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HÆMATOLOGY

Fœtal Hæmoglobin in the Monkey

A number of well-defined physico-chemical differences exist between human adult and fœtal hæmoglobins. These include their electrophoretic and chromatographic behaviour under defined conditions, a large difference in alkali denaturation rates, and the changed position and contour of the tryptophan fine-structure band.

The differences between the fœtal and adult hæmoglobins of such other mammals as have been examined, also show differences in electrophoretic and chromatographic mobility and alkali denaturation rates—in the latter case generally in the opposite sense to the human pigments[1]. Jope[2] showed that the shift in tryptophan band wave-length did not extend to any of the animal fœtal pigments which he examined. We have been concerned to establish whether the unique specific differences between human hæmoglobins *A* and *F* occur in other primates, especially since one important attribute of human adult hæmoglobin (the presence of a minor component hæmoglobin A_2) is found in some, though not all, species of monkey[3].

Electrophoretic behaviour in agar gel has been examined. At *p*H 6·2[4] human hæmoglobin *F* migrates much more rapidly than hæmoglobin *A* and gives a distinctive straight front. Fig. 1 shows that the hæmoglobins of the adult and fœtal rhesus monkey (*Macacus rhesus*) migrate in the reverse order, but that the characteristic zone shape is retained. Under these conditions the human and monkey fœtal pigments can also be separated without difficulty.

The position of the tryptophan fine-structure bands in the pure fœtal proteins has been established by direct examination of the zones in the gel with the aid of the moving-plate spectrograph[5]. Fœtal rhesus monkey hæmoglobin has its band at about 289·7 mμ compared with 289·6 mμ for the human fœtal and 291·0 mμ for both adult pigments. There is thus a close similarity between the monkey and human pigments in this unique respect. Alkali denaturation has also been studied, and it is found that monkey fœtal hæmoglobin has a greater alkali resistance than adult. When followed photometrically with a red filter (Wratten 29) the difference is of a similar order to that found in the corresponding human proteins, but the rate curve for adult monkey hæmoglobin deviates from linearity.

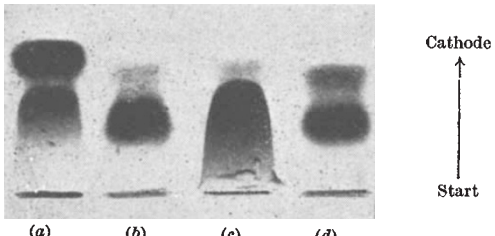

Fig. 1. Agar gel electrophoresis of human and monkey hæmoglobins at *p*H 6·4.
a, human hæmoglobins *A* + *F*.
b, *d*, monkey cord blood hæmoglobins.
c, maternal monkey hæmoglobin.

Further investigations on the fœtal pigments are in progress, and it is hoped to examine those of other primates if they can be obtained.

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Synthesis of Hæm by Circulating Blood Cells

It has been shown that hæm containing iron-59 can be crystallized from the reticulocytes of blood samples to which iron-59 has been added prior to incubation at 37°C.; but the mature mammalian erythrocyte does not synthesize hæm in this way[1,2]. The results of an investigation of the nature and kinetics of this phenomenon in reticulocytes and avian cells suggests that there are at least two phases; first the entry of iron into the cell and secondly the synthesis of hæm from this iron.

Blood was collected from rats five days after intraperitoneal injection of 2 per cent phenylhydrazine solution, and from other rats three days after removal of 5 ml. of blood by cardiac puncture. Human reticulocytes were obtained from patients with hæmolytic anæmia or with pernicious anæmia after treatment, while cardiac puncture of pigeons provided avian nucleated cells. Aliquots of 1 ml. of blood were placed in small vaccine vials sealed with rubber bungs and the vials were rotated three times per minute during incubation at 37°C. The solution of ferric chloride labelled with iron-59 solution was of high specific activity and was added in 0·1-ml. quantities containing approximately 0·5 μc. Before assay of radioactivity, the red cells were washed ten times with physiological saline solution and hæmolysed by the addition of distilled water. Hæm was extracted from the hæmolysates by Heilmeyer's method[3] and the radioactivity of the hæm and non-hæm fractions was measured.

The principal findings were as follows:

(1) In mammalian blood, approximately 90 per cent of the total uptake occurred within 2 hr. and hæm synthesis took place rapidly. The ratio of hæm iron-59 to non-hæm iron-59 in all hæmolysates was approximately 65 to 35. Uptake and hæm synthesis were also parallel in avian blood, but the rate was slower and was related linearly to time up to 8 hr.

(2) Incubation of blood prior to the addition of iron-59 reduced the total uptake of iron-59 and also its percentage in the hæm fraction. A typical

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