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FOURTH INTERNATIONAL CONGRESS ON RHEOLOGY BROWN UNIVERSITY, PROVIDENCE, RHODE ISLAND U.S.A. AUGUST 26–30, 1963

Under the auspices of the International Committee on Rheology

SYMPOSIUM ON BIORHEOLOGY

Organized and arranged by the Chairman of the Symposium, Professor A. L. Copley, New York Medical College, New York.

INTRODUCTION

THE editors-in-chief have asked eleven participants of the Symposium on Biorheology to write synopses of the discussions to each of the eleven sessions. We should like to thank the authors of each synopsis for their assistance in this compilation of reports. As it would not be possible to write an adequate report about the entire symposium, as no one could have been at more than one session at a time, this compiled report will not only acquaint the participants with what went on in the two simultaneous sessions, but will be of equal interest to those readers of BIORHEOLOGY who did not participate. Moreover those who will read the Proceedings of the two symposium volumes, to be published by John Wiley and Sons, New York and edited by A. L. Copley, will find this report useful, since the Organizing Committee of the Congress decided not to include any discussion remarks in the planned six volumes of the entire Proceedings.

It should be stated, however, that the coverage could not be complete, because no stenographic or other recordings of the discussion notes could be provided. Some speakers used up the entire time of 30 min, allotted to each paper, with the exception of Professor Weissenberg's 1 hr lecture. In general, 20 min were given for the delivery and 10 min for the discussion of each paper, so that unfortunately no time was left for discussion in the above few cases. In several other instances, the authors could not be present and their papers were read by other participants not familiar with the work presented.

There had been no time scheduled for discussion of the presentations given in the General Session by Professors Copley, Fåhraeus, Weissenberg and Scott Blair, as well as regarding the lectures before the entire Congress by Dr. R. L. Whitmore and Professor N. Kamiya. Because of his sudden illness, the General Lecture by Professor Aharon Katchalsky was not delivered and Dr. R. L. Whitmore substituted his General Lecture at about a day's notice.

We are grateful to John Wiley & Sons, Inc. Publishers, New York and London, for granting permission for the publication of the abstracts of the Symposium on Biorheology from the Fourth International Congress on Rheology. Abstracts which were not included in the mimeographed volume published by the Congress were supplied by A. L. Copley,

A. Katchalsky, R. L. Whitmore, A. H. Saks, and R. D. Allen. The abstract of the paper by Dr. L. C. Cerny is not reprinted from the above Congress volume of abstracts, because he had withdrawn his paper before the Congress had begun.

Although the three lectures given before the entire Congress by R. L. Whitmore, N. Kamiya and A. Katchalsky were not part of the Symposium, they have been included in this report, because they deal with biorheology and, therefore, will also be included in the two symposium volumes now in preparation.

The Symposium on Biorheology has been initiated as late as November 1962 by the original organizers of the 4th International Congress on Rheology, Dr. R. S. Marvin of the National Bureau of Standards, Washington, D.C., Professor R. S. Rivlin of Brown University, Providence, R.I., the two co-chairmen of the Congress and by Professor E. H. Lee of Stanford University of Stanford, Calif., the Editor-in-Chief of the four other volumes of the Proceedings. They asked Professor A. L. Copley to organize and arrange the Symposium on Biorheology and edit its proceedings.

In his Opening Address Professor Copley first welcomed the members attending the Symposium and then gave a brief account of the history of its organization. He thanked the various U.S. Government agencies and individuals whose generosity had made the venture possible and expressed particularly his thanks to the Office of Naval Research, United States Navy, which made it possible that twenty-seven biorheologists from Europe, Israel and Japan could be provided with free travel and with subsistence during the Congress in Providence.

He paid a special tribute to the work of a great pioneer in hemorheology, Professor Robin Fåhraeus of the University of Uppsala, Sweden. His proposal that the two volumes of the Proceedings of the Symposium be dedicated to Professor Fåhraeus was warmly applauded. The participants gave an ovation to Professor Fåhraeus who accepted the honour thus bestowed on him. Professor Copley regretted the absence of Dr. G. W. Scott Blair who was expected but unfortunately was unable to attend.

A total of fifty-eight communications were presented at the Congress, of which the majority were papers by invited authors. Professor Copley expressed the view that the programme of the Symposium mirrored the scope and extent of biorheological research as it is being practiced today and that most studies appear to be made in hemorheology. He regretted that the botanical sciences were represented by only four papers and that the vast majority of biological fields including genetics has not yet become accessible to rheological treatments.

In his second part of his Opening Address, the third part dealing with the scientific topic of which an abstract is included, Professor Copley referred to the pre-Socratic thinkers, among them Anaximander, Empedocles and Heraclitus whose thoughts around 560–450 B.C. not merely originated the natural sciences, but rheology as well. The famous $\pi\acute{\alpha}\nu\tau\alpha\ \dot{\rho}\epsilon\hat{\iota}$ ascribed to Heraclitus, written on the cover of the program was the motto of the Congress which proved to be a highly stimulating one for all its members and, in particular, to the participants of the Symposium.

In the following presentation of abstracts and synopses, we thought it best to follow the order of items as given in the original program.

The round table discussion on hemorheology took place after the closure of the Congress in the evening of August 30th and therefore was not part of the official business. However, because of its interest to our readers, we asked Professor J. H. Wayland to write a report of this discussion which will be published in the next issue of BIORHEOLOGY.

This is the first occasion on which a Symposium on Biorheology has formed part of any of the International Congresses on Rheology, although two independent symposia took place, the one at Lund, Sweden in 1950 and the other at Oxford, England in 1959. There were of course individual biorheological contributions at all the earlier international congresses and indeed, the term "biorheology" as first proposed by one of us (A.L.C.) at the First Congress in 1948 at Scheveningen, Holland. Since the congresses take place every 5 years, the Fifth International Congress on Rheology will be held in 1968, probably in Tokyo, Japan. Our Japanese colleagues hope that biorheology will again be well represented at this Congress and that rheologists and biologists from all parts of the world will be able to attend.

ALFRED L. COPLEY and GEORGE W. SCOTT BLAIR
New York and Reading, October 1963

GENERAL SESSION (W6)

Monday, 26 *August* 1963

Chairmen: Professor A. KATCHALSKY (Weizmann Institute of Science, Rehovot, Israel)
Professor G. L. BROOKS (Brown University, Providence, U.S.A.)
Professor S. OKA (Tokyo Metropolitan University, Tokyo, Japan)

No. 183

A. L. COPLEY: *On the validity of classical fluid mechanics in biorheology. Opening Address*

New York Medical College, New York, U.S.A.

RHEOLOGY as a discipline different from fluid mechanics is discussed, in that the latter concentrates on the study of flow of idealized simple media while the former is concerned with the flow of complex fluids.

It is contended that rheology should be considered as a fluid mechanics of higher complexity and that, within rheology, the rheology of biological fluids would present an even higher level of intricacy. However, the study of all flow phenomena, whether of simple or complex fluids, must be based on a certain number of axioms or assumptions, the number of which will be the smaller the simpler the behaviour of the fluid. In classical hydrodynamics of the incompressible fluid the principle of conservation of mass in conjunction with Newton's laws are sufficient for the construction of the complete theory.

Any further complication of the behaviour of the fluid, such as non-Newtonian viscosity, or the existence of a yield stress or the consideration of the flow of suspensions, where the suspended particles themselves may have certain characteristics, will lead to certain severe complications in the theoretical formulations. The validity of simple equations, when applied to rather simple problems, such as laminar flow in a capillary, becomes then highly problematic.

Some phenomena of the author's own sphere of interest are chosen in which an apparent deviation from the principles of classical fluid mechanics exists [1]. They point to the existence of the so-called plasmatic zone, a layer near the living blood vessel wall free of blood cellular elements in the circulation and to our observations that the "apparent viscosity" in capillary viscometers can be affected by coating the glass surface with different substances.

Following the fundamental work of HELMHOLTZ [2] and of JEFFERY [3], some of the extremely complicated phenomena of blood capillary flow can be viewed from the starting point of classical theory; in particular the anomalous radial distribution of corpuscles and the complex influence of the nature of the vessel walls. No contradiction with classical fluid mechanics appears to exist in the first above cited phenomenon. However the second cited phenomenon [4, 5] which produces a rate of flow through a capillary dependent on the character of the coating could be explained by the existence of slip along the wall, an assumption which is rejected in classical fluid mechanics. The replacement of the

Poiseuille equation would require an extended equation due to HELMHOLTZ published in 1868 [6].

The observed difference in the thickness of the immobile layer as a function of the characteristics of the wall coating is offered as an alternative explanation of the effect of coatings on apparent viscosity. It is surmised that, if there is wall adherence, there is no slip at the wall. The existence of wall adherence has been established only on the basis of an index of blood systems bordering air surfaces and travelling in a capillary tube. If wall adherence can be demonstrated in a closed system, it may then be comparable with Poiseuille's concept of an immobile layer for which some evidence in the living microcirculation in the hamster's cheek pouch has been found [7]. As an assumption, slip on the immobile layer would still be compatible with the assumption of zero velocity at the wall. A close relationship of classical fluid mechanics and rheology rather than a contradiction between them could thus exist.

Entirely new approaches in physics other than fluid mechanics may be found and applied to problems in biorheology. On the other hand, mechano-chemical interactions in living systems as well as in extracorporeal biological materials may occur which will invalidate the purely mechanical approach in fluid mechanics.

REFERENCES

[1] WHITMORE, R. L., *Biorheology* **1**, 201, 1963.
[2] HELMHOLTZ, H. V., *Wissenschaf. Abhandl. Leipzig* **1**, 223, 1882.
[3] JEFFERY, G. B., *Proc. Roy. Soc.*, A **102**, 161, 1922.
[4] COPLEY, A. L., In: *Flow Properties of Blood and Other Biological Systems*, Copley, A. L. and Stainsby, G. (editors), Oxford, Pergamon Press, 1960, p. 97.
[5] COPLEY, A. L., SCOTT BLAIR, G. W., GLOVER, F. A. and THORLEY, R. S., *Kolloid-Z.* **168**, 101, 1960.
[6] HELMHOLTZ, H.v., *Berlin. Monatsber*, 215, 1868; *Phil. Mag.* **36**, 337, 1868.
[7] COPLEY, A. L. and STAPLE, P. H., *Fed. Proc.* **18**, 30 1959; *Biorheology* **1**, 3, 1962.

