HÆMATOLOGY

Abnormal Transport of Vitamin B_{12} in Plasma in Chronic Myelogenous Leukæmia

RECENTLY[1] we demonstrated that two substances which we believe to be proteins carry the vitamin B_{12} in the plasma of normal subjects. These will be referred to as transcobalamin I and II. We then investigated their behaviour in the plasma of patients with chronic myelogenous leukæmia (CML) and found a major abnormality.

In the investigation of the control subject and of those with leukæmia, plasma which was taken at various times after intake of $^{57}CoB_{12}$ was fractionated by DEAE–cellulose anion-exchange column chromatography. Normally[1], almost all of the $^{57}CoB_{12}$ as it is taken into the plasma from injection, or from the intestine, is bound to a protein which was eluted pre-albumin, transcobalamin II. The B_{12} is rapidly lost from this binding site and little remains after the first day. A small amount of the B_{12} recently taken into the body and all the endogenous B_{12} which has been present in plasma for some time is bound to an alpha-1 globulin, transcobalamin I, the first binding substance to be described[2,3]. The loss from this binding site is quite slow.

When a patient with chronic myelogenous leukæmia was given 0·8 μg of $^{57}CoB_{12}$ by mouth, almost all the radioactive B_{12} was taken up by transcobalamin I, a complete reversal of the normal pattern. The plasma peak was not reached until 24 h in contrast to a peak at 8 h in normal subjects. There was little loss from this binding site during the next 24 h, and more than 50 per cent remained at 13 days. Two other subjects with CML were given 1·0 μg intravenously. Here, too (Fig. 1), almost all the $^{57}CoB_{12}$ was bound to transcobalamin I. In a normal subject almost all would have been bound to transcobalamin II. The investigation was repeated 3½ months later when the patient was in a good remission induced by 'Busulfan'. As shown in Fig. 2, transcobalamin II participated to a much greater extent than previously, an apparent return towards the normal. Usually we have found a sharp peak of $^{57}CoB_{12}$ in the transcobalamin II region, and while the peak in this case was in the expected position, it was unusually broad. The *in vitro* binding of 300 μμg/ml. of plasma was examined in 4 patients with CML in relapse. An abnormal binding pattern was found which was identical to that found when the $^{57}CoB_{12}$ was added *in vivo*.

The abnormality of the binding of B_{12} in the plasma in CML could be due to an increase in transcobalamin I, to a decrease in transcobalamin II, to a change which alters the binding capacity of either, or to some chemical change in the plasma which alters the union of B_{12} and transcobalamins which carry it. Because they give up their B_{12} at very different rates, the two transcobalamins appear to have different functions. The abnormality of plasma transport of B_{12} in CML could therefore alter the distribution of B_{12} within the body.

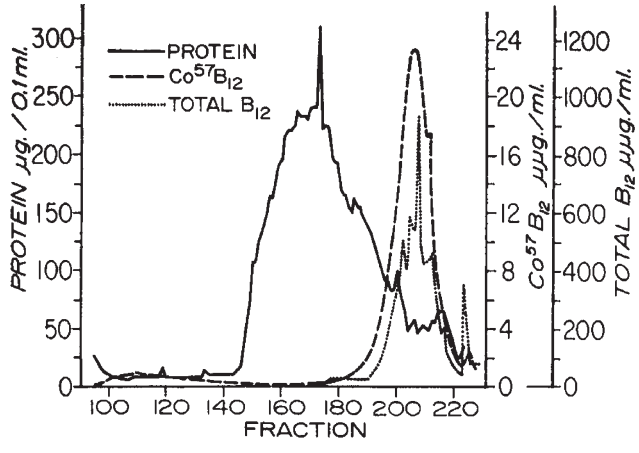

Fig. 1. Fractionation of plasma taken 1·5 min after i.v. $^{57}CoB_{12}$ from a subject with chronic myelogenous leukæmia in relapse. Total B_{12} includes both endogenous and recently injected B_{12}. Both are bound to transcobalamin I (peak in fractions 207–208) with only a trace of $^{57}CoB_{12}$ in transcobalamin II (peak in fraction 109). Fractions 0–95 contained γ and β globulin but no B_{12}

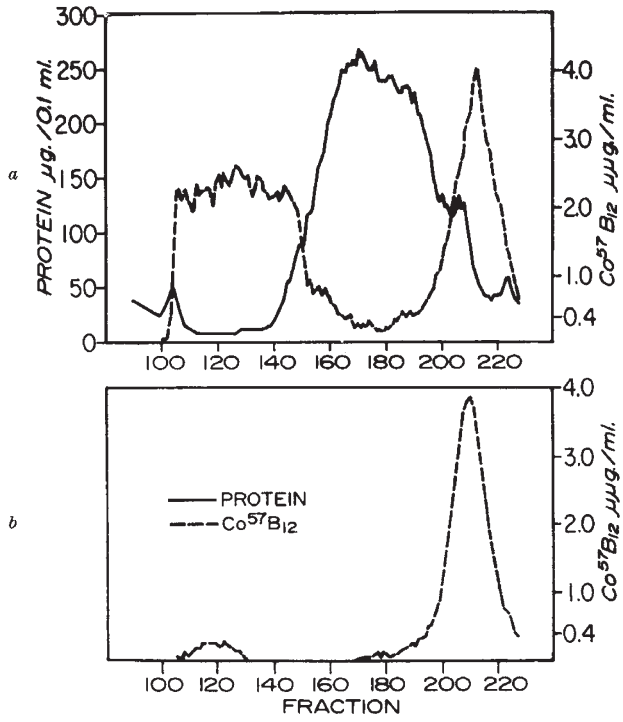

Fig. 2. A study of the same patient as Fig. 1 during remission. Note the rapid loss from transcobalamin II and the slow loss from I. (*a*) Plasma taken 1·5 min after injection, (*b*) plasma taken 90 min after injection

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In vivo Maturation of Immature Reticulocytes transfused into a Normal Rabbit

WE have recently published the results of an investigation of polyribosomes and the loss of synthesis of hæmoglobin in maturing rabbit reticulocytes fractionated by buoyant density centrifugation in an albumin gradient[1]. Several cytological and biochemical criteria were applied to show that this procedure fractionates the reticulocyte population according to their degree of physiological maturity. This communication presents additional proof, using *in vivo* maturation of a fraction of the youngest reticulocytes, that the position of the cells in the albumin gradient is a function of their age. In addition, these investigations provide an estimate of the life-span of the reticulocytes produced in phenylhydrazine-induced anæmia.

Reticulocyte fractionation by buoyant density centrifugation in bovine serum albumin (BSA) gradients and *in*