phenomenon, however, this factor could be important in the net response of human malignant tumours to fractionated radiotherapy, for many tumours are known to contain a sizable fraction of stationary cells.

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Alcohol-induced Malabsorption of Vitamin B_{12} in Man

INTOXICATION with alcohol is frequently associated with diarrhoea, and disturbances of intestinal function have been reported to be common in chronic alcoholics studied shortly after drinking-bouts[1–5]. Because the normal diet of alcoholics is characteristically poor, it is not clear whether the transient malabsorption frequently found can be attributed to a direct toxic effect of ethanol on the small intestine, or to a nutritional deficiency. We therefore studied the effects of the experimental ingestion of ethanol in man on vitamin B_{12} absorption under controlled metabolic ward conditions in the absence of nutritional deficiency.

Our experimental design was similar to that of previous studies[6,7] in which toxic effects of ethanol on liver and bone marrow in man were demonstrated. Four asymptomatic, haematologically normal adult male volunteers with normal liver biopsies and a history of chronic alcoholism were studied. Throughout each of three study periods (pre-ethanol control, ethanol and post-ethanol control), they received daily multivitamin supplements including pharmacological doses of folic acid[7]. Protein intake comprised 12·5 per cent of total calories in two, and 25 per cent in two others. Ethanol was substituted isocalorically for carbohydrate for 3 to 8 weeks, the intake having the same calorie value. The maximal daily dose varied from 158 to 253 g ethanol.

Vitamin B_{12} absorption was studied during control and ethanol periods by the method of Schilling[8]. ^{57}Co-cyanocobalamin (0·75 μg; specific activity 1 μCi/μg) was given orally with intrinsic factor concentrate. The urinary excretion of ^{57}Co-vitamin B_{12} during ethanol testing periods was less than that of any of the control values for each subject (Table 1). Comparison of control and ethanol values revealed an average decrease in B_{12} excretion during the alcohol period of 41·5 per cent (range 22·9–52·7 per cent) for 24 h urines, and 34·7 per cent (range 17·1–47·5 per cent) for 48 h ($P < 0·005$ for 24 h and $P < 0·01$ for 48 h). In two subjects the 24 h excretion during the ethanol period fell below what we consider as normal (7 per cent or greater). Urine volumes did not differ between periods. In subject 1, faecal radioactivity was determined for two weeks after three of the Schilling tests, and was higher during the ethanol period (pre-ethanol 17·7 per cent of administered dose; ethanol 41·3 per cent; post-ethanol 34·4 per cent). Serum vitamin B_{12} levels[9], and urinary indican excretion[10], remained normal throughout the study.

Our results indicate that the administration of ethanol for two weeks or more along with a proper intake of protein and vitamin interferes with the absorption of vitamin B_{12} by the human ileum. That impairment

Table 1. PER CENT URINARY EXCRETION OF ^{57}Co-VITAMIN B_{12} DURING CONTROL PERIODS AND ETHANOL ADMINISTRATION IN HUMAN VOLUNTEERS

Subject	Urinary ^{57}Co-vitamin B_{12} excretion (per cent)				Days on ethanol when tested (per cent)	Maximal ethanol dose (total calorie intake)
	Control (pre- and/or post-ethanol)		Ethanol			
	24 h	48 h	24 h	48 h		
1	42·4	51·4	27·4	33·0	13	46
	40·7	50·6	11·9	20·6	26	
2	12·1	16·2	5·9	9·1	21	60
	12·1	16·8	6·7	11·0	31	
	11·2	17·5				
3	17·0	21·0	13·1	17·4	21	60
4	10·5	15·4	5·9	10·2	34	66

of ileal function occurred was further suggested by the presence of striking ultrastructural abnormalities (dilated endoplasmic reticulum and focal cytoplasmic degradation) in an ileal biopsy obtained from subject 2 on the fifty-first ethanol day. Light microscopy histological findings were normal. (These changes will be reported in detail by B. Rybak, E. Rubin, J. L. and C. S. L. elsewhere.) Whether the "toxic" effect of ethanol is limited to B_{12} assimilation or to ileal function in general remains to be determined. In animals, depression of active jejunal transport of amino-acids by ethanol has been reported[11,12].

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Control of Degradation and Synthesis of Induced Tyrosine Aminotransferase studied in Hepatoma Cells in Culture

WE have been studying the mechanism of tyrosine aminotransferase (TAT) induction by adrenal steroids in hepatoma (HTC) cell cultures[1,2]. The hormones increase the rate of enzyme synthesis resulting in an increased intracellular TAT concentration[3]. The enzyme is continuously turning over with a half-time of degradation of 3 to 7 h (measured as loss of either enzymic or antigenic activity), depending on the experiment and the conditions.

We show here that when the nutritional level of the medium is suddenly reduced, a transient phase of more rapid TAT degradation appears. This "enhanced degradation" is inhibited by actinomycin *D* and cycloheximide,