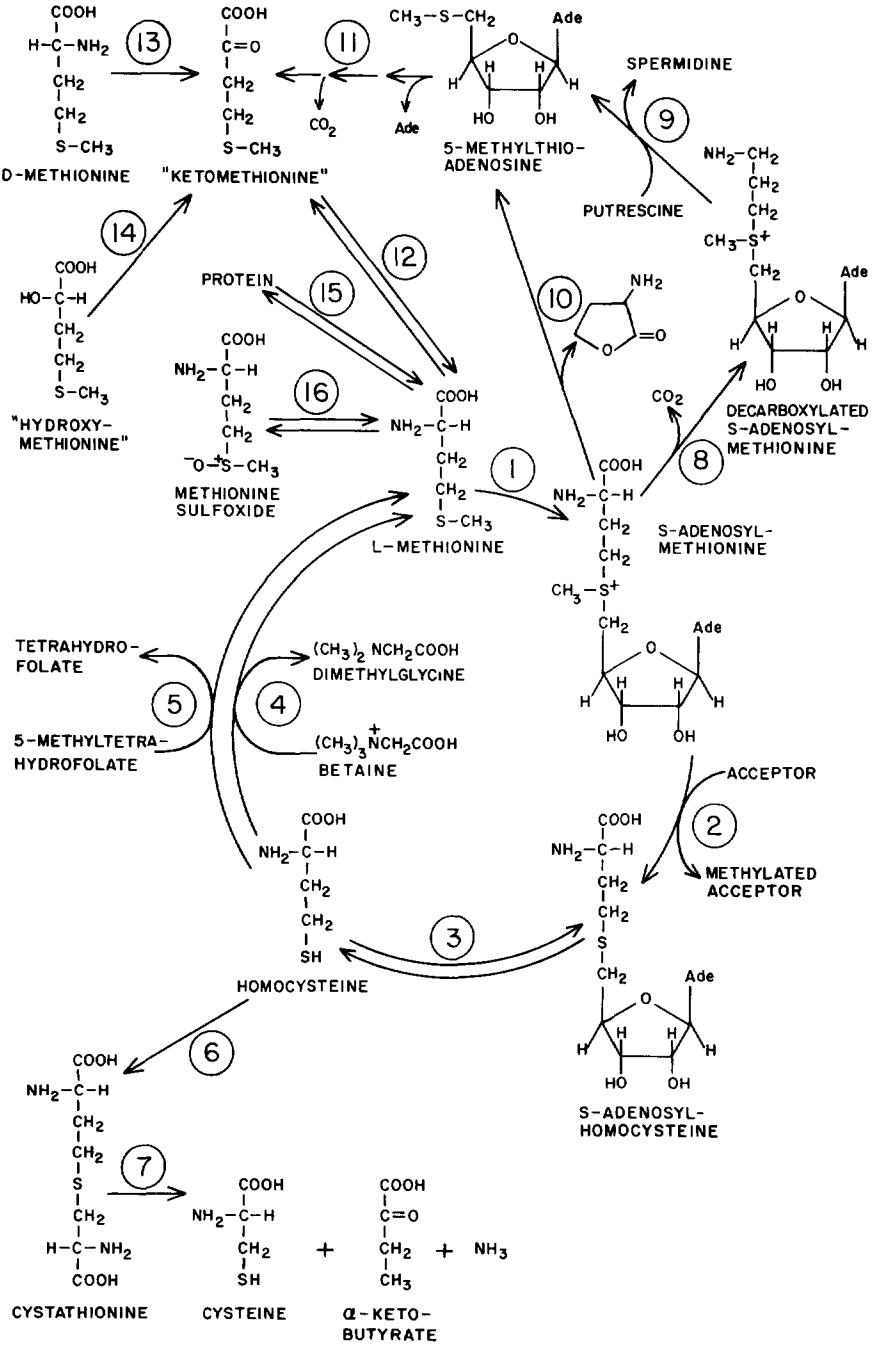
[6] W. B. Jakoby, J. Stevens, M. W. Duffel, and R. A. Weisiger, *Rev. Biochem. Toxicol.* **6,** 97 (1984).

