special slide chamber and phase microscopy. The titer was defined as the dilution of antiserum which killed 90% of the cells.

The rabbit anti-dog lymphocyte serum was toxic to the cells in all 5 cultures (Table). The cells of MOORE No. 5287 were the most sensitive (titer 1:3000) and of Burkitt's lymphoma, HRIK, the least sensitive (titer 1:30). Cultures CEE, MOORE and CORMACK were derived from normal persons and culture BARNES from a patient with acute leukemia. The degree of toxicity did not seem to be correlated with the derivation of the culture.

In recent parallel experiments, the rabbit anti-dog lymphocyte serum had titers up to 1:40 for lymphocytes of 6 normal persons (median > 1:10) and up to 1:1000 for lymphocytes from 12 patients with chronic lymphocytic leukemia (median 1:100). These findings are in accord with the previous study[1].

The rabbit anti-dog lymphocyte serum plus rabbit complement was, on the average, more toxic to the human cells in cultures than to blood lymphocytes of patients with chronic lymphocytic leukemia[3].

Titer of rabbit anti-dog lymphocyte serum which killed 90% of cells in established human cell cultures and in lymphocyte suspensions

Cell cultures	*Titer (median)*
Derived from blood of normal persons	
CEE No. 1120	1:300
CORMACK No. 8068	1:1000
MOORE No. 5287	1:3000
Derived from patients with acute leukemia or lymphoma	
BARNES No. 4277	1:1000
BURKITT's lymphoma – HRIK	1:30
Lymphocyte suspensions	
Lymph nodes of 2 dogs	1:10,000
Derived from blood of	
6 normal persons	> 1:10
12 patients with chronic lymphocytic leukemia	1:100

Zusammenfassung. Die Kombination von Kaninchen Anti-Hund Lymphozytenserum und Kaninchen Komplement war für menschliche Blutzellen in in-vitro-Kultur sowie für Blutlymphozyten von Patienten mit chronischer lymphatischer Leukämie toxisch.

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Rheogoniometric Viscosity Measurements of Whole Human Blood at Minimal Shear Rates Down to 0.0009 sec^{-1}

Low shear rates down to 0.052 sec^{-1} applied to certain blood systems led some investigators to the conclusion that blood has Newtonian characteristics. Our modifications to the Weissenberg rheogoniometer permitted measurements down to 0.0009 sec^{-1} and, in some cases, down to 0.0006 sec^{-1}. The data obtained at these low shear rates demonstrate that blood has non-Newtonian behavior and exhibits a yield stress. These findings are considered significant in the physiology and pathology of blood circulation.

Blood viscosity is markedly augmented as the flow of blood approaches a standstill and the shear rate progresses to zero. Such situations exist physiologically in the living circulation, when the flow velocity is extremely low, such as in post-capillary vessels and with the occurrence of stasis or cessation of blood flow. Therefore, it needs to be established whether or not blood has a yield stress and to determine what the flow characteristics are at extremely low shear rates.

One of us (A.L.C.) proposed in 1942 that blood behaves as a non-Newtonian fluid and might well have a yield stress[1]. Since at that time techniques were not available for the measurement of viscosity at very low shear rates, this problem could only be speculated upon. MERRILL, WELLS et al.[2] studied whole blood viscosity at 'low' shear rates and concluded, according to CHIEN, GREGERSEN et al.[3], that whole blood exhibited a yield stress. CHIEN et al.[3], who repeated some of these studies, reported in 1966 that the results at low shear rates with the GDM viscometer were not reliable, because of limitations of

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this instrument. With their improvement of the mechanical and electrical components of the GDM viscometer, they succeeded in securing reproducible measurements at shear rates as low as 0.052 sec^{-1} and finally down to 0.01 sec^{-1}. On the basis of their data, they concluded that whole blood possesses no yield stress and that it exhibits Newtonian behavior. In our appraisal, the low shear rates, which these authors employed, were not low enough[4]. We attempted therefore to secure data at shear rates as near to zero as the Weissenberg rheogoniometer, which we modified[3] for this purpose, would permit. These modifications allowed the measurement of the viscosity of whole human blood in all cases down to 0.0009 sec^{-1} and in some cases down to 0.0006 sec^{-1}.