No. 129

R. FÅHRAEUS: *Archaic haemorheology. The historical significance of blood sedimentation*

University of Uppsala, Uppsala, Sweden

THERE is no other symptom of disease which has exerted such a deep influence upon pathology and therapy as variations of the blood sedimentation. From time immemorial up to the middle of the last century, probably the most important medical observation referred to the appearance of the letted blood. Even for the ignorant man it was obvious that the content of the blood vessels was a complicated mixture, which, some time after venesection, separated into different parts. The Greek physician came to the conclusion that one could distinguish four different fluids, namely the black bile (melancholia, the dark-red lower part of the clot), the yellow bile (cholera, serum), haima (later cold sanguis, the light red part of the clot) and finally the phlegm. The last-named fluid was of particular significance for the pathogenesis in two respects. Firstly, experience showed that the phlegm (the fibrin) had increased in almost all diseases. The blood clot was then covered with a more or less thick layer of phlegm, a phenomenon due to an increased sedimentation rate of the red corpuscles, which, as we now know, is perhaps the most common of general symptoms. The second and pathologically more important characteristic of the phlegm

was—in contrast to the three other fluids—its ability to congeal. The "cold and humid" phlegm corresponded to water, the element, which was made firm and immovable by cold. The behaviour of shed blood thus reflected the alterations which the content of the veins tended to undergo. The Greeks had certainly no idea about the circulation of the blood, but they were naturally convinced that, under physiological conditions, the content of the blood vessels was liquid. It seems to me probable that the Greeks sometimes made post mortem examinations. Then they found their suspicions confirmed. The heart and large vessels, e.g., in cases of pneumonia, were found almost entirely filled with congealed phlegm. The therapeutic consequences of this doctrine are easily understood. One tried to keep the phlegm liquid by warmth, locally and generally. Fever was welcomed as nature's own remedy to neutralize the injurious effects of the phlegm. But there existed one even more rational treatment, namely venesection. In this way the diseased body could be relieved of large amounts of the harmful fluid and one could observe with satisfaction the congealing process of the phlegm in the receptaculum. This erroneous conception of disease became the tragic foundation for the greatest mistake of ancient medicine, i.e., the enormously exaggerated use of blood-letting.

No. 130

K. WEISSENBERG: *Research in haemorheology—an introductory lecture*

The Royal Institution, London, England

IN presenting my introduction to the session on haemorheology it gives me great pleasure to acknowledge here my indebtedness to some of the pioneers in haemorheological research, and in particular to Drs. KNISELY, COPLEY, HARDERS, GELIN, DAVIS and LANDAU, who acted as my teachers and friends.

In 1853 POISEUILLE started a combination of *in vivo* and *in vitro* studies of the flow of blood, and this combination is characteristic for the modern conception of Haemorheology, which recognizes that in all processes occurring inside the living organism the rheology *in vivo* is constantly interacting with the rheology *in vitro* occuring through the intake of food, water and air, and the expulsion of the waste products by way of the digestive organs. Similar interactions occur in the modern techniques of blood transfusions, injections, and in the use of the artificial heart, lung and kidney machines during operation on vital organs.

The studies of Haemorheology have so far been dominated by the classical scheme of mechanics. This scheme is based on a number of assumptions which postulate that the macroscopic behaviour of a material can be approximated by that of a continuous medium with a consistency that is either ideally solid and then has only elastic properties obeying Hooke's law, or ideally fluid and then has only viscous properties obeying Newton's law. Testing of the said properties can then be carried out by means of simple instruments such as capillary viscometers for which Newton's law for fluids appears in the form of Poiseuille's law. Unfortunately, the classical scheme leads to a onesided and distorted description of macroscopic behaviour. This is because in a material of any consistency (solid, fluid or intermediate) there is inevitably a coexistence of elastic and viscous properties, which means for fluid blood e.g. that the classical characterization by the viscous property alone misses

entirely the characterization by the equally important elastic property which is always present even if the tests in capillary viscometers show no appreciable deviation from the viscosity laws of Newton and Poiseuille*. Moreover, the approximation of a material by a continuous medium is justified only if the flow patterns of the various structural components of the material appear to coincide in the statistical average of macroscopic observations. In blood rheology, however, there is no such coincidence as in the flow through the blood vessels there is already a macroscopically visible separation of the flow pattern of the serum from that of the red and white cells, and the separation is even more pronounced in the cross currents which carry some blood components through the membranes of the vessel walls and cells into the surrounding tissue.

For future studies of Haemorheology it is suggested that in the discussion of macroscopic behaviour one should replace the scheme of classical mechanics by an improved scheme based on a generalized continuum theory. The laws of this theory are derived from the fundamental principles of Thermodynamics and Mechanics, and provide for every material exact definition of the coexisting elastic and viscous properties. The continuous medium which approximately represents the material will have to be compounded from various coincident continuous media whenever different flow patterns are macroscopically observed for different structural components. The determination of all the properties requires highly elaborate testing instruments which are described together with the theory itself and illustrated in a discussion of the blood rheology *in vivo* and *in vitro*. It is noted that one can now establish a much closer relation than previously between the constitution of the blood and its viscous and elastic properties in flow.

* According to Maxwell's theory one has always to regard viscosity as an elasticity which decays in time.

No. 131

G. W. Scott Blair: *Some aspects of rheological theory as applied to biological systems*

University of Reading, Reading, England

The same rheological principles apply to all systems, whether of biological or of inanimate origin. There can be no rheological "vitalism". Nevertheless, certain aspects of rheological theory are more appropriate and certain branches of mathematics are more useful for some types of system than for others.

This is seen historically in the parallel growths of rheology and of thermodynamics. The first quantitative rheological studies (Hooke) were concerned with the stretching of metal wires and of springs. Under stress, all the energy is retained in potential form as a result, as we now know, of a disturbance of equilibrium between attractive and repulsive forces between the atoms. On release of stress, strain almost completely disappears and energy is conserved with negligible heat losses. Newton's concept of flow virtually introduces the second law of thermodynamics, since applied stress is degraded quantitatively into heat. Cooling a viscometer does not cause the liquid in it to flow backwards!

High-elasticity introduces specifically the concept of entropy, elastic recovery being due to the greater probability of short than of elongated configurations.

So far, we have been concerned essentially with classical thermodynamic considerations.

Living things maintain their precarious existence by absorbing negative entropy and so delay the inevitable rise in entropy which we call death. It seems likely then, that a valuable tool for the study of biorheology will be the new irreversible or non-equilibrium thermodynamics and it is encouraging that some rheologists are specializing in this field.

Another feature of biorheology is that we must expect a different kind of invariance among highly complex systems than that characteristic of simpler rheological materials. Structural materials of biological origin hardly come within the biorheological field, yet we require nine elastic constants (independent components of the fourth rank elasticity tensor) to describe even the linear reversible strain behaviour of wood under small stresses.

In most biorheological studies, we gain little by measuring invariant physical properties such as elastic coefficients in the classical sense. When blood flows through a capillary, even under the simplified conditions of rigid, cylindrical and impermeable tubes, the equation which appears best to fit the relationship between pressure and flow-rate is that of Casson, plotting square-roots of these quantities against one another. "Fundamental physical equations" do not contain square-roots. (As P. A. M. Dirac points out, one reason for supposing that, of the three fundamental physical quantities, c, $\hbar$ and e, it is c and e that will eventually prove to be fundamental and not $\hbar$, is that the latter contains a square-root).

But in complex systems, especially biological materials either *in vivo* or *in vitro*, it is processes rather than properties that must be designated by our characteristic parameters. Thus the Casson slope and intercept represent not static properties of blood but dynamic characteristics of its behaviour as it flows along a tube. If we reverse the direction of flow, we must "start all over again", so to speak: a mere reversal of sign would introduce an imaginary quantity into the flow parameters in one direction but not in the reverse direction.

Biorheologists should, therefore, seek new types of invariants. The tensorial background, invaluable in the study of stress-strain and stress-flow relations in simpler systems, may prove to be quite unsuitable for biorheological analysis.

No. 132

M. JOLY: *Agrégation provoquée par l'écoulement dans les solutions de macromolécules d'origine biologique*

Institut Pasteur, Paris, France

APRÉS avoir rappelé certains faits expérimentaux bien connus qui montrent que l'état de dispersion des suspensions dépend fréquemment de leur état d'écoulement, on précise les relations entre fréquence de collision des particules et durée de vie moyenne des agrégats d'une part, et vitesse de cisaillement des suspensions d'autre part. On définit ainsi pour cette vitesse de cisaillement deux valeurs critiques qui délimitent les domaines des divers types de comportement des suspensions en écoulement. Ces valeurs particulières dépendent des dimensions des particules et de leurs énergies d'interaction. A partir de ces notions une théorie générale de l'agrégation est proposée et les calculs sont développés dans quelques cas simples: particules sphériques et particules ellipsoidales allongées.

Les résultats de cette analyse permettent de prévoir quantitativement le comportement rhéologique et rhéooptique des suspensions et de préciser les conditions dans lesquelles

l'écoulement laminaire d'une suspension peut entrainer des variations très notables de son état de dispersion. On en déduit des méthodes de détermination experimentale du volume moyen des agrégats dans une suspension en écoulement et on montre qu'en contrepartie ces méthodes rhéologiques et rhéooptiques fournissent un procédé relativement commode pour évaluer les énergies d'interaction entre les particules d'une suspension.

On étudie en détail les résultats expérimentaux obtenus avec des solutions de virus de la mosaïque du tabac, de sérum albumine de boeuf et de cheval, native et dénaturée, de protéines musculaires et de quelques autres systèmes protéiques. Cette étude est faite en fonction des concentrations, du pH, de la force ionique et de la nature des ions. On présente surtout deux types de résultats: d'une part les variations du volume moyen des agrégats en fonction de la durée de l'écoulement à vitesse de cisaillement constante, mais pour différentes valeurs de celle-ci, ce qui fait apparaître la diversité des comportements possibles; d'autre part les variations du volume moyen des agrégats en fonction de la vitesse de cisaillement pour des durées d'écoulement suffisantes pour que la distribution des tailles des agrégats ait atteint un état stationnaire. On est conduit á distinguer différents cas selon que l'agrégation provoquée par l'écoulement est plus ou moins réversible en fonction de la vitesse de cisaillement. Un choix convenable des systèmes étudiés et des paramètres de l'écoulement permet d'observer, avec une bonne reproductibilité, toutes les étapes depuis la réversibilité totale de l'agrégation dynamique jusqu'à une précipitation complète et définitive.

La comparaison des courbes expérimentales et des courbes théoriques permet une étude critique de la validité pour les systèmes réels des diverses hypothèses introduites dans les calculs qui, évidemment, sont relatifs à des modeles schématiques.

La discussion des résultats expérimentaux obtenus avec des systèmes artificiels conduit á envisager le rôle de l'écoulement dans l'élaboration des structures dans certains systèmes biologiques naturels, et á s'interroger sur certains aspects de la corrélation mouvement-organisation dans les cellules vivantes.