[7] L. Flohé, *Ciba Found. Symp.* [N.S.] **65,** 95 (1979).

[8] J. E. Packer, *in* "The Chemistry of the Thiol Group" (S. Patai, ed.), p. 481. Wiley, New York, 1974.

[9] W. P. Jencks, "Catalysis in Chemistry and Enzymology." McGraw-Hill, New York, 1969.

[10] S. W. Schaffer, S. I. Baskin, and J. J. Kocsis, eds., "The Effects of Taurine on Excitable Tissues." Spectrum Publications, New York, 1981.


D-METHIONINE
"KETOMETHIONINE"
5-METHYLTHIO-ADENOSINE
SPERMIDINE
PUTRESCINE
"HYDROXY-METHIONINE"
PROTEIN
METHIONINE SULFOXIDE
L-METHIONINE
DECARBOXYLATED S-ADENOSYL-METHIONINE
S-ADENOSYL-METHIONINE
TETRAHYDRO-FOLATE
5-METHYLTETRA-HYDROFOLATE
DIMETHYLGLYCINE
BETAINE
ACCEPTOR
METHYLATED ACCEPTOR
HOMOCYSTEINE
S-ADENOSYL-HOMOCYSTEINE
CYSTATHIONINE
CYSTEINE
α-KETO-BUTYRATE

This chapter briefly summarizes the mammalian metabolism of methionine and cysteine with emphasis on the chemical transformations of sulfur; the metabolism of inorganic sulfur compounds is reviewed separately elsewhere in this volume.[11] Extensive reviews of the metabolism of sulfur in mammals are available.[2,12,13]

Methionine Metabolism

As noted, methionine metabolism is initiated by the formation of *S*-adenosylmethionine (AdoMet),[14] a sulfonium compound in which each of the carbons attached to sulfur is activated toward nucleophilic attack (reaction 1, Fig. 1). In most cases, AdoMet reacts by transfer of the *S*-methyl group to one of several possible acceptors including glycine (forming sarcosine), guanidinoacetate (forming creatine), phosphatidylethanolamine (forming lecithin), the lysine residues in specific proteins (forming ε-*N,N,N*-trimethyllysine, the precursor of carnitine), pyrimidine and purine bases of tRNA (leading to ribothymidine and other methylated nucleosides), and various xenobiotics bearing hydroxyl, amino, or sulfhydryl groups (reaction 2). It is estimated that methyl transfer reactions as a group consume about 95% of the AdoMet formed[15]; guanidinoacetate and glycine are believed to be the quantitatively most important acceptors.[15,16] In addition to the methylated acceptor, transmethylation yields *S*-adeno-

[11] J. A. Schiff and T. Saidha, this volume [58].
[12] T. P. Singer, *in* "Metabolic Pathways" (D. M. Greenberg, ed.), Vol. 7, p. 535. Academic Press, New York, 1975.
[13] A. J. L. Cooper, *Annu. Rev. Biochem.* **52,** 187 (1983).
[14] J. L. Hoffman, this series, Vol. 94, p. 223.
[15] S. H. Mudd and J. R. Poole, *Metab., Clin. Exp.* **24,** 721 (1975).
[16] H. Ogawa and M. Fujioka, *Biochem. Biophys. Res. Commun.* **108,** 227 (1982).

