by a macrophage in tissue culture. We now report evidence of the phagocytosis of free merozoites of *Plasmodium falciparum* by human polymorphonuclear leukocytes.

Blood was drawn from young men, recently returned from Vietnam, who entered the hospital as a result of a relapse of falciparum malaria. Small amounts of heparin (Panheprin, Abbot) which contained no preservative was used as an anticoagulant. A small drop of blood was placed on a cover slip (22 by 40 mm) sandwiched onto a glass slide and sealed with 360 silicone fluid, 350 centipoise (Dow Corning) (*3*). Cells in such preparations remained viable for many hours and afforded good phase-microscopic images.

The slides were studied on a Leitz microscope equipped with phase optics and time-lapse cinephotomicrographic apparatus (Sage Instruments). The temperature of the preparation was maintained at 36°C with an air-curtain incubator (Sage Instruments). The parasitized red cells were observed under a × 90 phase objective and photographed on Plus X negative 16-mm film (Kodak) at eight frames per minute under tungsten illumination with a green-yellow filter at 5.2 volts, requiring 1.25 seconds for exposure.

The parasite is easily made visible in the red cell by phase microscopy and is a highly motile, freely moving flattened structure. The extreme freedom of motion suggests that the interior of the parasitized red cell is fluid or semifluid. The parasite apparently produces no changes in the red-cell surface that can be recognized by the monocyte or polymorphonuclear leukocyte (Fig. 1). Monocytes and polymorphonuclear leukocytes repeatedly pass within a few red-cell diameters from the parasitized red cell, even up to a few minutes before rupture of the diseased red cell. In Fig. 2, a red cell has ruptured, releasing its merozoites. A polymorphonuclear leukocyte which had passed the red cell moments before the rupture rapidly reversed its direction and in a purposeful fashion returned to ingest the released organisms. Digestive vacuoles appear within moments after the phagocytosis of the merozoites.

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16 August 1968

Red Blood Cells: Why or Why Not?

Abstract. *It is commonly stated that, if hemoglobin were dissolved in the blood plasma rather than enclosed in corpuscles, the viscosity of the blood would be greatly increased. We found that when the corpuscles of dog or goat blood were disrupted with ultrasound, giving a solution with the same hemoglobin concentration, the relative viscosity was drastically reduced. It appears, therefore, that the existence of blood corpuscles does not contribute to a reduced viscosity of blood.*

Some animals carry hemoglobin in blood corpuscles, and others do not. Possible advantages of blood corpuscles have been the subject of much speculation. Animals which possess blood of high oxygen-carrying capacity, notably vertebrates, always have hemoglobin located within corpuscles (*1*). It has therefore been inferred that the existence of corpuscles is a necessary prerequisite for a high oxygen-carrying capacity. One reason often stated is that, compared to the more easily flowing fluid obtained by enclosing the hemoglobin in small packages (the red blood cells), a hemoglobin solution with the same oxygen capacity as mammalian blood would be highly viscous, and therefore would require much greater pumping efforts of the heart. This explanation is found at all levels, from specialized monographs to the elementary textbooks (*2*).

We wanted to know whether this contention is reasonable, but a literature search revealed no experimental evidence. We therefore examined the problem by comparing blood with intact red cells and the same blood after disruption of the cells. Comparison of these two fluids, which have identical concentrations of hemoglobin, showed that the assumed effect of the corpuscles on viscosity is wrong.

Blood was taken from the jugular vein of mongrel dogs and domestic goats with sodium heparin as an anticoagulant (10 unit/ml). A range of hemoglobin concentrations was obtained by withdrawing or adding plasma to the samples. Viscosity at 37°C was determined in these samples, before and after hemolysis, by means of Ostwald viscometers (*3*). The corpuscles were disrupted by ultrasound (Branson Sonifier model W-140C) with a Rosett cell used to prevent overheating. Any cell fragments formed remained in the solution, which we will refer to simply as a hemoglobin solution. Treatment with ultrasound had no effect on the viscosity of plasma alone (*4*). Hemoglobin concentration was measured in all samples, both before and after hemolysis, by the cyanomethemoglobin method (*5*).

Disruption of the corpuscles of dog blood by ultrasound caused a conspicuous decrease in the relative viscosity (Fig. 1). However, at very high concentrations of hemoglobin, outside the normal physiological range (hemoglobin more than approximately 20 g/100 ml), disruption of the corpuscles yielded a hemoglobin solution which gelled, and its viscosity could not be measured.

At the normal hemoglobin concentration of dog blood (14.8 g/100 ml), the relative viscosity of blood with cells was 4.7 (Fig. 1, *A*), and disruption of the cells reduced this to a relative viscosity of 3.3 (Fig. 1, *B*). Thus, if the hemoglobin were carried in solution in the plasma, its contribution to the viscosity would be 47 percent less than it is when carried in cells (as related to plasma viscosity, Fig. 1, *C*).