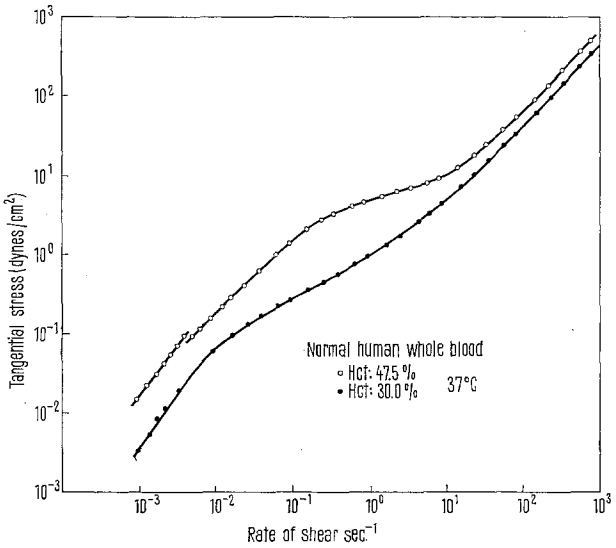
Blood was secured from the antecubital vein of 12 male and female healthy human subjects, ranging from 25 to 40 years of age. After the first 10 ml of blood were discarded, the donation was collected through a Plexitron set into a test tube containing EDTA (ethylenediaminetetraacetic acid) in dry form, so that there was a final concentration of 1.2 mg of this anticoagulant per ml. The tube containing the blood was swirled, care being taken to avoid bubble formation and to secure good mixing with the anticoagulant.

The blood samples were maintained at 37 °C throughout the testing. The lowest shear rates were measured first, and, between each shear increment, the platens were given a high speed spin to remix sedimented red blood cells. A blanket of moist air was applied to the blood sample under investigation to prevent drying of the topmost layer of blood[5].

The Figure represents plots of data obtained with the samples of whole blood from 2 donors with hematocrits of 30.0 and 47.5%, respectively. These plots are typical of the results obtained with the blood of any of the donors and show some of the variations encountered in healthy persons. Since no blood was studied from subjects suffering from any pathological condition, the variations which we found are considered to be within normal limits.

Peak values of tangential stress were plotted and no consideration has been given to apparent time-dependent behavior due to the development of a cell free plasma layer at the sample geometry interface and sedimentation at lower speed settings.

It can be seen from these curves that there is an inflection between 0.004 and 0.009 sec^{-1}. We consider this to be due to the collapse of a three-dimensional structure of red blood cells, existing up to this point, and to represent a true measurement of the yield stress. When the yield stress measured from the relaxation curve of the torque trace, recorded after the instrument has stopped, as described by MERRILL et al.[2], is compared with the torque value at the discontinuity point in the Figure, almost exact agreement is found. Below this shear rate, slip may occur at the 2 interfaces of the geometry, possibly on a thin layer of plasma, and a plug of red cells may behave like a plastic solid. Between 0.04 and 30.0 sec^{-1} there is a region of non-Newtonian behavior which possibly can be explained by the gradual breakdown of red cell aggregates[6]. A second inflection is seen at about 30.0 sec^{-1}, which may be the point where complete desaggregation of red blood cells is reached and the viscosity no longer decreases. We found the inflection points to vary slightly with the blood of different human subjects. MORRISON and HARPER[7] have shown with measurements of suspensions of fibrous particles exhibiting a yield stress, that, when using differing radial gaps, different values of yield stress are obtained. Their comments may very well apply to our experiments with whole blood. We, therefore, plan to investigate this possibility by using different gap widths and cone angles to ascertain the effects that they may have on the flow characteristics of whole human blood. Our findings demonstrate that, contrary to the conclusion of CHIEN et al.[3], human blood exhibits a yield stress and that plug flow occurs below the yield point. These findings appear to be of utmost significance in the physiology and pathology of the circulation[8].



A shear stress/shear rate plot of the measurements made on the whole blood of 2 donors. This plot is typical of the results obtained with the blood of other subjects.

Zusammenfassung. Messungen menschlichen Gesamtblutvolumens bei sehr niedrigen Schubzeiten bis 0,0009 sec^{-1} (modifizierter Weissenberg-Rheogoniometer). Es wird gefunden, dass das Blut kein Newton'sches Verhalten und bei diesen niedrigen Schubzeitableitungen eine Fliessspannung aufweist.

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