FIG. 1. Mammalian methionine metabolism. The circled numbers correspond to the following enzymes or metabolic processes (Enzyme Commission numbers are shown in parentheses): 1. Methionine adenosyltransferase (EC 2.5.1.6), an ATP-dependent reaction; 2. Various *S*-adenosylmethionine methyltransferases (EC 2.1.1.?); 3. Adenosylhomocysteinase (EC 3.3.1.1); 4. Betaine–homocysteine methyltransferase (EC 2.1.1.5); 5. 5-Methyltetrahydrofolate–homocysteine methyltransferase (methionine synthase) (EC 2.1.1.13); 6. Cystathionine β-synthase (EC 4.2.1.22); 7. Cystathionine γ-lyase (EC 4.4.1.1); 8. Adenosylmethionine decarboxylase (EC 4.1.1.50); 9. Spermidine synthase (EC 2.5.1.16); 10. Adenosylmethionine cyclotransferase (EC 2.5.1.4); 11. A multienzyme pathway including methylthioadenosine phosphorylase (EC 2.4.2.28) and probably two additional enzymes; 12. Various transaminases including particularly glutamine transaminase; 13. D-Amino-acid oxidase (EC 1.4.3.3); 14. Possibly (*S*)-2-Hydroxy-acid oxidase (EC 1.1.3.15) and D-2-Hydroxy-acid dehydrogenase (EC 1.1.99.6); 15. Ribosomal protein synthesis and various proteases; 16. Methionine-*S*-oxide reductase (EC 1.8.4.5).

sylhomocysteine, a product reversibily hydrolyzed to adenosine and homocysteine (reaction 3). Since the equilibrium constant of reaction 3 favors *S*-adenosylhomocysteine synthesis, proper flux through the "methionine cycle"[2] depends on maintenance of a low *in vivo* concentration of homocysteine. Pathological conditions that cause homocysteine accumulation (e.g., cystathionine β-synthase deficiency or disorders of homocysteine methylation) result in *S*-adenosylhomocysteine (AdoHcy) accumulation; AdoHcy is a potent inhibitor of transmethylation reactions.[2,17]

As shown in Fig. 1, homocysteine occupies a branch point in methionine metabolism. In both the rat and human about half of the homocysteine formed is irreversibily converted by transsulfuration to cysteine, α-ketobutyrate, and ammonia (reactions 6 and 7) whereas the remainder is remethylated to methionine (reactions 4 and 5).[15,18] 5-Methyltetrahydrofolate is believed to be the quantitatively important methyl donor *in vivo* under normal nutritional conditions.[18–20] Methionine synthetase,[21,22] the enzyme catalyzing reaction 5, accounts for the final metabolic step in the *de novo* synthesis of methyl groups[2,12] and enjoys a wide tissue distribution. In contrast, activity of betaine–homocysteine methyltransferase (reaction 4) is confined to the liver in most species. Its activity is increased by high protein diets, and the enzyme probably serves mainly in betaine catabolism and, under conditions of high methionine intake, helps to dispose of excess homocysteine.[18–20] Transamination or oxidation of homocysteine to the corresponding α-keto acid is believed to be of limited importance under normal circumstances but may assume a more significant role in disorders of homocysteine metabolism.[2,15] The product, α-keto-γ-mercaptobutyrate, is a reactive and possibily toxic metabolite that *in vivo* is reduced in part to α-hydroxy-γ-mercaptobutyrate (reactions not shown).[23,24]

In humans polyamine biosynthesis[25] consumes 2–5% of the AdoMet pool[5] and is initiated by the decarboxylation of AdoMet (reaction 8).

[17] P. K. Chiang, *Methods Pharmacol.* **6,** 127 (1985).
[18] J. D. Finkelstein, *Metab., Clin. Exp.* **23,** 387 (1974).
[19] J. D. Finkelstein, W. E. Kyle, and B. J. Harris, *Arch. Biochem. Biophys.* **146,** 84 (1971).
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[23] A. J. L. Cooper and A. Meister, *Arch. Biochem. Biophys.* **239,** 556 (1985).
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[25] H. Tabor and C. W. Tabor, eds., this series, Vol. 94.