No. 133

R. L. WHITMORE: *An application of particle/fluid mechanics to blood flow*

University of Nottingham, Nottingham, England

THE observed fall in both the viscosity of blood and the concentration of erythrocytes when the diameter of a glass capillary tube down which the blood is flowing is decreased, has frequently been attributed to the presence of a "plasmatic layer" free of erythrocytes adjacent to the tube wall. It appears to be confirmed by the experiments of SEGRÉ and SILBERBERG [1] and by OLIVER [2] who demonstrated that neutral-density spheres moved away from the wall of a tube down which they were being carried by a fluid. However, BAGNOLD [3] has shown that when a mass of particles is sheared, a dispersive pressure is developed at right angles to the direction of shear and that the dispersive pressure increases with the rate of shear and the particle concentration. A similar pressure must be expected to develop in closely-spaced erythrocytes flowing down a tube and it should be greatest at the walls where the rate of shear is highest.

Although the magnitude of the dispersive force can be calculated for hard spherical particles, no satisfactory theory is available to explain, quantitatively, the inwardly directed force on particles near a tube wall [1]. However from published experimental work on the flow of suspensions of spheres it has been possible to obtain the parameters which indicate the conditions of flow rate and concentration under which a particle of a flowing suspension should leave the tube wall.

On applying the parameters to data on the flow of blood in glass capillaries it can be shown that at normal haematocrits the outwardly-directed dispersive pressure exerted on an erythrocyte at the wall by the flowing blood should be many times greater than the inward force which the red cell can develop, even under the most favorable conditions. Thus the development of a "plasmatic layer" at the wall of a capillary tube down which blood is allowed to flow is unlikely and the layer which is observed *in vivo* must be the product of some other interaction or force.

REFERENCES

[1] SEGRÉ, G. and SILBERBERG, A., *J. Fluid Mech.* **14**, 136, 1962.
[2] OLIVER, D. R., *Nature, Lond.* **194**, 1269, 1962.
[3] BAGNOLD, R. A., *Proc. Roy Soc.* A **225**, 49, 1954.

SYNOPSIS

Discussions were limited to two papers in the session.

Paper 132: M. JOLY: Agrégation provoquée par l'écoulement dans les solutions de macromolécules d'origine biologique.

On a demandé si une étude de l'agrégation provoquée par l'écoulement a été faite avec des cellules ou des globules sanguins?

Le professeur JOLY a répondu que les expériences ont porté uniquement sur des suspensions artificielles de particules submicroscopiques: protéines dénaturées ou virus de la mosaïque du tabac en présence de diverses concentrations salines. D'ailleurs la théorie du phénomène n'a été développée que dans le cas ou les particules constitutives initiales du système sont suffisamment petites pour que l'agitation thermique y joue un rôle important. It est toutefois probable que dans le cas de suspensions de cellules ou de globules on observe des comportements présentant certaines analogies avec ceux que nous avons décrits. Le problème serait néanmoins assez différent car les terms de collision spontanée et de dissociation spontanée sous l'effet de l'agitation thermique seraient nègligeables; il ne subsisterait que ceux relatifs aux collisions provoquées par l'écoulement et aux dissociations provoquées par les forces de cisaillement. Par contre on ne pourrait plus négliger la possibilité de déformation des particules.

La 2ème question: Il a été fait état dans l'exposé de systèmes réversibles; de quelle sort de réversibilité s'agit-il?

La Résponse: Il ne s'agit évidemment pas de la réversibilité au sens thermodynamique stricte du mot. Il s'agit plutôt d'une inversabilité de l'agrégation. Dans certains cas les agrégats qui se sont formés pendant l'écoulement se dissocient spontanément plus ou moins rapidement dès que l'écoulement est arrêté, et cette dissociation est plus ou moins complète selon les systèmes considérés. D'autre part, avec certaines suspensions si l'on fait varier

la vitesse de cisaillement, en la faisant alternativement crôitre et décrôitre, mais suffisamment lentement, on observe un renversement de la variation de la grosseur des agrégats, avec une hystérèse plus ou moins grande selon la rapidité de variation de la vitesse de cisaillement. Cette hystérèse correspond au temps nécessaire pour que l'état stationnaire du processus association-dissociation soit atteint.
La 3ème question: De quelle nature sont les énergies impliquées dans les agrégats considérés?
La Résponse: Il s'agit exclusivement des énergies dues aux forces électrostatiques et aux forces de cohésion de van de Waals. Dans le cas des protéines dénaturées, il a été montré que des liaisons hydrogène pouvaient occasionnellement intervenir.

Paper 133: R. L. WHITMORE: An application of particle/fluid mechanics to blood flow.

Dr. S. ROWLANDS asked whether one could allow for the possible effects of blood cell flexibility in the theory and the reply was that at present this was not possible because information regarding the effect of cell flexibility on the forces present was not available, even for single cells, and the theory was developed for concentrations where interference between cells could also be expected.

Professor SEGRÉ noted that reference was made in the paper to the tubular pinch effect which Dr. SILBERBERG and he had shown to be present in dilute suspensions of rigid neutrally-buoyant spheres and recommended that the greatest care should be taken in translating their results to the case of blood flow.

Dr. GOLDSMITH commented on the possible effect of particle shape on the transverse forces experienced by a body moving down a tube and the author readily agreed that more information on this problem was required. It did not, however, alter the basic point that as the concentration of bodies moving down a tube increased, an outwardly-directed dispersive force must almost certainly develop although at the moment it was extremely difficult to estimate its magnitude.

SESSION I (X6)

Tuesday, 27 August 1963

Laminar Flow of Biological Fluids

Chairmen: Professor K. WEISSENBERG. The Royal Institution, London, England
Professor A. M. FREUDENTHAL, Columbia University, New York, U.S.A.

No. 134

H. L. GOLDSMITH and S. G. MASON: *Physical aspects of the flow of biological suspensions through vessels*

McGill University and Pulp and Paper Research Institute of Canada, Montreal, Canada

AN investigation of the flow behaviour of suspensions of model rigid and deformable particles is described. The experiments refer to steady, laminar flow in rigid straight tube at low Reynolds number for particles which are (i) small, and (ii) large compared to the tube width. Individual particle motions and their interactions in suspensions from 0 to 40 per cent by volume were investigated.

Single small rigid spheres flowing in large tubes rotated with steady angular velocity; rigid discs and rods with variable angular velocity without the particles migrating axially. However, single small liquid drops which were deformed into prolate spheroids during flow migrated towards the tube axis at a rate determined, in a given system, by the extent of deformation and the variation in the velocity gradient across the ends of the drops. Two body collisions between small rigid spheres were symmetrical. Those between liquid drops were unsymmetrical, thus causing radial displacements of both colliding particles. At concentrations above 20 per cent by volume, the measured velocity profiles in flowing suspensions of rigid spheres became blunted, the velocity gradient near the wall being greater and that near the tube center smaller than that calculated from Poiseuille flow. The distribution of spheres across the tube was uniform.

The flow and deformation of large liquid bubbles suspended in wetting liquids flowing through small tubes were studied. It was shown that the bubbles travelled axi-symmetrically through the tube surrounded by a film of liquid of constant thickness between the bubble ends. The thickness of the film and the velocity profiles in bubble and film were measured as a function of tube radius, bubble velocity and the ratio of bubble to suspending liquid viscosity. The existence of vortex patterns in the liquid between the ends of a series of flowing bubbles was demonstrated.

The relevance of the findings to the flow of blood and other systems is discussed.

No. 135

S. OKA: *Theoretical considerations on the flow of blood in a capillary*

Tokyo Metropolitan University, Tokyo, Japan

SCOTT BLAIR (G. W. SCOTT BLAIR, *Nature, Lond.* **183**, 613, 1959) has shown that an equation proposed by Casson for varnishes and which was later applied by Steiner to molten chocolate, gives excellent straight lines for bovine, rabbit and human blood, on both glass and fibrin surfaces. Following this equation, straight lines are obtained when the square root of the shear rate is plotted against the square root of the shear stress. On the assumption that Casson's equation is applicable to blood, we treated theoretically the rheological behaviour of blood flowing in a capillary. We have obtained both the velocity distribution across the capillary and the volume of flow in unit time as a function of pressure difference. The result was compared with the rheological behaviour of a Bingham system and other non-Newtonian systems.

As is well known, Poiseuille demonstrated microscopically that the axial stream of red cells in capillary blood vessels was separated from the wall of the vessel by a plasmatic zone. Similar observations have been made on various non-biological suspensions by many workers, and axial accumulation of suspended particles with a formation of a particle-free zone is a phenomenon characteristic of certain types of suspensions under shear. From observations of injected graphite particles and of blood platelets in plasma-skimmed vessels, COPLEY and STAPLE demonstrated a component of force normal to the direction of flow acting on suspended particles when blood flows (A. L. COPLEY and P. H. STAPLE, *Biorheology* **1**, 3, 1962). Although various theories of the axial drift have been reported in the literature, the mechanism of axial drift has not yet been well established from the physical point of view. The theories may be roughly classified into hydrodynamical and thermodynamical ones. According to the theory of fluid mechanics, the lift experienced by a particle in a viscous flow depends on various factors—the type of flow, the shape of the particle, the boundary surface, the approximation of calculations and whether the particle is rigid or deformable—and it is difficult to draw a simple conclusion. Since these results are scarcely known except by specialists of fluid mechanics, we will put the results in order and further state our opinion about them. This will be useful for the physical interpretation of the mechanism of axial drift of red cells in a capillary. According to the principle of minimum dissipation of energy in an irreversible process, a particle initially situated at a point in a velocity field at which the gradient is not zero is expected to move with a velocity component normal to the direction of flow toward the region of lower velocity gradient. The validity of the above-mentioned principle will be discussed.

In the study of the flow of blood in a capillary, mutual interaction of the red cells must be taken into account, since the relative cell volume of blood is as large as approximately 0·4. The mutual interaction of the particles has been discussed quantitatively for an ideal case from the standpoint of fluid mechanics. The result may prove useful for studying the phenomenon of sedimentation of red blood cells.

No. 136

G. SEGRÉ: *Necklace-like formations in the Poiseuille flow of a suspension of spheres*

Cartiera Vita Mayer & Co., Milan, Italy

WHEN a dilute suspension of rigid spherical particles is carried along a tube in laminar flow, rearrangements of the particles are observed to take place. In addition to the previously described tendency of the particles to shift radially towards a position at about two thirds of the tube radius, ("tubular pinch effect"), one observes that, at non-vanishing concentrations, neighboring particles interact and tend to form regular linear groups ("necklaces"). These necklaces consist of equally spaced particles, aligned in the direction of motion, of a rather stable configuration.

