

ON THE DISTRIBUTION OF QUININE IN THE BLOOD.—By O. S. GIBBS, M. B., CH. B., Pharmacology Dept., Dalhousie University, Halifax, N. S.

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Quinine is a substance having the remarkable powers of forming films of high concentration at an interface. As was pointed out by Ramsden¹ it may actually produce solid films.

If quinine be filtered some always becomes absorbed on the filter, and if a celloidin thimble is used to filter a dilute solution, no quinine may appear in the filtrate. Furthermore the concentration inside the thimble falls.

These facts led me to examine the distribution of quinine in the blood; since if quinine were absorbed on the erythrocytes, thus forming a film, though perhaps very thin, of high concentration, it would offer further explanation of its value in the treatment of malaria.

The method of analysis used was described by Ramsden and Lipkin² which utilizes the relative insolubility of quinine in a saturated solution of ammonium sulphate to form clouds with Tanret's reagent. The same solution being used to obtain protein free extracts from the blood. Like King and Acton³ I was unable to confirm the accuracy of this method, which has very many fallacies, and even using a better extraction method was only able to obtain between 70-80% yield of the quinine.

The results of these experiments show clearly that quinine is very difficult to extract completely from the blood debris, and as is to be expected the greater the amount of debris, the greater the loss. In my experiments in which 10 cc. of blood, to which quinine was added, was centrifuged into two layers, the upper one being clear serum, I found like King & Acton

¹Ramsden, W. Proc. Roy. Soc. 1904, 72, 156-164.

²W. Ramsden & Lipkin, I. J., B. M. J. 1918, Vol. I, p. 560.

³King & Acton, Biochem. Jour. 1921, XV, 53.

more or less equal amounts were extracted from the serum, and the blood cells. It should be noted however that the cell debris is much larger than that of the serum.

When the blood is haemolysed, and then centrifuged, the two layers (upper 5 cc. and lower 5 cc.) appear identical, although the lower one contains the 'ghosts' of the cells. They also give an approximate amount of debris. Under these conditions however more quinine is always found in the lower layer, varying from 6-40% more.

This fact appears most easily explained by assuming the adsorption of quinine onto the 'ghosts', and if this be true onto the intact cells. In any case the diffusion of quinine into the cell, even if it occurs, would probably be a very slow process; whereas, as Rona & Block⁴ point out, the distribution of quinine takes place with "unmeasurable rapidity."

Summary.

1. King and Acton's results on the use of Ramsden & Lipkin's method are completely confirmed.
2. Using a modified technique very similar to these authors between only 70-80% of the added quinine has been recovered.
3. Under the conditions of the experiments the yield from the serum approximately equals that from the blood cells.
4. Quinine is probably adsorbed onto the blood cells.

⁴P. Rona & Block E. Biochem. Zeit. 1922. 128, p. 169.