LETTERS TO THE EDITORS

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Fetuin, a New Globulin Isolated from Serum

DURING a study on the fractionation of serum with ammonium sulphate, I thought it worth while to try whether some of the serum proteins could be isolated more easily from the serum of a newly born animal. Serum from calves not more than two weeks old was used for these fractionation experiments, which immediately indicated a pronounced difference between the serum from the calf and that from the cow. Ultracentrifugal examination of the different fractions revealed the presence of large amounts of a globulin with the sedimentation constant, s_{20}, of the order $3S$ ($1S$ (Svedberg) $= 1 \times 10^{-13}$ C.G.S.) as compared with the normal $s_{20} \sim 7S$ for serum globulin. The main part of the new protein was precipitated between the salt concentration limits 0·37 and 0·45 saturated ammonium sulphate. It was purified further by fractionation with ammonium sulphate and centrifugation in a high-speed air-driven centrifuge. Molecular weight determination gave a value of the order 50,000 [1].

Experiments with serum from calves of different ages have shown that the amount of this globulin has its highest value in the newly born calf, and decreases with time. In the adult cow, its presence may be demonstrated in the fractions which correspond to those from the newly born calf where the new globulin is the predominant component. It seems reasonable to assume that the concentration of the new protein shows its maximum value in the fœtus and that it is in some way associated with the period when the greatest building and development of the animal takes place. I therefore propose that this new protein be called 'fetuin'. The name is derived from the Latin name for fœtus, namely, *fetus*.

Later experiments with fœtal sera from cow and sheep have shown that the 'total globulin' obtained from these liquids mainly consists of fetuin, whereas the presence of ordinary globulin with $s_{20} \sim 7S$ can just be demonstrated. Serum from human umbilical blood was also examined, but its contents of fetuin was only a few per cent. The same serum, however, contained considerable amounts of globulin with $s_{20} \sim 7S$. A similar result was obtained with rabbit fœtal serum, whereas foal serum behaved similarly to that from the calf.

The same grouping of the species (cow, horse and sheep on one side, and man and rabbit on the other) is found in one of their immunological properties. Thus placental transmission of antibodies takes place in the latter group, while the newly born animal of the former group receives its antibodies with the colostrum, when it is suckled for the first time (see ref. 2). There is also a distinct difference between the two groups in the construction of the placenta. In the case of ruminants, the placenta consists of three layers of cells, whereas in rodents and man the maternal blood is separated from the fœtal by only a single layer of cells.

It is still an open question whether or not fetuin is generally present in embryonic serum. In this connexion, it is of interest to note that Svedberg and Andersson [3] several years ago, in an unpublished investigation, found that no component with $s_{20} \sim 7S$ was present in serum from chicken embryo after 11–15 days incubation. The 'albumin peak' in the sedimentation diagram, however, was very asymmetrical and gave comparatively low values for the sedimentation constant. The low value for s_{20} in this case may perhaps be explained by the possible presence of fetuin in the embryonic serum. After 18 days of incubation the globulin amounted to 22 per cent of the protein, and the 'albumin peak' had become more symmetrical.

Differences between haemoglobins from adult and from fœtal blood have been reported from time to time, and it was generally supposed that they were to be found in the protein moiety of the molecule. Several years ago, G. S. Adair [4] found that maternal and fœtal hæmoglobin from sheep could be easily distinguished in electrophoresis. Quite recently, Wyman *et al.* [5] have demonstrated great differences in the solubility of maternal and fœtal hæmoglobin from the cow. At the same time, Andersch *et al.* [6] showed that the electrophoretic mobility is not the same for hæmoglobin from a newly born infant as that from an adult. The two sedimentation constants were also unlike ($s_{20} = 2{\cdot}5S$ for the infant and $4{\cdot}7S$ for the adult).

It is thus evident that in the case of the respiratory proteins and also in the serum proteins, great differences exist between their properties in the embryonic state and in the adult animal. This investigation is being continued, and details will be published elsewhere.

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[1] Pedersen, K. O., in "The Svedberg 1884 30/8 1944" (Uppsala: Almqvist and Wiksell, 1944), 490.
[2] Kuttner, A., and Ratner, B., *Amer. J. Dis. Child.*, **25**, 413 (1922).
[3] Svedberg, The, and Andersson, K. I. J., private communication.
[4] Cf. Tiselius, "The Harvey Lectures" XXXV, 1939–1940, 67.
[5] Wyman, J., Rafferty, J. A., and Ingalls, E., *J. Biol. Chem.*, **153**, 275 (1944).
[6] Andersch, M. A., Wilson, D. A., and Menten, M. L., *J. Biol. Chem.*, **153**, 301 (1944).

Permeability of Keratin Membranes

BARRER [1] has suggested that the diffusion of vapours through media in which sorption and swelling occur are governed by a generalized form of Frick's Law, in which the diffusion constant is a function of the vapour concentration in the specimen.

Recent measurements in these laboratories of the diffusion constant of water vapour in keratin have provided an example of this phenomenon. At water contents below 6 per cent on the dry weight, the diffusion constant becomes extremely small in comparison with its value at higher concentrations.

This property of keratin may be demonstrated very simply as follows. Two compartments A and B, separated by a film of horn a few thousandths of an inch thick, are both evacuated. Then on introducing water vapour into A the subsequent rise in pressure in B follows Curve a. The diffusion is slow until the film acquires a water content of about 6 per cent throughout, when a rapid increase in transport occurs, despite the decreasing pressure difference across the membrane, because of the large increase in the diffusion constant.

If, after equilibrium is attained, the water vapour is rapidly removed from A, the fall in pressure in B