Our observations have been made with neutrally buoyant spheres of uniform diameter ($2r = 0{\cdot}8$–$1{\cdot}7$mm for the different fractions employed), in concentrations of $0{\cdot}5 \sim 2$ particles per cc of liquid, the suspensions being made to flow in a tube 150 cm long. Two tube diameters have been used, $2R = 11{\cdot}2$ mm and $8{\cdot}5$ mm respectively. By changing the viscosity of the liquid and its flow velocity, a range of tube Reynolds numbers from 30 to 600 has been obtained. Stereoscopic photography has been employed to detect and to analyse the necklaces in detail.

The equilibrium distance d between the particles, for a system and given flow conditions, decreases regularly as one passes from groups of 2 to 3 and 4 particles, probably reaching a constant value for the longer groups. It is strongly correlated with the Reynolds number, decreasing from $d/R \simeq 1$ to $d/R \simeq 0{\cdot}5$ as the Re value increases from 100 to 600. On the other hand dependence of the equilibrium distance on the particles' dimensions is weak, a change by a factor 2 in their diameter giving an increase of only 20 per cent for d.

The observations permit also of a statistical study of the necklaces' formation, and of a qualitative description of the dynamics of the phenomenon.

The average number of particles in the groups obviously increases with increasing concentration, as well as with increasing distance from the tube mouth. The number of necklaces increases initially with increasing Reynolds number, reaches a maximum and then decreases, certainly because incipient turbulence tends to hinder their formation.

There is the evidence that air bubbles also, carried in Poiseuille flow, tend to form similar regular groups along the axis of the tube.

No. 137

A. SILBERBERG: *Hydrodynamic interaction between particles in suspension*

Weizmann Institute of Science, Rehovot, Israel

INFORMATION about particles suspended in a viscous liquid is often derived from a study of the overall visco-elastic behaviour of the suspension. The interpretation of the results in terms of particle shape and size, orientation and aggregation depends on a knowledge of the solution of the Navier-Stokes equations of flow under the boundary conditions imposed. An exact solution of the problem is in general prohibitively difficult, but with the aid of approximations, both to the boundary conditions and to the differential equations themselves, models can be proposed and calculated which have in part been very successful in interpreting observations.

In most of these cases the solutions were approximated by replacing the particles with point centres of disturbance and by regarding the general flow pattern to arise from a linear superposition of the solutions for each of these centres acting alone. The flow pattern resulting from such an isolated centre of disturbance is approximated by the so called Oseen tensor.

It will be pointed out that this tensor is equivalent to the first term of Stokes' solution of the simplified Navier-Stokes equation for creeping motion of a rigid sphere of finite radius. It corresponds to the Stokes solution in cases where the radius of the sphere is vanishingly small. In regions close to the rigid particle whose motion causes the disturbance the Oseen tensor is thus only an approximation. Use of the Oseen tensor in these regions constitutes the replacement of the good Stokes approximation to the solution of the full differential equation by a poorer one. At points far from the sphere, the Stokes solution and the Oseen tensor become identical. In those regions, however, use of the Stokes solution is associated with serious deviations from the exact solution even in cases where the Reynolds number is small.

In past discussions of the behaviour of suspensions use has been made of the Oseen tensor at points both close to and far from the suspended particles. An analysis of the conditions under which the approximations, thus introduced, can be justified has thus been undertaken.

Some of the points which arise will be discussed with particular reference to suspensions of spheres and randomly coiled linear macromolecules. Considered will be the inter-action of particles, one with another, and the interaction of particles and suspending medium with the walls.

No. 138

E. A. Fox and E. Saibel: *A formulation of the problem of flow through tubes.*

Rensselaer Polytechnic Institute, Troy, U.S.A.

The study of the flow of blood in the circulatory system requires a re-examination of the mechanics of tube flow problems. The usual formulations in the past have been unnecessarily restricted and difficulties have arisen which are due solely to these restrictions. In the present formulation the authors consider a finite length of tube enclosing any fluid continuum. The tube may be deformable in any manner. The flow may be time dependent, laminar or turbulent, but not cavitating. Basically the treatment is general and not restricted to axial symmetry. Later however for mathematical simplicity it may be so restricted· In its finite form the results are suitable for digital calculation, but, if so desired, by passing to the limit the differential equation of flow is obtained.

No. 139

G. R. Cokelet, W. Margetts, E. W. Merrill and E. R. Gilliland: *The Casson equation and rheology of blood near zero shear*

Massachusetts Institute of Technology, Cambridge, U.S.A.

As a continuation of previous studies, (Cokelet *et al. Trans. Soc. Rheology* 7) this paper is concerned with assessing the relevance to blood rheology of the model upon which N.

CASSON (Chap. 5 in *Rheology of Disperse Systems*, C. C. MILL (Editor) Pergamon, New York, 1959) derived the equation:

$$\tau^{\frac{1}{2}} = S\dot{\gamma}^{\frac{1}{2}} + b,$$

where
$S = [\eta_0/(1 - c)^{a\alpha - 1}]^{\frac{1}{2}}$,
$b = [(a\beta)/(a\alpha - 1)]\,[(1 - c)^{1 - a\alpha/2} - 1]$,
τ = shear stress; γ = shear rate; η_0 = viscosity of suspending medium,
c = volume fraction of dispersed particles,
a = factor depending on average orientation of aggregate,
α, β = constants.

On the one hand the *form* of the equation serves well in correlating the low shear rate data on blood near and at zero shear. On the other hand the model on which the equation is based does not allow for attraction between ,or three dimensional structural organization of, the rod-like aggregates (rouleaux). Thus it is impossible to obtain unequivocal values of the face-to-face and edge-to-edge attractive forces between red cells. Alternative models are proposed, based on recent studies.

SYNOPSIS

GOLDSMITH and MASON presented some excellent film material on the behaviour of single particles and concentrated suspensions flowing through cylindrical vessels. They discussed the relevance of these findings to the flow of blood.

OKA presented some theoretical considerations of the flow of blood when its bulk properties can be expressed by the Casson equation, and when a finite plasma layer exists at the wall.

SEGRÉ described his observations of fascinating stable necklace-like formations of particles in a suspension flowing through a tube.

Unfortunately, there was hardly any discussion on these three papers, and an opportunity was lost for an obviously interested audience to pursue some implications of very intriguing results.

SILBERBERG presented some theoretical considerations of the intrinsic viscosity-concentration relationship for a suspension, and in particular he considered the effects of the particle interactions. Considerable discussion centred around the magnitude of the coefficient of the quadratic term in the expanded series for this relationship, and both WAYLAND and OLIVER could refer to their own precise results which gave a value for this coefficient close to the theoretical value mentioned by SILBERBERG.

SAIBEL and FOX presented a very generalised formulation of the problem of flow through tubes, which allowed considerable flexibility in formulating both the properties of the fluid and the boundary condition at the wall. The paper was too theoretical and general to be appreciated by most of the audience, but one or two members commented favourably on the approach adopted by the authors.

MARGETTS *et al.* discussed the applicability of the Casson equation to the rheology of blood near zero shear stress. Whilst the equation is found empirically useful, they now consider the theoretical basis to be unsound, at least for blood. During a short lively discussion, MARGETTS reviewed the main factors which contribute to the yield stress of red cell suspensions.

SESSION II (X7)

Tuesday, 27 August, 1963

Cytoplasmic Streaming. Hemolysis. Sap Movement

Chairmen: Professor N. KAMIYA, Osaka University, Osaka, Japan and Princeton University, Princeton, U.S.A.

Professor D. DANON, Weizmann Institute of Science, Rehovot, Israel and Columbia University, New York, U.S.A.

No. 140

S. ABE: *The visco-elasticity of slime mold protoplasm*

Osaka University, Osaka, Japan

SINCE the plasmodium of the slime mold grows as an enormous mass of naked protoplasm, it is considered to be one of the most suitable materials for the study of rheological properties of living protoplasm. The plasmodium forms smooth strands which sometimes amount to 900 μ in diameter under favourable conditions. In the present studies plasmodial strands of *Physarum polycephalum* 500–750 μ in diameter and 4–20 mm in length were used.

Visco-elasticity of the plasmodial strands was investigated by applying certain torques around the longitudinal axes of the strands. This method was adopted because torsion around the longitudinal axis of a cylinder brings about far less change both in its length and in diameter than longitudinal tension.

(1) By analysing a damped oscillation shown by the plasmodial strands, viscosity and elasticity of the protoplasm were estimated independently of each other.

(2) On the basis of creep and recovery of the plasmodial strands, it was found that rheological behaviour of the slime mold protoplasm can be well represented in terms of a four-element model.

(3) When a torque was repeatedly applied on a plasmodial strand at short intervals, it was observed that the strain corresponding to each torque increased successively. This fact indicates that the slime mold protoplasm is thixotropic in nature.

No. 141

N. KAMIYA and K. KURODA: *Rotational protoplasmic streaming in* Nitella *and some physical properties of the endoplasm*

Osaka University, Osaka, Japan and Princeton University, Princeton, U.S.A.

WHAT is usually called rotational streaming designates that kind of motion where the cytoplasm in a band-like form goes around close to the wall of a cell, the central space being occupied with a large vacuole. A crucial point in the mechanism of this motion is the location of the seat of the motive force responsible for the streaming.

By an operation combining centrifugation and subsequent ligation of an internodal cell of *Nitella*, it is possible to make artificially a cell fragment the whole interior of which is filled with protoplasm without visible vacuoles. Even in such a cell fragment rather vigorous streaming takes place. An important fact revealed by such streaming is that the rate of streaming is highest in the outermost layer of the endoplasmic sol, i.e., at the contact area of the endoplasm with cortical gel layer. The velocity profile of the endoplasmic flow in this case shows that a parallel displacement force is generated at the boundary between the endoplasm and the cortical gel layer in such a way that the outer edge of the endoplasm tends to be shifted along the inner surface of the cortical gel layer in one direction on one longitudinal half of the cell and to the opposite direction on the other half. This active shearing force, the nature of which is still unknown, is responsible for the rotational streaming.

Endoplasmic drops isolated from the *Nitella* cell by means of a suitable technique developed by ourselves survive for a couple of days in an artificial solution *in vitro*. They serve as a favorable object for the study of physical properties of the living cytoplasm.

Through the analysis of the profile of the naked drop, and by measuring the densities of the drop and the external medium, it was found that the tension at the surface of the naked endoplasm is usually as low as 0·002–0·004 dyn/cm.

Since the naked endoplasmic drops can be introduced in a capillary without giving rise to any observable ill effect, they provide unique opportunities to characterise rheological properties of the living cytoplasmic sol.

No. 142

R. D. ALLEN: *Rheological properties of slime mold endoplasm*

Princeton University, Princeton, U.S.A.

