A SECOND COAGULATION OF THE BLOOD DUE TO A
SUBSTANCE THAT IS NOT IDENTICAL WITH FI-
BRINOGEN AND IS COAGULABLE BY SATURATION
WITH NEUTRAL OXALATE.

BY EDWARD T. REICHERT, M.D.

(From the Physiological Laboratory of the University of Pennsylvania.)

That the oxalated bloods of certain species may undergo
coagulation, even in the presence of an excess of oxalate, has
been known for some years. A plausible explanation has been
suggested in the probability that the oxalate does not cause the
plasma to become lime-free, but leaves sufficient lime salts in
solution to be slowly effective. It was during an investigation
of this problem that I discovered that the oxalate may not only
hinder or prevent coagulation, but actually cause it; and that
the oxalate is anticoagulative to one substance and coagulative
to another.

The experiments were carried out chiefly with the bloods of
the *necturus* and *amia*, which bloods were oxalated in the usual
proportion, or defibrinated.

If to the oxalated blood either neutral ammonium or potas-
sium oxalate be added to saturation, in the course of several
minutes, the time varying with the freshness of the blood and
other conditions, a thickening begins which gradually increases
until there is formed a solid, very elastic, and slightly contractile
cogulum. The question at once arose as to whether or not the
coagulation is due to the plasma-fibrinogen, or to another sub-
stance, or to both. To determine this point the fibrinogen was
removed from the plasma by beating, and then the oxalate was
added to saturation. This defibrinated blood was found to
coagulate as before defibrination, thus showing that the coagula-
tive principle that is caused to undergo coagulation by saturation
with oxalate cannot be, unless in minor part, the plasma-fibrinogen. To prove if the oxalate to saturation has a coagulative action on the plasma-fibrinogen, oxalated blood was centrifugalized, and the clear plasma then saturated with oxalate, with a negative result. Having thus determined that the plasma-fibrinogen is not the coagulative substance affected by the oxalate, it seemed clear that a second principle exists which is not only not identical with the plasma-fibrinogen, but which belongs to the corpuscles. Tests made with centrifugalized blood rendered it obvious that the chief or sole source must be in the red cells. The upper layer of corpuscles, rich in colorless cells and poor in red cells, reacted to saturation with oxalate poorly, if at all; the middle layer, poor in colorless cells and rich in red cells, reacted well; and the lowermost layer, which consisted essentially of red cells, yielded a coagulum more quickly and of firmer consistency than even the normal blood. Moreover, that the coagulative substance is contributed by the red cells is further indicated by the fact that when the cytoplasm of these cells is caused to disintegrate, as by agitation with ethyl ether, coagulation occurs more promptly, and the coagulum is firmer and more elastic than when the corpuscles are practically intact. This observation also shows that the clot formed in defibrinated blood is not merely an agglutination of the corpuscles caused by the deposition of some substance of the plasma, or from the colorless cells, but is due to a principle of the red cells.

My experiments with mammalian bloods, although as yet very limited, indicate that two clot-forming substances, one coagulable by saturation with neutral oxalate and the other not, may be common to all or nearly all bloods, and that the corpuscular principle, like the plasma-fibrinogen, varies in percentage not only in the bloods of different species, but in the bloods of the same species, and even in the bloods of different vessels of the same individual.

That the red corpuscles yield such a coagulative material seems evident also from a number of facts, as, for instance: The red corpuscles of certain mammals have been found to yield a fibrinogenous substance; the fibrinogenous material of the
bloods of certain amphibia and birds is stated to originate in the breaking down of the red cells; the quantity of fibrin formed in mammalian blood is greater when the red corpuscles are present than when absent; agents which cause a partial or complete disintegration of the red cells increase the rapidity of clotting and the quantity of fibrin formed, etc. In connection with the foregoing it is of interest to note that the results of recent research indicate that the chief source of the plasma-fibrinogen is probably the leucocytes, especially those of the intestinal tract.

The fact that the red cells undergo gradual dissolution in the shed blood, and even with considerable rapidity in certain bloods, makes it probable that the coagulative substances of both plasma and red corpuscles constitute together, in some cases at least, the normal fibrin-yielding material, the proportions of the two varying in different bloods under different conditions. This view is in accord with such facts as pertain to the differences in the composition of the fibrins obtained from the plasma and from the whole blood; the differences in the fibrins from the bloods of different species, and from the bloods of different vessels of the same species; and the occurrence of coagulation of bloods which contain an ordinary amount (1:1000), or an excess, of oxalate.

The fact that the fibrinogen of the plasma is not coagulated by saturation with neutral oxalate, and that the coagulable substance of the red corpuscles is so coagulated, can scarcely leave a reasonable doubt as to their non-identity.