Subsequent transfer of the 3-aminopropyl moiety to putrescine, the product of ornithine decarboxylation, yields spermidine and 5-methylthioadenosine (reaction 9). Transfer of another 3-aminopropyl moiety to the unsubstituted putrescine nitrogen of spermidine yields spermine; in mammals this reaction is catalyzed by a distinct enzyme, spermine synthase.[26,27] 5-Methylthioadenosine is also formed by cyclization of AdoMet (reaction 10).[28] Although the pathway by which 5-methylthioadenosine is metabolized to methionine is not fully elucidated for mammals, the initial reaction appears to be phosphorylytic cleavage to adenine and 1-phospho-5-methylthioribose. The latter intermediate is metabolized to 2-oxo-4-methylthiobutyrate ("ketomethionine") and formate (from C-1 of the ribose) by an enzyme or enzymes that have not been purified (reaction 11).[29,30] "Ketomethionine" is transaminated to reform methionine (reaction 12). Although there does not appear to be a methionine-specific transaminase in mammalian cells, methionine formation is effectively catalyzed by several transaminases, most notably the glutamine transaminases isolated from liver and kidney.[31]

The transamination of methionine to form "ketomethionine" has been suggested as an important process *in vivo;* "ketomethionine" may be further metabolized via oxidative decarboxylation to 3-methylthiopropionate, methanethiol, and additional catabolites[32–34] (reactions not shown, see Refs. 2 and 13 for a contrasting view). Nutritional studies indicate that "ketomethionine" is also formed from both D-methionine (reaction 13) and DL-2-hydroxy-4-thiomethylbutyrate ("hydroxymethionine") (reaction 14)[35]; "ketomethionine" from these sources is converted in large part to L-methionine, thereby accounting for the observation that these compounds can replace L-methionine in the diet. The spontaneous formation and enzymatic reduction of methionine sulfoxide (reaction 16) have been reviewed.[36]

[26] P. Hannonen, J. Janne, and A. Raina, *Biochem. Biophys. Res. Commun.* **46,** 341 (1972).
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[31] A. J. L. Cooper and A. Meister, "Chemical and Biological Aspects of Vitamin B_6 Catalysis: Part B," p. 3. Alan R. Liss, Inc., New York, 1984.
[32] N. J. Benevenga, *Adv. Nutr. Res.* **6,** 1 (1984).
[33] N. J. Benevenga and A. R. Egan, "Sulfur Amino Acids: Biochemical and Clinical Aspects," p. 327. Alan R. Liss, Inc., New York, 1985.
[34] G. L. Case and N. J. Benevenga, *J. Nutr.* **106,** 1721 (1976).
[35] D. H. Baker, this volume [55].
[36] N. Brot, H. Fliss, T. Coleman, and H. Weissbach, this series, Vol. 107, p. 352.

Cysteine Metabolism

In contrast to methionine, an essential amino acid, cysteine is synthesized by mammals; as shown in Fig. 1, cysteine sulfur is derived from methionine whereas the carbon and nitrogen of cysteine are derived from serine. It is notable that the dependence on methionine sulfur implies that cysteine remains a nonessential amino acid only if methionine intake is sufficient to meet the total sulfur amino acid requirement. Conversely, the dietary requirement for methionine is reduced, but not eliminated, when cyst(e)ine intake is adequate.[35]

As shown in Fig. 2, mammalian cysteine metabolism is complex. Cysteine participates conventionally in ribosomal protein synthesis (reaction 1), but posttranslational disulfide bond formation causes both cysteine and cystine to be released during protein degradation (reaction 2). As discussed below, cystine is reduced to cysteine by transhydrogenation with glutathione (reaction 18); direct reduction of cystine by NADH or NADPH has not been observed in mammals.

Several enzymes catalyzing cysteine transamination (reaction 3) have been isolated from mammalian tissues,[37–43] but the relative or absolute importance of the various activities *in vivo* is not established. Although much of the activity in liver and kidney homogenates is attributable to mitochondrial aspartate aminotransferase,[38–40] the contribution of this enzyme *in vivo* is unclear since the K_m for cysteine is 22 m*M*,[39] a value about 100-fold greater than its physiological concentration. β-Mercaptopyruvate, the product of cysteine transamination, is efficiently converted to pyruvate and a reduced sulfur species by β-mercaptopyruvate sulfurtransferase (reaction 4).[44] The sulfur product formed depends on the composition of the medium, but it is probable that any reduced sulfur species formed *in vivo* is ultimately converted to sulfate. In considering the partitioning of β-mercaptopyruvate between transamination (reaction 3) and conversion to sulfate and pyruvate (reaction 4) it is notable that rats given D-cysteine form sulfate but apparently do not form L-cysteine.[45]