BEFORE the advent of the electron microscope, biologists interested in the general problem of cytoplasmic structure often resorted to centrifugation, quantitative analysis of Brownian motion and other procedures to measure "protoplasmic viscosity". While the techniques for studying the rheological properties of cytoplasm have not improved very much in recent years, modern rheology has made biologists aware that a great deal more information than "apparent viscosity" it required to characterize the rheological properties of cytoplasm. Early studies of "protoplasmic viscosity" were misleading in two important respects (cf. Allen, 1960). First, the internal shearing forces in cells were greatly underestimated, so that some of the very low apparent viscosities measured were for shearing forces at which cytoplasmic structure had been destroyed, and second, cells subject to centrifugation or to compression for some Brownian motion studies were not in a normal state when studied.

Plasmodia of the acellular slime mold, *Physarum polycephalum*, contain cytoplasma in at least two states: gelated channel wall material, which was the subject of Dr. Abé's paper. and more fluid endoplasmic material which streams back and forth with a characteristic periodicity. In some recent, incomplete experiments done in collaboration with Stephen Cox and Jonathan Belcher, an attempt has been made to determine some of the rheological properties of the endoplasm *in vivo*, under as normal conditions as possible. Iron spheres

3–8 in. dia. were injected into plasmodial blobs in a Kamiya double-chamber mounted on the rotating stage of a horizontal microscope. After resumption of normal streaming, some of the iron spheres were seen to pass along the channel connecting the blobs. When a suitable sphere appeared in view, a balance pressure was applied to one of the chambers and changed continuously so that the cytoplasm was prevented from streaming and the spheres kept in view. By rotating the stage, spheres of various sizes could be made to fall either across the endoplasmic stream or parallel to its axis at any point along the diameter in such a way that their displacements were recorded cinematographically.

It was invariably found that the iron spheres slowed down to 50–80 per cent of their initial velocity when they reached approximately the central third of the channel. In the axial region of the endoplasm, the fall was discontinuous (or "bumpy") as though interrupted by obstacles. After passing through this region, the spheres again fell more rapidly. The same regional difference in resistance to fall was found when the spheres fell parallel to the axis of the channel. The variability in velocities in orthogonal directions, and variability in the apparent viscosities calculated from Stokes' law for data on spheres of different diameters was such that it was not possible to establish a force-flow curve or determine whether the endoplasm was structurally anisotropic. Apparent viscosity values (calculated from Stokes' law with suitable corrections for channel dimensions) ranged from 0·2 to 1·5 P, with very great variability between serial determinations. It was quite clear from these simple observations that streaming endoplasm of *Physarum* could in no way be considered to be a "watery" fluid, but rather a complex fluid in a highly unstable state and partially structured. Present rheological techniques which can be applied *in vivo* do not offer much hope of further analysing this structure.

In a separate study to be reported elsewhere, Dr. Hiromichi Nakajima and I have examined slime mold plasmodia in polarized light. The ectoplasm contains positively birefringent fibrillar structures similar to those demonstrated electron microscopically by Wohlfarth-Bottermann, as well as diffuse birefringence due to unresolved structures. An unexpected finding, however, was a negative birefringence in the endoplasm which remains whether or not streaming is taking place. This finding emphasizes the dilemma that while the ground cytoplasm is sufficiently structured to be birefringent even during cytoplasmic streaming, the birefringence observed is not the immediate result of flow, as is the flow birefringence of solutions.

No. 143

E. W. TAYLOR: *Brownian motion and saltatory movements of cytoplasmic granules*

University of Chicago, Chicago, U.S.A.

THE cytoplasm of many cell types contains granules one to a few microns in diameter which may be expected to show Brownian movement. A number of authors have examined granule movements as a means of estimating cytoplasmic viscosity. (J. PEKAREK, *Protoplasma*, **10**, 510, 1930). It must be recognized that cytoplasm shows non-Newtonian behaviour so that the viscosity obtained from Brownian movement may apply only to motions at very low shear gradients. Nevertheless an estimate of the viscosity is important for considerations of the energy requirements for the slow movement of chromosomes during mitosis.

A study was made of the movements of granules in fibroblast cells of the newt (*Triturus viridescens*). Measurements were made on time lapse films of interphase and mitotic cells and the viscosity was obtained by the "first passage time" method (R. FURTH, *Ann. Phys.* **53**, 177, 1917). The reliability of this method for viscous solutions was evaluated by determining the viscosity of glycerol–water mixtures containing a low concentration of mastic particles. The error did not exceed 30 per cent for viscosities up to 300 cP.

The values obtained for about 25 cells were in the range from 100 to 1000 cP with an average value of about 300 cP. There were no striking changes for the various stages of mitosis although the average viscosity decreased about 30 per cent from metaphase to anaphase.

In the collection of the experimental data it was noted that occasionally a particle executed a very long jump, as large as 6 μ. The probability of such jumps occurring by Brownian movement, in a medium of viscosity at least 100 cP, was far too small to account for the frequency of their occurrence. This type of movement has been described by REHBUN (L. I. REHBUN, *Ann. N.Y. Acad. Sci.*, **90**, 357, 1960) and named saltatory movement.

The mechanism of saltatory movement is obscure. A number of hypotheses will be discussed: (1) Particles move in viscosity "holes". (2) Particles are self propelled. (3) Particles are attached to contractile elements of the cytoplasm.

No. 144

J. A. KOCHEN: *Flow properties of hemoglobin in the hemolysing red cell*

Albert Einstein College of Medicine, New York, U.S.A.

A CLEAR understanding of the nature of red blood cell lysis has been limited by the virtual disappearance from view of the red cell and its contents during hemolysis.

The present study was undertaken to determine whether the flow of hemoglobin from the lysing red cell could be visualized by the precipitation and fixation of the emerging intracellular material.

Alizarin red S, an anionic dye with the capacity to form insoluble dye-protein complexes was selected as the preciptitating agent. Under appropriate isotonic conditions this dye did not itself cause lysis or appreciable alteration of the osmotic fragility or morphologic appearance of red cells. However, when red cells were exposed to conditions known to produce hemolysis, the presence of this reagent resulted in the precipitation and fixation of the emerging intracellular material in the regions of membrane breakdown.

Hypotonic hemolysis under these conditions, was found to be associated with the appearance of a single discrete stream of escaping hemoglobin in each lysing red cell. This stream emerged with sufficient force to propel the lysing red cell in the reverse direction. Similar propulsive movements have also been noted in red cells undergoing hypotonic lysis in the absence of precipitating agents.

The flow rate of the emerging stream of hemoglobin was determined by microcinematography and related to the apparent size of the membrane defect. These findings permitted the derivation of the diffusion coefficient of hemoglobin in individual cells undergoing hemolysis. This value was found to correspond to the previously reported diffusion coefficient of hemoglobin solutions in the concentration range of 25 per cent or less.

This is consistent with the finding that red cells under hypotonic conditions swell to about 170 per cent of their original volume before undergoing lysis. This may be expected to result in a corresponding dilution of the intracellular hemoglobin from a concentration in the 32 per cent range to a concentration of less than 25 per cent.

These studies indicate that the influx of water which precedes hypotonic red cell lysis results in swelling of the cell and a corresponding dilution of its hemoglobin content. The increase in red cell volume is presumably accompanied by the development of stresses in the cell membrane, which lead to the formation of a single localized region of membrane breakdown. It is through this single region of membrane breakdown, and across the resulting concentration gradient, that the outward flow of hemoglobin occurs by a process of passive diffusion.

No. 145

M. H. ZIMMERMANN: *Sap movements in trees*

Harvard University, Petersham, U.S.A.

THE most spectacular movements of liquids found anywhere in the animal or plant kingdom are sap movements in trees and lianas. Water and mineral nutrients are taken up by the roots and ascend via xylem (the wood) into the leaves, where most of the water is lost by transpiration. Transpiration from leaves pulls up the water; movement is presumably along a gradient of negative pressures (tensions). The conductive tissues are uniquely adapted to negative pressures. They contain rigid tubes which acquire a strong cellulose and lignin reinforced wall during growth. These cells die before they become functional. The whole water-conduction tissue is continuous throughout the plant, rapid movement takes place through xylem tubes, slow movement through walls of all the cells, even living ones. The transpiration stream is very low in concentration, it usually contains less than 0·5 per cent solutes. However, the rapid rate of movement (up to around 40 m/hr), and loss of water by transpiration from leaves, carry sufficient quantities of mineral nutrients into the leaves.

Most of the plant material is made of carbohydrates which are formed in green parts (leaves) by photosynthesis. Growth of branches, stem and roots can only take place if building materials (photosynthetic products) are translocated from leaves downward. This type of long-distance movement is quite different from the one described above. It takes place in the phloem (the inner bark); the conducting channels are living but enucleate cells. Velocities of translocation are slower (ca. 1 m/hr), the concentration of the moving solution is higher (10–20 per cent, mostly sugars), and the pressures are positive. During recent years entomologists have developed an effective new method for sampling this descending nutrient stream of plants. Aphids, feeding on these channels, are anaesthetized and cut from their mouth parts. The high pressure within the phloem keeps exudation from the mouth parts going for many days, and the exudate can be collected from the stylet stump for analysis.

SYNOPSIS

Dr. S. ABE. (No. 140)

Dr. R. D. HARKNESS: Under the conditions of the present study, could you exclude a possibility that the characteristics of visco-elasticity are due only to the external layer of the slime mold? Did you study the properties of the internal protoplasm?
Dr. S. ABE: We can not estimate, at this stage of the study, what is the contribution of the external and internal plasma respectively.
Dr. D. DANON: Did you try to carry out your measurements at different ionic strengths and/or at different pH in the medium surrounding the slime mold?
Dr. ABE: These studies have not yet been performed but they are planned for the future.

Drs. N. KAMIYA and K. KURODA. (No. 141)

Drs. Kamiya's and Kuroda's experimental system provides a potent tool for further studies of this kind, especially in connection with the possibilities of micro-cinematography that have been so beautifully demonstrated.

Dr. R. D. ALLEN. (No. 142)

Dr. Allen took the trouble to analyse in his introduction the theoretical as well as the experimental difficulties in the study of the rheological properties of endoplasm. After the presentation of his own experiments and results, he ended his lecture by asking for suggestions to improve the studies under discussion.
Dr. DANON: Since you have demonstrated the possibility of inserting iron balls into the endoplasm of the slime mold while maintaining it alive, and then determining the viscosity by measuring the rate of dropping of the iron balls through the endoplasm, I would suggest the use of the viscoelastometer of Dr. Behar and Dr. Frei from the Weizmann Institute, for measurement of the viscoelasticity of the endoplasm. In their system a pulse of horizontal magnetic field is applied which displaces the iron ball from its initial line of dropping in the material under study. If no elastic component exists the ball would continue dropping vertically from its new position. If there is an elastic component the ball will undergo a certain recoil, after the magnetic field is stopped, while continuing its drop. The rate of dropping and the amount of recoil can be recorded.
Dr. ALLEN: Thank you for your suggestion, it seems simple and we may try it. As a matter of fact Dr. Kamiya has already suggested the use of electro-magnetic fields perpendicular to each other and alternately activated in order to displace the iron balls inside the cytoplasm, for the measurement of visco-elasticity.

