

EFFECTS OF SEVERE VITAMIN B<sub>12</sub>-DEFICIENCY  
ON TISSUE FOLATES IN SHEEP

W.S. OSBORNE-WHITE\* and R.M. SMITH\*

Severe vitamin B<sub>12</sub>-deficiency in sheep leads to loss of appetite and death from inanition. In the terminal stages excretion of excessive amounts of formiminoglutamate in the urine indicates a systemic deficiency of folic acid as well and at slaughter liver folates are found to be severely depleted (Smith and Osborne-White, 1973). The cause of the secondary depletion of liver folates in vitamin B<sub>12</sub>-deficiency is not known but has been variously attributed to a reduced capacity to form pteroyl polyglutamates (Chanarin et al., 1974), a fault in folate transport (Gawthorne and Smith, 1974) or an inability of methyl tetrahydrofolate to form polyglutamates coupled with an excessive proportion of folates present in this form in vitamin B<sub>12</sub>-deficiency (Shane et al., 1977). The present experiments were designed to see whether tissues other than liver also suffer depletion of folates in vitamin B<sub>12</sub>-deficiency.

Sheep were made severely deficient of vitamin B<sub>12</sub> by feeding a cobalt-deficient diet (Smith and Osborne-White, 1973) and the folate content of tissues was compared at slaughter with individually pair-fed controls that received adequate vitamin B<sub>12</sub>. Two experiments were carried out involving respectively three pairs and four pairs of deficient and control animals. Total folates were assayed with *Lactobacillus casei* (Osborne-White and Smith, 1973) in liver, kidney cortex and pancreas (all folate-rich tissues) and, in the first experiment, in the wall of the small intestine as well.

In comparison with their pair-fed controls the deficient animals showed significant depletion of total liver folates, but depletion in the other tissues was either absent or statistically non-significant (ns). Thus in the two experiments respectively mean folates were depleted in B<sub>12</sub>-deficient liver by 93% and 87% (both  $P < 0.01$ ) but kidney cortex folates were depleted by only 21% and 27% (ns). Mean folate concentrations in B<sub>12</sub>-deficient pancreas were 4% lower than the controls in experiment 1, but they were 19% higher in experiment 2 (ns). The concentration of folates in the wall of the small intestine was less than 5% that in liver and although the mean concentration was 42% lower in the deficient tissue the effect was erratic and non-significant.

It is concluded that the severe depletion of folates in the livers of vitamin B<sub>12</sub>-deficient animals may not occur generally in other folate-rich tissues.

- CHANARIN, I., PERRY, J. and LUMB, M. (1974) Lancet 1: 1251.  
 GAWTHORNE, J.M. and SMITH, R.M. (1974) Biochem. J. 142: 119.  
 OSBORNE-WHITE, W.S. and SMITH, R.M. (1973) Biochem. J. 136:  
 265.  
 SHANE, B., WATSON, J.E. and STOKSTAD, E.L.R. (1977) Biochim.  
Biophys. Acta 497: 241.  
 SMITH, R.M. and OSBORNE-WHITE, W.S. (1973) Biochem. J. 136:  
 279.

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\* CSIRO Division of Human Nutrition, Adelaide, S.A. 5000.