[37] M. P. C. Ip, R. J. Thibert, and D. E. Schmidt, Jr., *Can. J. Biochem.* **55,** 958 (1977).
[38] T. Ubuka, Y. Ishimoto, and R. Akagi, *J. Inherited Metab. Dis.* **4,** 65 (1981).
[39] T. Ubuka, S. Umemura, S. Yuasa, M. Kinuta, and K. Watanabe, *Physiol. Chem. Phys.* **10,** 483 (1978).
[40] R. Akagi, *Acta Med. Okayama* **36,** 187 (1982).
[41] S.-M. Kuo, T. C. Lea, and M. Stipanuk, *Biol. Neonate* **43,** 23 (1983).
[42] M. Taniguchi, Y. Hosaki, and T. Ubuka, *Acta Med. Okayama* **38,** 375 (1984).
[43] A. J. L. Cooper, M. T. Haber, and A. Meister, *J. Biol. Chem.* **257,** 816 (1982).
[44] B. Sörbo, *in* "Metabolic Pathways" (D. M. Greenberg, ed.), Vol. 7, p. 433. Academic Press, New York, 1975.
[45] E. J. Glazenburg, I. M. C. Jekel-Halsema, A. Baranczyk-Kuzma, K. R. Krijgsheld, and G. J. Mulder, *Biochem. Pharmacol.* **33,** 625 (1984).