E. W. TAYLOR. (No. 143)

Dr. TAYLOR presented cinematographic illustrations of intracellular Brownian and saltatory movements. In discussing three hypothesis for the mechanism of saltatory movements, he conveyed the impression that not a single one is completely satisfactory..

Dr. J. A. KOCHEN: (No. 144)

Prof. H. HARDERS: The jerky movement of the erythrocytes hemolysed with distilled water, as we have seen in the micro-cinematographic presentation of Dr. Kochen, was obvious.

It seems that in this kind of shock lysis a single relatively large opeining occurs in one point of the cell membrane through which the hemoglobin is released. The demonstration with the Alizarin red S, although under different conditions of pH, demonstrates again the single opening in shock lysis.

I have recently seen a cinematographic film made by Dr. Danon in which osmotic hemolysis was achieved by gradual decrease of the salt concentration of the medium surrounding the erythrocytes. The cells changed gradually from bi-discoids to spheres and then faded out without any jerky movement. Have you tried the method of gradual hemolysis in the presence of Alizarin red S? I would expect that the single tail at one point will not be seen there.

Dr. KOCHEN: We did not try the gradual hemolysis method in the presence of Alizarin red S. However the saponin hemolysis usually gives an image similar to that received by the shock lysis, but when saponin hemolysis is carried out very slowly by the right dilution of saponin, instead of a single "tail" of precipitate of Alizarin with hemoglobin, numerous "buds" appear all over the surface of the cell membrane. I agree with Dr. Harders that a similar picture would be expected when hemolysis will be carried out by Danon's method in which the rate of increasing pressure inside the cell is lower that that of shock lysis.

Dr. DANON: The cinematographic presentation we have seen to day without the Alizarin red is probably the same kind of observation that Comandon and De Fonbrune have reported in 1929 and that has been much disputed since. The use of Alizarin red by Dr. Kochen provides additional argument in favor of the concept that in shock lysis a single opening occurs in the membrane through which the hemoglobin rushes out.

SESSION IIIA (X8)

Tuesday, 27 August, 1963

Hemorheology of Pulsatile Flow

Chairmen: Dr. R. L. WHITMORE, University of Nottingham, Nottingham, England
Professor H. HARDERS, University of Hamburg, Hamburg, Germany

No. 146

D. A. McDONALD: *The flow properties of blood as a factor in the stability of pulsatile flow*

The Medical College of St. Bartholemew's Hospital, London, England

THE topic discussed here will cover, briefly, some aspects of the problem of "turbulence" in the mammalian vascular system. This is, at present, highly speculative but I present it in the hope that it may form a closer link between rheologists and those who are studying pulsatile flow behaviour mainly from hydrodynamic principles.

Some aspects of the problem were touched on in my contribution to the discussion on the "*Flow properties of blood*" of 1959 [1]. COULTER and PAPPENHEIMER [2] made a stimulating contribution to this work by studying the critical Reynolds' number (Re) for blood in steady flow. The pipe was 2·5 mm in diameter, and pressure-flow studies gave an "orthodox" critical Re of 1,960 + 160. On the other hand, they could find no corresponding change in the longitudinal electrical resistance. This they interpreted as continuing stability of the red cell orientation ("floating like a log in a stream"). Other experimental evidence has been reviewed [3].

TAYLOR [4] made an important theoretical contribution by showing that the assumption that blood is a Newtonian fluid would only lead to an error of a few per cent in the pressure-flow equations for oscillatory flow if the "asymptotic" viscosity (i.e. at high rates of shear) in a tube of the same size were used. WOMERSLEY [5] also made some (unpublished) calculations of the steady flow paraboloid of blood assuming various forms of change of the viscosity with radial distance from the wall. While this "blunts" the axial region of the profile, the reduced viscosity near the wall increases the maximum rate of shear.

Applying these concepts to the profiles of oscillatory flow we find in the larger vessels that the region of marked rates of shear is virtually confined to the boundary zone. The size of the "plasmatic zone" would thus be of great importance if the development of instability was determined by the maximal rate of shear. On the other hand, there is evidence that instabilities originate at points of inflexion in the profile. As these occur closer to the axis than the region of highest shear, the presence of "packing of cells' would tend to diminish these inflexions and hence increase stability.

Recent work discussed at a Symposium on pulsatile flow in Philadelphia [6] has shown that pressure, at least, shows a persistence of pulsation into vessels of arteriolar dimensions that is much more marked than was previously thought. These are vessels where the effects of the anomalous viscosity of blood are very much more marked than in the larger arteries

and veins. Previously, flow in such small vessels has always been considered to be laminar but this work suggests that it should be looked into again. Also no-one has really followed up an interesting suggestion by TAYLOR [7] that in very small vessels the rotation of the red cells themselves could be considered as distorting the conditions of laminar flow.

On balance the fact that the effect of the axial accumulation of cells is confined to a narrow zone near the wall suggests that the structure of the blood is one of the lesser factors among the many that are to be considered in determining the stability; but this conclusion is certainly uncertain enough to warrant further thought—and investigation.

REFERENCES

[1] *Flow Properties of Blood and other Biological Systems*, COPLEY, A. L. and STAINSBY, G. (editors), Pergamon, London, 1960.
[2] COULTER, N. A. and PAPPENHEIMER, J. R., *Amer. J. Physiol.* **159**, 401, 1949.
[3] MCDONALD, D. A. *Blood Flow in Arteries*, Arnold, London: Williams and Wilkins, Baltimore, 1960.
[4] TAYLOR, M. G., *Phys. Med. Biol.* **3**, 273, 1959.
[5] WOMERSLEY, J. R., *J. Physiol.* **127**, 38P, 1955.
[6] *Symposium on Pulsatile Flow*, ATTINGER, E. O. (Editor), McGraw Hill, New York (in press).
[7] TAYLOR, M. G., *Austral. J. Exptl. Biol. Med. Sci.* **33**, 1, 1955.

No. 149

A. H. SACKS: *A study of auscultatory blood pressures in simulated arteries*

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A LARGE-SCALE pulsating flow system has been constructed and various simulated arteries of 1 in. inside dia. have been tested under varying conditions of pulse rate, pressure level, and pulse pressure using, first, various mixtures of water and glycerol and, finally, whole steer blood as the fluid. The oscillatory intra-arterial pressures were recorded by pressure transducers which were attached to both static and total pressure probes in the flow itself, and these are compared with measurements of the systolic and diastolic pressures which were obtained by the clinical auscultatory technique, using a stethoscope and a specially designed pressure chamber. In addition, simultaneous measurements were made of arterial wall displacements and the velocity of the pulse wave along the tube. The simulated system has exhibited many of the qualitative features of a living human subject. The entire spectrum of characteristic Korotkoff sounds was produced in the artery, and changes in quality and intensity ordinarily associated with such clinical conditions as aortic insufficiency and hypertension were produced in the laboratory by changes in arterial wall and flow conditions. The phenomenon known as the "auscultatory gap" was observed at very high pulse rates and/or high mean pressure levels.

The test results indicate that the systolic pressure as determined with a sphygmomanometer is consistently higher than the peak intra-arterial pressure by an amount which depends on the stiffness and thickness of the arterial wall. The auscultatory diastolic pressure reading, however, may be either higher or lower than the minimum intra-arterial pressure, depending primarily on the pulse rate. This result is independent of whether the fourth or fifth phase of the Korotkoff sounds is used as an indication of diastolic pressure. The auscultatory readings with whole steer blood are in agreement with those

using water and glycerol for the same conditions. Measured arterial wall displacements and wave velocities are in approximate agreement with theory except during transient changes in mean pressure level.

No. 147

W. G. FRASHER, JR., J. H. WAYLAND and S. S. SOBIN: *Visco-elastic behaviour of the main pulmonary artery segment*

Loma Linda University, Los Angeles and California Institute of Technology, Pasadena, U.S.A.

THE main pulmonary artery segment has been studied in dogs maintained by extracorporeal perfusion and with circulation to the segment wall intact. Segment preparation resulted in a closed sac whose proximal end was attached to a rigid delivery tube. Initial contained volume was measured at a fixed reference pressure. Pressures generated in the specimen in response to known volume inputs were recorded both statically and with sinusoidal oscillations in the normal heart rate frequency (40–180 count/min). The complex geometry of the interior of the specimen at varying levels of distention was preserved by preparing casts using known volumes of a silicone elastomer.

Results in 47 experiments may be summarized as follows:

1. At steady state, in the normal frequency and pressure range, pressure volume response is linear.

2. From the unstressed state a viscous component results in a decrement of pressure from the initial input toward an asymptotic value at the steady state. The viscous term is a function of time in quasi-static loading and a function of the number of loadings in the dynamic state.

3. Pressure-volume responses measured directly differ from computed values derived from other dimensional changes. The most likely explanation is the unique geometry of the segment which can be described as progressing from an ellipsoidal towards a spherical configuration.

No. 148

S. E. CHARM, W. MCCOMIS and G. KURLAND: *Dimensional analysis of pulsating blood flow*

Massachusetts Institute of Technology, Cambridge, U.S.A.

PULSATIONS occur in arteries, arterioles and perhaps even capillaries. A theoretical analysis of the flow shows that unless a number of assumptions are made, the resulting differential equations describing the flow are unsolvable. The assumptions normally made are:

(1) The flow is laminar.

(2) The flow is through a cylinder of constant diameter.

(3) The blood is a homogeneous fluid without anomalous viscous properties.

(4) There is no "slip" at the wall.

The validity of the first assumption is questionable in large arteries but is generally

accepted as adequate in smaller vessels. In order to clarify assumption number two, further study is needed on the effects of tube taper and elasticity on the energy losses occurring in blood flow.

Assumptions three and four have been found quite inadequate in calculating steady flow. Although it has been shown from theoretical considerations that these assumptions are probably justified in the case of pulsating flow through the larger arteries, there has been no experimental work to determine the effect of the anomalous properties of blood viscosity on flow especially in the smaller arteries and arterioles and veins where it would be most pronounced.

The non-linear partial differential equations, which result from a theoretical analysis of the problem where the non-Newtonian properties are retained, make it clear that a rigorous solution is not possible at this time. This is true even when the simplification is made that the flow is through rigid tubes. Therefore, the application of dimensional analysis appears appropriate for describing the energy loss in the pulsating flow of blood through small tubes.