Disruption of the red cells in goat blood (Fig. 2) caused an even greater reduction in relative viscosity than it did for dog blood. This is primarily because the curve for whole goat blood is located above that of dog blood. The curves for plasma and for the hemolyzed blood are approximately the same for the two animals, and the difference in the whole blood must therefore depend on cell characteristics. Another difference is that very concentrated solutions of goat hemoglobin did not gel as dog blood did. Even at a hemoglobin concentration of 25.2 g/100 ml, the viscosity of the goat hemoglobin solution (relative viscosity, 18.2) was

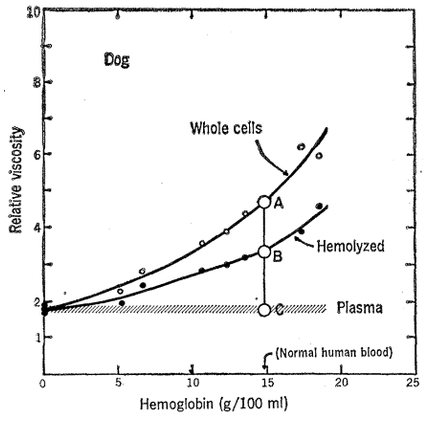

Fig. 1. Relative viscosity (water = 1.00) of dog blood (four animals) with whole cells (upper curve) and of the hemoglobin solution obtained by disrupting the corpuscles of the same samples with ultrasound (lower curve) at various hemoglobin concentrations. The horizontal, hatched area refers to the range of observed plasma viscosity of the blood samples. Points *A* and *B* denote the viscosities at the hemoglobin concentration of normal dog or human blood, 14.8 g/100 ml.

much less than that of the red cell suspension (relative viscosity, 30.1).

In goat blood, at 14.8 g of hemoglobin per 100 ml, the contribution of the hemoglobin to blood viscosity was reduced by 57 percent when the hemoglobin was carried in solution rather than in cells. The relative reduction is approximately the same at the normal concentration of hemoglobin in goat blood (about 12.6 g/100 ml).

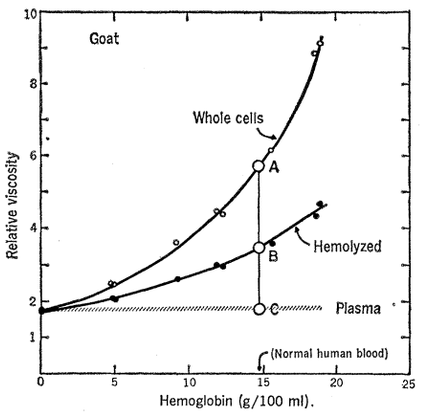

Fig. 2. Relative viscosity (water = 1.00) of goat blood (two animals) with whole cells (upper curve) and the hemoglobin solution obtained by disrupting the corpuscles of the same samples with ultrasound (lower curve) at various hemoglobin concentrations. The horizontal cross-hatched area refers to the range of observed plasma viscosity of the same blood samples. Points *A* and *B* denote the viscosities at a hemoglobin concentration of 14.8 g/100 ml.

The conspicuous reduction in relative viscosity which we found was measured in a glass capillary 0.63 mm in diameter and 70 mm long. In narrower tubes (less than about 0.5 mm), however, the viscosity of blood decreases relative to that of water in the same tube (the Fåhraeus-Lindquist effect) (*6*). If the relative viscosity of blood is measured by perfusion of the hind limb of a dog, it is lower than the relative viscosity measured in an Ostwald viscometer (*7*), probably due to the Fåhraeus-Lindquist effect. It is therefore desirable to extend our observations with determinations of the viscosity in small tubes with a diameter similar to the capillaries of the living organism.

If the red cell contributes a greater increase in blood viscosity than a hemoglobin solution of the same oxygen carrying capacity, what is the rationale for the existence of red blood cells? Perhaps the most convincing argument is that without the red cells the dissolved hemoglobin would cause the colloidal osmotic pressure of mammalian blood to be about three times as high as that caused by plasma proteins alone. This would have profound effects on movement of fluid through capillary walls, and, in particular, on the filtration process in the renal glomerulus, which would require a correspondingly higher filtration pressure and therefore also blood pressure. There is, however, a way out of this dilemma. The contribution of respiratory pigments to the colloidal osmotic pressure could be reduced by carrying the proteins as large-size molecular aggregates. This is the situation in many invertebrates which carry their respiratory proteins in aggregates with molecular weights of several million (*1*).

One possible function of red cells may be related to the fact that they cause the liquid flow in the capillary to change from a laminar to a bolus flow. This may have advantages for the gas exchange in the capillary because with bolus flow there is no stagnant layer of fluid along the capillary wall.

Another consequence of the existence of red blood cells is that various blood components, such as enzyme systems, are kept localized and in high concentration within the cell in close proximity to the hemoglobin. For example, the action of the enzyme glutathion reductase (which normally reduces the respiratory inactive methemoglobin to normal oxygen-carrying hemoglobin) is facilitated when both reactants are present in high concentration within the confined space of the red cell. Whatever reason there may be for the existence of red blood cells, our conclusion must be that experimental evidence does not support the assumption that their existence contributes to a reduced blood viscosity.

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Rheological Comparison of Hemoglobin Solutions and Erythrocyte Suspensions

Abstract. *Hemoglobin solutions prepared from hemolyzed human erythrocyte packs have Newtonian flow properties. Diluted solutions are also Newtonian. All solutions have a viscosity lower than the apparent viscosity of erythrocyte suspensions of equal oxygen-carrying capacity. The presence of cell debris in hemoglobin solutions causes non-Newtonian (pseudoplastic or rheopectic) flow behavior.*

It has been reported (*1*) that the viscosity of blood is considerably less than that of a hemoglobin solution of comparable oxygen-carrying capacity. It has been argued from this that hemoglobin packaged in red blood cells has evolved as a means of reducing the heart work