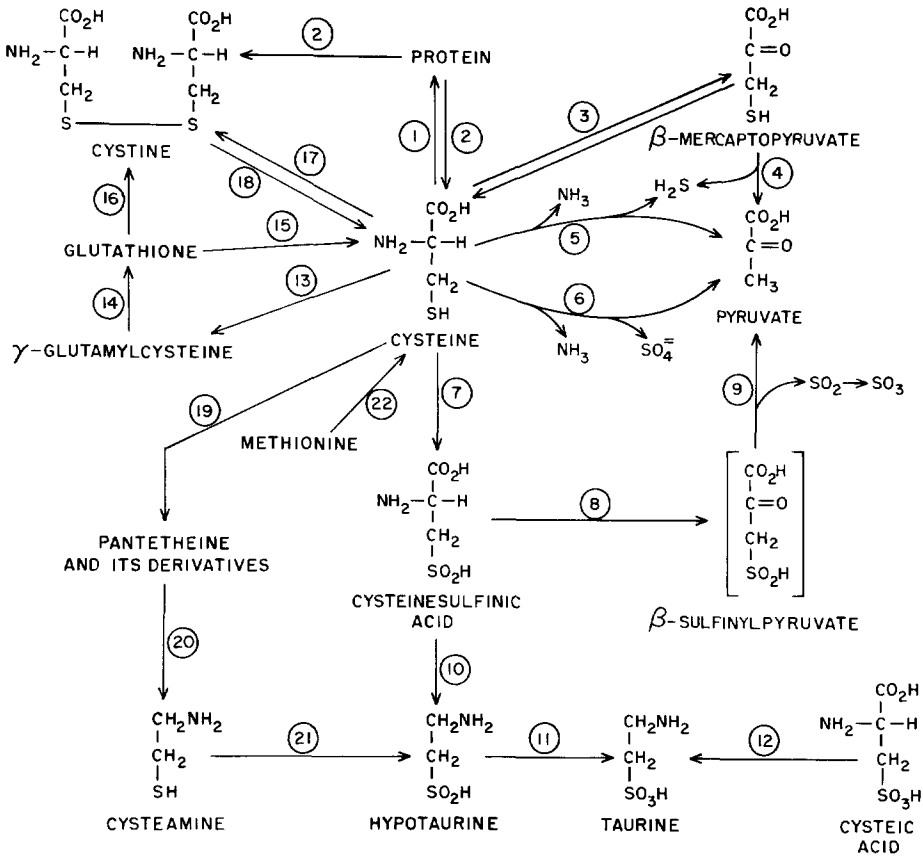

FIG. 2. Mammalian cysteine metabolism. The circled numbers correspond to the following enzymes or metabolic processes: 1. Ribosomal protein synthesis; 2. Formation of protein disulfide bonds; 3. Cysteine aminotransferase (EC 2.6.1.3) and probably other aminotransferases (see text); 4. 3-Mercaptopyruvate sulfurtransferase (EC 2.8.1.2); 5. Cystathionine γ-lyase (EC 4.4.1.1) (accounts for mammalian cysteine and cystine desulfhydrase activities, see text); 6. Poorly characterized mitochondrial activity (see text); 7. Cysteine dioxygenase (EC 1.13.11.20); 8. Aspartate aminotransferase (EC 2.6.1.1); 9. Spontaneous reaction; 10. Cysteinesulfinate decarboxylase (EC 4.1.1.29, sulfinoalanine decarboxylase); 11. "Hypotaurine oxidase" (mammalian enzyme not yet clearly identified); 12. Cysteinesulfinate decarboxylase (EC 4.1.1.29, sulfinoalanine decarboxylase); 13. γ-Glutamylcysteine synthetase (EC 6.3.2.2, glutamate–cysteine ligase); 14. Glutathione synthase (EC 6.3.2.3); 15. Combined activities of γ-glutamyltransferase (EC 2.3.2.2) and various dipeptidases acting on cysteinylglycine; 16. Enzymatic and nonenzymatic oxidation of glutathione to glutathione disulfide followed by the cleavage reactions listed as reaction 15 (see Ref. 75); 17. Various thiol oxidases; 18. Enzymatic and nonenzymatic transhydrogenations (disulfide interchange reactions) with glutathione coupled to glutathione reductase (EC 1.6.4.2); 19. Pantetheine and coenzyme A biosynthesis; 20. Pantetheine and coenzyme A catabolism; 21. Cysteamine dioxygenase (EC 1.13.11.19); 22. Transsulfuration pathway.

Assuming that the initial metabolism is to β-mercaptopyruvate (catalyzed by D-amino-acid oxidase), the findings suggest that the β-mercaptopyruvate sulfurtransferase reaction is greatly favored. The chemistry and biochemistry of β-mercaptopyruvate have been reviewed.[43]

Cysteine is converted to pyruvate by several additional pathways. Cysteine desulfhydrase (reaction 5) is an activity now attributed largely to cystathionine γ-lyase (γ-cystathionase), an enzyme which degrades, in addition to cystathionine, both cysteine and cystine. Whereas cysteine is converted directly to pyruvate, ammonia, and H_2S, cystine yields pyruvate, ammonia, and *S*-mercaptocysteine, a product reduced *in vivo* to cysteine and H_2S.[46–48] Although the intracellular concentration of cystine is low, it is notable that the K_m value for cystine is lower than that for cystathionine and much lower than that for cysteine.[49] Cystathionine β-synthase also catalyzes reaction 5 *in vitro*,[50,51] but its role in cysteine catabolism remains uncertain. The suggestion has been offered that reactions 3 and 4 together may account for cysteine desulfhydrase activity.[52] Although oxidative degradation of cysteine to pyruvate, ammonia, and sulfate (reaction 6) is reportedly catalyzed by an activity present in rat mitochondria,[53] a specific enzyme has not been identified; it is possible that the activity is due to the combined action of other enzymes of cysteine metabolism.

Oxidation of cysteine to cysteinesulfinate (reaction 7) is believed to be the major pathway of cysteine catabolism in mammals, particularly when cysteine availability is high.[54–56] The metabolic partitioning of cysteinesulfinate between transamination (reaction 8) and decarboxylation (reaction 10) shows considerable species variation. In mice, about 85% of parenterally administered cysteinesulfinate is converted to hypotaurine,[57]