SYNOPSIS

The Session began with the paper of McComis, Charm and Kurland on "Dimensional analysis of pulsating blood flow". The following members took part in the discussion: Dr. Wiener, Dr. Kurland, Dr. Munro, Dr. Whitmore, Dr. Cohen, Dr. Sacks, and Dr. Gelin.

The discussion especially centered around technical and mathematical details, the frequency of pulsation, flow velocity, rigidity of tubes and the necessity to anticoagulate the blood for experimental purposes.

Lecture No. 2 was that of Drs. Frasher, Wayland and Sobin on "Visco-elastic behavior of the main pulmonary artery segment".

The discussion of Dr. Wiener and Dr. Kurland was aimed towards the clarification of technical details of the experimental procedures of the authors.

Finally before the intermission the paper of Dr. Sacks on auscultatory blood pressure in simulated arteries was presented. Discussion: Hartert, Monro, Harders, Frasher, Whitmore. Dr. Monro and Dr. Harders emphasized the similarity of some pulse curves with those obtained clinically in aortic insufficiency. Dr. Sacks answered that unlike aortic insufficiency, no sounds were obtained without compression of the tube segment undergoing auscultation. Dr. Whitmore asked for the reason for employing such enormous amounts of blood as were indicated by the author. The answer was that the attempt was to be made to simulate the situation within the arteries as naturally as possible.

Paper No. 146 (McDonald) was not read because of the absence of the author.

In the 2nd part of the Session after the break Dr. Whitmore acted as Chairman.

SESSION IIIB (X8)

Blood Flow in Branching and Tapered Tubes

Chairmen: Professor L. E. GELIN, University of Gothenburg, Gothenburg, Sweden
Mr. S. D. CARLILL, Royal Free Hospital, School of Medicine, London, England

No. 150

A. A. PALMER: *Plasma skimming in human blood flowing through branching glass capillary channels*

Kanematsu Memorial Institute, Sydney, Australia

FRESH human blood with acid citrate dextrose solution added as an anticoagulant was passed through branching glass channels and the haematocrit of the blood issuing from the branches was measured. The channels were rectangular in cross section and branched in the plane of the smaller dimension which was of the order of 100 μ. Variable resistances were connected to the branches to control the ratio of the outflow.

Partial plasma skimming (i.e. a difference in the haematocrit of the blood from each branch), occurred if the flow from the branches was unequal and the skimming increased with increasing outflow ratios.

At low absolute rates of flow, skimming was related inversely to the flow rate but above an apparent shear rate at the wall of about 250 sec ^{1} (calculated assuming a velocity profile in accordance with Poiseuille's law) skimming became almost independent of the rate of flow.

Addition of dextran (Mol.Wt. 200,000–275,000), which increases rouleau formation and sedimentation rate, greatly increased skimming.

No. 151

C. SONG, S. E. CHARM and G. KURLAND: *Energy losses for blood flowing through tapered tubes and curved tubes*

Massachusetts Institute of Technology, Cambridge, U.S.A.

THE microcirculatory system contains numerous tapered and curved vessels. Little is known about the energy losses associated with blood flow in such vessels.

The energy loss for blood flowing through tapered and curved glass capillary tubes was experimentally determined.

The energy losses in tapered tubes were calculated by considering the tapered tubes to be made up of a number of incremental straight tubes. The energy losses for the incremental straight tubes were calculated by applying equations derived through dimension analysis. The results in tapered tubes were compared to the energy losses in straight tubes.

SYNOPSIS

Dr. A. A. PALMER, Sidney Hospital of Australia: "Plasma skimming in human blood flowing through branching glass capillary channels". In the absence of Dr. PALMER, Mr. CARLILL made the presentation. Dr. Palmer had made a capillary device with branching channels from two pieces of glasses. The channels were rectangular in cross section. The diameters studied were of the order of 100μ. Through this branching capillary device fresh human blood, with acid citrate dextrose solution added as anticoagulant, was perfused. The differences in haematocrit of the blood issuing from each branch were measured. The outflow from the branches of the device could be partially obstructed by compression in order to control the flow rate through the channels.

Partial plasma skimming occurred when the flow rate through the branches was unequal. Skimming increased with increasing outflow rate. At high absolute flow rates (about 250 sec^{-1}) skimming was almost independent of flow rate. At low absolute flow rates skimming was inversely proportionate to the flow rate.

Addition of high molecular weight dextran (average molecular weight 250,000) increased the sedimentation rate and the aggregation of cells, and greatly increased skimming.

In the discussion of this paper Dr. GELIN from Gothenburg, Sweden, reported on his studies on a similar capillary device with branching capillary tubes varying in diameter from 500 to 50 μ (*Biorheology* **1**, 119, 1963). This model had channels which were circular in cross section. Blood with normal suspension stability did not show significant skimming as long as the capillary channels were wider than 200 μ. Plasma skimming increased with decreasing width of the channels, decreasing flow rate, increasing aggregation of the cells and with increasing viscosity of plasma. The concentration of cells did not influence skimming significantly. In postcapillary tubes, connected to the outflow channels of the device, stasis of cells relative to plasma occurred when there was pronounced aggregation of cells. Observations on the flow rate of cells and of plasma in the pre- and the postcapillary flow showed that in precapillary flow the red cells were concentrated to the faster axial stream, but in postcapillary flow the plasma had a higher flow rate than the cells especially when aggregation was pronounced. This was not significant when the blood was of normal suspension stability.

Dr. GREGERSEN, New York, emphasized the physiologic significance of this separation of plasma flow and cell flow in smaller capillary vessels. In the understanding of differences of large vessel haematocrit and small vessel haematocrit this is quite evident. The importance of this separation is especially to be considered in blood volume determinations. Dr. GREGERSEN also wanted to know the skimming tendency in capillary devices with angles of more and less than 90 degrees.

Dr. KURLAND, asked for numbers on skimming in capillary tubes less than 50 μ.

Dr. GELIN remarked that there are no data yet available on branching capillary devices with diameters less than 50 μ. This depends on technical problems in perfusing such narrow tubes with whole blood. Nor are there any results yet available on other branching capillaries than at right angled branches. The data from these model studies, however, emphasizes the significance of aggregation for the separation tendency and for the distribution of cells in the capillary system. The experiments also made evident that stasis of cells may occur independent of vascular or perivascular reactions just because of

alterations in the flow properties of blood. The *Fåhraeus-Lindquist* effect is only valid for precapillary flow systems but nor for postcapillary flow systems.

Drs. SONG, CHARM and KURLAND, Massachusetts Institute of Technology, USA, presented a paper on the energy losses for blood flowing through tapered and curved tubes. In order to get an idea about the energy losses associated with flow through tapered vessels experiments were performed on blood flowing through tapered and curved glass capillary tubes. The energy losses in such tapered tubes were calculated on the assumption that the tapered tubes were made up of a number of incremental straight tubes. The energy losses for the incremental straight tubes were calculated by applying equations derived through dimensional analysis. The results from tapered tubes were compared with the results obtained from straight tubes. For convergent flow the resistance factor versus the Reynolds' number gave smooth logarithmic curves. For divergent flow similar graphical curves showed a discontinuity. In the discussion there were arguments which questioned the assumption made that tapered tubes could be made up from a number of incremental straight tubes, especially since flow in these small vessels is extremely sensitive to even small alterations in the geometry of the tubes. This argument was felt to be especially significant during divergent flow.

SESSION I (Y6)

Thursday, 29 August, 1963

Biorheological Measurements and Observations

Chairmen: Professor M. REINER, Technion, Haifa, Israel
Professor J. H. WAYLAND, California Institute of Technology, Pasadena, U.S.A.

No. 152

K. WEISSENBERG: *Development of instrumentation for the testing of extracorporeal flow and deformation of biological materials**

The Royal Institution, London, England

AT THE start one assumed validity of the scheme of classical mechanics which allowed testing by simple instruments as it attributed to solids a constant elasticity according to Hooke's law and to liquids and gases a constant viscosity according to Newton's law. In this way e.g. Poiseuille studied the flow of blood through glass capillaries and deduced from Newton's law the Poiseuille law for the volume of the flow. Subsequently, Copley, Scott-Blair, Gelin, Kamiya, Bayliss, Mason and many others obtained biologically valuable results by making the capillaries conform closer to in vivo conditions. The results were, however, unsatisfactory for the testing of viscosity because of the presence of "anomalies" i.e. deviations from the classical laws on which the evaluation of the experiments was based. To deal with these anomalies one replaced in the classical laws the constant coefficients by variable ones, and then tested the variable "apparent" properties over wide ranges of shear by instruments developed by Couette, Mooney, Shirley-Ferranti, Dintenfass, Merrill and others. Substantial progress was thereby made but the results presented only a one-sided view, because the above procedure could not detect the viscous properties exhibited by solids, nor the elastic ones, exhibited by liquids. Thus e.g. the important elastic properties in the flow of blood have hardly ever been considered.

An improved scheme was then introduced and based on the Continuum theory of Rheology which derived its laws from the fundamental principles of Thermodynamics and Mechanics, and accounted then for the macroscopic rheological behaviour in all its variety and complexity by approximating materials of all consistencies (solid, liquid, gaseous or intermediate) by continuous media with elastic as well as viscous properties exactly defined by the two parts of the external work, one (elastic) which is reversibly stored, and the other (viscous) which is irreversibly dissipated as heat. For the study of infinitesimally small shears it sufficed to use instruments which produced only harmonic vibrations, and allowed measurements only in one dimension of space (tangential to the shear-plane). These instruments were developed by Weissenberg, Lebedenko and Philippoff, Hartert, Fukada and others but were insufficient for the general case of shears of any amounts, small

* For the discussion here the term "material" will be used for brevity instead of "biological material"

or large (as in the flow of blood), and for this purpose K. Weissenberg, helped by J. Roberts, introduced an instrument termed Rheogoniometer which allowed approximation to the ideal comprehensive testing in which one considered the movements and forces which coexisted in the material, and measured them

(i) at each point in their development in time, and in their distribution over the full solid angle in all three dimensions of space.
(ii) over the envisaged ranges of temperatures (−40°–+400°C) and rheological states, and for
(iii) the various kinds and amounts of consistencies encountered between 0·0005 and 10^8 P

while the material was subjected to either vibrational or unidirectional shearing movements, or any combination of the two (corresponding to a pulsating flow of blood) with shear rates varying over six orders of magnitudes. The advantages of such a comprehensive testing and further developments are discussed.

