

compared. The illumination (small automatic feed carbon arc), magnification, etc., were kept constant. To exclude the subjective factor, the observations were always checked by 2 observers, whose readings coincided within 0.5 cm.

The amount of light reflected is indicated by the thickness of the wedge of opaque fluid necessary to obliterate the particle from view, *i. e.*, by the readings on the wedge, in centimeters.

The apparatus described enables us to compare the appearance of a series of lyophilic colloids with one another under standardized conditions, and should be useful for a considerable number of investigations, particularly for investigation of the degree of hydration of the particles.

We are using it in the investigation of the effects of antiseptics and of various drugs upon blood plasma. Investigations of the blood plasma in various pathological conditions, and of the effects of hydrating and dehydrating agents upon protein and lipid suspensions, are in progress.

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Effects of Neoarsphenamine and of Mercurochrome Upon the Ultramicroscopic Appearance of the Blood Plasma.*

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In a previous communication¹ we have shown that the addition of a great variety of antiseptics to solutions of purified egg albumin *in vitro* causes the appearance of the albumin particles to change from the bubble-like picture given by egg albumin and other lyophilic colloids, to the punctate, star-shaped and comet-like picture given by lyophobic colloids. We have assumed that this may be regarded as evidence of aggregation and probably also of dehydration.

The conditions observed with blood plasma are, however, somewhat different. The proteins of plasma are probably not like the particles of egg albumin in sodium chloride, naked protein, but certainly represent a better state of dispersion, which is probably in part due to the presence of the plasma lipoids. Under the ultra-

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¹ Wright, H. N., and Hirschfelder, A. D., *Proc. Soc. Exp. Biol. and Med.*, 1929, xxvi, 790.

microscope the visible particles never appear as large or as brilliant as those seen in an egg albumin solution, but are smaller and less brilliant.

When neoarsphenamine or mercurochrome solutions are added to oxalated rabbit's plasma (2 mgm. oxalate per cc. of whole rabbit's blood) the spherical particles become definitely more brilliant than they were before. This seems to correspond qualitatively, but not quantitatively, with the actions of these drugs upon egg albumin solution, *i. e.*, there is probably an alteration of the colloid with a partial dehydration and perhaps a small degree of aggregation. When mercurochrome (10 mgm. per kilo) is injected intravenously in a rabbit, and the blood removed 5 minutes or even an hour and a half later, the particles seen when the oxalated plasma is viewed with the ultra-microscope, show the same increase in brilliancy that we observed when the drug was added *in vitro*. Using the wedge photometer² for comparing the plasma of the normal rabbit with that of the rabbit injected with mercurochrome, we have obtained the following readings, which are typical for several experiments:

Normal plasma	Rabbit injected with 10 mgm. mercurochrome per kilo, intravenously
4.5—5.0 cm	6.5—7.0 cm.

In harmony with these results we have found that mercurochrome, when injected intravenously, is definitely fixed by, and probably adsorbed on the blood colloids. Though the plasma becomes a deep pink, the mercurochrome will not pass through a viscose sausage skin dialyzer as does an aqueous solution of mercurochrome. An aqueous solution of mercurochrome will stain yeast cells pink; the pink plasma obtained after injection of mercurochrome will not stain yeasts at all.

We are, therefore, forced to the conclusion that mercurochrome, when injected into the veins, converts the plasma colloids, probably the proteins, into aggregates which are foreign to the animal. Since intravenous mercurochrome gives rise to chills and fever similar to that resulting from the injection of foreign proteins, we believe that these new aggregates formed within the patient's own vessels by the intravenous injection of protein act much as though they were foreign proteins; though the reactions are probably not absolutely identical. We believe that it is this foreign protein-like action, rather than an antiseptic action of a drug in concentrations too weak

² Hirschfelder, A. D., and Wright, H. N., *PROC. SOC. EXP. BIOL. AND MED.*, 1930, **xxvii**, 547.

to be either bactericidal or bacteriostatic, which is responsible for any therapeutic effect which may occur in the blood and tissues after the injection of mercurochrome. (Conditions after excretion through the kidney are different, for the mercurochrome is then freed from the protein.)

Since the injection of nearsphenamine is not so commonly followed by febrile reactions as is that of mercurochrome, it might be expected that the changes which it would produce in the plasma colloids would also be less marked. This is exactly what we have observed with the specimens of nearsphenamine thus far tested.

After the intravenous injection of 20 mgm. nearsphenamine per kilo into the rabbit, the plasma particles seem to become definitely more brilliant, but the change is much less marked than that observed after mercurochrome.

We are, therefore, investigating the relation of colloidoclastic reactions observed after the intravenous injection of drugs and in pathological conditions, upon the ultramicroscopic appearance of plasma proteins.

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Effects of the Commonly Used Anticoagulants on the Ultramicroscopic Appearance of Frog's Plasma.

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A series of investigations are in progress in this laboratory dealing with the changes brought about in the blood plasma by the injection of drugs and also by various pathological conditions.

Since some method of preventing the coagulation of the blood plasma has to be employed, it became essential to study the effects of the commonly used anticoagulants on the appearance of plasma under the ultramicroscope. In previous communications^{1, 2} oxalated rabbit's plasma had been used.

Samples of frog's blood (*Rana catesbiana*) were collected into oiled tubes without the use of any anticoagulant, centrifuged, the

¹ Wright, H. N., and Hirschfelder, A. D., *PROC. SOC. EXP. BIOL. AND MED.*, 1929, xxvi, 790.

² Hirschfelder, A. D., and Wright, H. N., *PROC. SOC. EXP. BIOL. AND MED.*, 1930, xxvii, 547, 548.