[46] J. Loiselet and F. Chatagner, *Biochim. Biophys. Acta* **89,** 330 (1964).
[47] M. T. Costa, A. M. Wolf, and D. Giarnieri, *Enzymologia* **43,** 271 (1972).
[48] D. Cavallini, C. DeMarco, B. Mondovi, and B. G. Mori, *Enzymologia* **22,** 11 (1960).
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[51] M. H. Stipanuk and P. W. Beck, *Biochem. J.* **206,** 267 (1982).
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but the fraction decarboxylated in humans is much less.[58] The cat, which is cysteinesulfinate decarboxylase deficient,[59] forms little or no hypotaurine and in the absence of dietary taurine becomes blind.[60,61] β-Sulfinylpyruvate, the product of cysteinesulfinate transamination, spontaneously decomposes to pyruvate and sulfite (reaction 9); sulfite is oxidized by sulfite oxidase to sulfate. At least 90% of the hypotaurine formed from cysteinesulfinate is oxidized further to taurine (reaction 11); a small portion of the hypotaurine formed is transaminated to β-sulfinylacetaldehyde and catabolized, presumably through acetaldehyde, to CO_2 (not shown).[57,62] The mechanism by which hypotaurine is converted to taurine remains poorly understood, and both enzymatic[63] and nonenzymatic[64] pathways remain under consideration. Cysteic acid (cysteinesulfonic acid) is apparently not a mammalian metabolite but is contained in the diet as the result of nonenzymatic oxidation of cysteine and the action of enteric bacteria. As an alternative substrate of cysteinesulfinate decarboxylase, cysteinesulfonate is decarboxylated directly to taurine (reaction 12). Transamination of cysteinesulfonate, catalyzed by aspartate aminotransferase, yields β-sulfopyruvate; that product is reduced by malate dehydrogenase to β-sulfolactate (reactions not shown).[65]

Intracellular concentrations of cysteine are of the order of 30–200μM, values that are among the lowest observed for any of the protein amino acids.[66,67] Higher concentrations of cysteine are potentially dangerous to cells since cysteine forms a thiazolidine derivative with pyridoxal phosphate and thereby may deplete cells of that coenzyme. Cysteine is also easily oxidized nonenzymatically to cystine (reaction 17), an insoluble amino acid which is toxic if allowed to accumulate (c.f. cystinosis).[68] The multiple pathways of cysteine catabolism function efficiently to prevent

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[63] P. Kontro and S. S. Oja, *in* "Taurine: Biological Actions and Clinical Perspectives," p. 83. Alan R. Liss, Inc., New York, 1985.

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[68] J. A. Schneider and J. D. Schulman, *in* "The Metabolic Basis of Inherited Disease" (J. D. Stanbury, J. B. Wyngaarden, D. S. Fredrickson, J. L. Goldstein, and M. S. Brown, eds.), p. 1844. McGraw-Hill, New York, 1983.

toxic accumulations of cysteine. Glutathione biosynthesis (reactions 13 and 14) serves, in part, to preserve a pool of cysteine in a nontoxic, metabolically active form that can be easily transported between organs.[67,69,70] Thus, glutathione is actively synthesized in liver, a tissue rich in both dietary and biosynthetic cysteine, and is released into the plasma[70,71] and, to a lesser extent, bile.[72–74] Cysteine and cystine are then released from glutathione and its disulfide by enzymes localized on the external plasma membrane surfaces of cells throughout the organism (reactions 15 and 16).[67,75] Both cysteine and cystine are efficiently taken up by most cells. Cystine is reduced to cysteine intracellularly by transhydrogenation with glutathione (reaction 18). Since the glutathione pool is maintained in a highly reduced state by glutathione reductase, the cyst(e)ine pool is also maintained in a reduced state (>90% cysteine).

As shown in Fig. 2, cysteine is required for the biosynthesis of pantetheine and coenzyme A (pathway 19); the enzymes involved have been extensively studied and reviewed by Brown[76] and Abiko.[77] Catabolism of pantetheine and coenzyme A yield cysteamine, an intermediate metabolized to hypotaurine and taurine (reactions 20, 21, and 11). The possibility that this pathway accounts for quantitatively significant amounts of taurine biosynthesis has been considered.[78] Cysteamine and its disulfide, cystamine, may also play a role in mediating intracellular disulfide bond formation *in vivo*.[79]

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