HOMOCYSTINURIA

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• homocysteine is an intermediate in the metabolism of methionine to cysteine but can also be used to reform methionine
• homocysteine is linked to both folate and vitamin B_{12} metabolism
• homocystine is formed by joining 2 homocysteines
• excessive accumulation of homocystine (homocystinuria) is caused by decreased metabolism of homocysteine through either its link to folate metabolism (Figure 1) or through its link to cysteine formation (Figure 2)
**Figure 1.** Methionine is formed from homocysteine by methionine synthase using methyl B<sub>12</sub>. Methyl B<sub>12</sub> is made from vitamin B<sub>12</sub> using methyl tetrahydrofolate (THF). Methyl THF is made from methylene THF by methylenetetrahydrofolate reductase (MTHFR). Homocysteine is also used to make cysteine. In this form of homocystinuria (right), MTHFR is deficient (X) so that methylene THF accumulates. Hence there is no methyl THF to make methyl B<sub>12</sub> and homocysteine accumulates because it cannot be converted to methionine, even though it can still make cysteine. Excess homocysteine is converted to homocystine (see preceding slide).

**Figure 2.** Methionine is formed from homocysteine by methionine synthase as described in the legend for Figure 1. Cystathionine is formed from homocysteine by cystathionine β-synthase that requires vitamin B<sub>6</sub>. Cystathionine is then converted to cysteine. In this form of homocystinuria (right), cystathionine β-synthase is deficient (X) so that homocysteine accumulates. Excess homocysteine is converted to homocystine (see preceding slide).