No. 153

J. HARKNESS and R. B. WHITTINGTON: *A new capillary-type viscosimeter: Comparison with the classical Ostwald viscosimeter, and a general consideration of capillary-type instruments*

Musgrove Park Hospital, Taunton and The University of Liverpool, Liverpool, England

A NEW viscosimeter will be described. A mercury-containing device supplies a standard head of pressure to force the test liquid through a capillary-tube of specified dimensions; the mercury device measures the standard volume of flow; it also activates the electronic digital timer which displays the time of flow. A technique has been devised which excludes the need to clean and dry the viscosimeter between samples.

The most widely-used capillary viscosimeter is the U-tube known as Ostwald's. When introducing the new viscosimeter it was felt appropriate to compare it in all aspects with the established instrument.

To facilitate these comparisons, the basic theory of both instruments is given briefly, beginning with the general case of motion under gravity of a viscous Newtonian liquid in a U-tube.

Ostwald's instrument is seen as an "overdamped" case of motion under gravity: the new viscosimeter as an instance of motion under an arbitrary pressure-system.

At first, only the primary phenomenon is dealt with; that is to say, the loss of energy due to viscous flow through the capillary.

Later, the secondary phenomena are considered. These include the effects of kinetic energy, curvature of the capillary, viscous losses in other parts of the instrument, and surface tension.

It is shown that the time of flow is approximately proportional to the viscosity in the new instrument, and to the kinematic viscosity (or ratio of viscosity to density) in Ostwald's viscosimeter.

The pressurizing and timing device incorporated in the new viscosimeter is described.

The accuracy of the whole assemblage, both as an "absolute" and as a calibrated instrument, is considered.

The exposition, to this point, has been concerned only with Newtonian liquids: some remarks on the rheology of non-Newtonian systems now follow, with particular reference to the problem of comparability of numerical results. The standardization of hypothetical "rates of shear" or of "wall shear-stresses", and of observational temperatures, is advocated.

Some reference is made to the use (and mis-use) of Ostwald's instrument in rheology.

The new instrument was designed for the rapid and accurate estimation of the viscosity of human blood plasma and serum. Reference will be made to the changes in the plasma viscosity in disease and how their estimation may be used in clinical pathology to diagnose the presence of a disease and to assess its severity. Changes in the plasma viscosity reflect changes in the plasma protein fractions.

The paper concludes with a brief account of some applications of the new viscosimeter to the rheology of solutions of protein fractions prepared from human blood plasma and serum.

No. 154

H. KAWAI, E. FUKADA, T. IBE and H. SHONO: *A new capillary viscometer for measuring the viscosity of small amounts of blood*

Kobayasi Institute of Physical Research and Rion Co. Ltd., Tokyo, Japan

A GLASS tube with a diameter of 5 mm and a length of 10 cm is closed at both ends by syringe needles. The pressure inside the tube is reduced by pressing a hollow rubber ball which is connected to the upper side of tube. The lower needle is vertically immersed in the blood to be tested and the upper needle is open to air. The blood is then sucked up into the tube through the lower needle and the air is drawn into the tube through the upper needle.

The highest level of blood sucked into the tube depends primarily on the viscosities of blood and air, the volume of the hollow rubber ball and the dimensions of the glass tube and the two syringe needles. Since the quantities, other than the viscosity of the blood, can be determined by the calibration experiments, using liquids with known viscosity, such as silicone oils, the observation of the highest level of blood measures the value of the viscosity of the specimen.

The relation between the level of blood sucked in and the degree of inclination of the glass tube from the vertical position is investigated. It has been found that ignoring the change in the density of blood does not affect appreciably the accuracy of measurement.

The minimum volume of blood required is about 1 cm^3 and the time necessary for one measurement is about 10 sec. The concurrent measurements of sedimentation rate of blood cells and the viscosity of blood have been carried out for a number of blood specimens taken from patients in a hospital. The hematocrit, i.e. the volume fraction of cells is determined by a centrifugation method. The viscosity of plasma separated from cells is also measured by the same viscometer. The relations between hematocrit and the viscosity of blood and between sedimentation rate of cells and the viscosity of plasma have been investigated.

The viscometer is easily handled and even available for clinical use. The measurement of

viscosity of blood *in vivo* is also undertaken by injecting the syringe needle of the viscometer into the vein of an animal where the blood pressure approaches zero.

No. 155

L.-E. GELIN: *Rheological disturbances following tissue injury*

University of Gothenburg, Gothenburg, Sweden

THE flow properties of blood are highly dependent on the composition of blood and the rate of shear. Using a Brookfield synchro-lectric viscosimeter model LVT with an adapter for small blood samples, we have studied the rheological properties of blood in relation to tissue injuries of various kinds. At different time intervals after injury, arterial samples of blood have been drawn into dry-heparinized or oxalated bottles. Injury is followed by marked alterations of viscous properties of whole blood and of plasma.

For an analysis of the interrelationship between the concentration of corpuscles and the vehicle viscosity for the rheology of a suspension, the following model experiments were performed. Twice washed human red cells were added to different vehicles in a concentration to give a hematocrit varying from 0 to 70. The following vehicles were used: saline, a 4% solution of a dextran fraction with an average molecular weight of 40,000, a dextran fraction with an average molecular weight of 80,000, a dextran fraction with an average molecular weight of 800,000, plasma, albumin and fibrinogen solutions. These experiments show that the viscosity of a red cell suspension increases with (a) increasing hematocrit, (b) increasing vehicle viscosity and (c) decreasing rate of shear. This increase of the suspension viscosity is, however, not a simple addition of the two factors of hematocrit and of vehicle viscosity. It is a disproportional increase, termed "viscosity plus factor", which has been calculated for different vehicles. It increases with decreasing rate of shear, increasing hematocrit and increasing vehicle viscosity.

An increase in the viscous properties of blood will play an important role for venous return and postcapillary flow where there is a small pressure head and a slow flow rate, especially in pathophysiologic conditions. An increase in the viscosity of whole blood means a tendency to stagnation.

Studies have been made in a system with branched capillaries, varying in diameter between 500 μ and 25 μ, to analyse the separation tendency between plasma flow and cell flow. These model experiments show that an increased plasma viscosity together with a decreased flow rate produces stasis of cells in postcapillary flow.

No. 156

H. WAYLAND and M. INTAGLIETTA: *Streaming birefringence study of the interaction of submicroscopic particles*

California Institute of Technology, Pasadena, U.S.A.

MANY liquids of biological importance contain mixtures of macromolecules of varying shapes and sizes. In particular, blood plasma contains highly elongated macromolecules

(fibrinogen) and ellipsoidal macromolecules (globulin and albumin). The rheological properties of such heterogeneous systems will be influenced by both the chemical and hydrodynamic interactions of the macromolecular components. This paper reports a portion of a study aimed at evaluating the extent of the hydrodynamic interactions between elongated and spherical particles, as a model of the plasma system.

Tobacco mosaic virus (TMV) was used as the elongated particles and southern bean mosaic virus (SBMV) for the spherical particles. The effect of the presence of the spherical particles on the orientation distribution of the rods was studied by means of streaming birefringence.

An apparatus was developed using Faraday cell modulation and photoelectric detection in which the output signal near the null is linear with respect to the angular distance from the null. With this equipment it was possible to establish the position of the angle of isocline with an accuracy of one degree in a relative retardation of 10^{-9} cm/cm.

Because of reported anomalies in the position of the angle of isocline [1] for TMV at small shear rates, this was studied, making corrections for all extraneous birefringence, by means of a computer routine. The corrected results showed no significant deviation from the monotonic increase of the angle of isocline as the shear stress approached zero.

For mixtures of TMV and SBMV the amount of retardation measured for a given shear stress and TMV concentration was lower than that for pure TMV. This is consistent with the viscometric studies of COLLINS and WAYLAND [2] which can be explained on the basis of an increase in randomness of orientation of the rods due to the presence of the spheres.

REFERENCES

[1] LERAY, J., *J. Chim. Phys.* **316**, 1961.
[2] COLLINS, D. J. and WAYLAND, H., *Proc. Rheol. Soc.*, 1962.
In press.

SYNOPSIS

Paper 152: K. WEISSENBERG: Development of instrumentation for the testing of extra-corporeal flow and deformation of biological materials.

Dr. M. JOLY raised the question if Prof. WEISSENBERG's idea of a general field theory for complex rheological fluids could take account of structuring of certain constituents of the fluid by the flow (e.g., the macromolecules or the formed elements in the blood). This was not directly answered, but Prof. WEISSENBERG pointed out that in a biological system one must consider the parallel flow of a variety of materials, and any satisfactory theory must take this into account. For example, the flow of oxygen or that of water or that of carbon dioxide could be separately followed, although their intimate interrelationship is also important.

Paper 153: JOHN HARKNESS and R. B. WHITTINGTON: A new capillary type viscometer.

As an example of the use of this viscometer in a clinical application, Dr. HARKNESS discussed the increase in blood plasma viscosity with progress of tuberculosis. Dr. MELVIN KNISELY raised the question as to the problem of sampling: is the plasma sample representative

Dr. HARKNESS stated that in their clinical work they could find no measureable difference between samples taken from either arm of the patient.

Dr. WILLIAM ROSE raised the question as to how the progress of the disease was measured.

The reply was that the British Medical Council has set criteria which are accepted in British medical practice.

Paper 154: H. KAWAI, E. FUKADA, T. IKE and H. SHONO: A new capillary viscometer . . .

The discussion on this instrument was centered around technical problems, particularly the role of operator skill in squeezing the rubber ball to obtain reproducible results. It was pointed out that other more reproducible sources of reduced pressure could be used.

Paper 155. LARS-ERIK GELIN: Rheological disturbances following tissue injury. (Discussion not recorded).

Paper 156. HAROLD WAYLAND and MARCOS INTAGLIETTA: Streaming birefringence study of the interaction of submicroscopic particles.

Dr. A. SILBERBERG raised the question as to the relationship between the behaviour of the angle of isocline and the amount of birefringence in rod-sphere mixtures as a function of sphere concentration. It was pointed out that uncertainties in measurement of the isocline angles led to deferring reporting on this effect until more experimental work has been done, although these difficulties do not invalidate the retardation measurements.

SESSION II (Y7)

Thursday, 29 August, 1963

Hemorheology of Red Cell Suspensions

Chairmen: Professor R. FÅHRAEUS, University of Uppsala, Uppsala, Sweden
Professor S. G. MASON, McGill University, and Pulp and Paper Research Institute of Canada, Montreal, Canada

No. 157

S. E. CHARM, W. MCCOMIS and G. KURLAND: *Rheology and structure of blood suspensions*

Massachusetts Institute of Technology, Cambridge, U.S.A.

A STRUCTURAL model developed for kaolin suspensions was applied to blood in order to determine the structure and strength of the red cell suspensions.

The yield stress of red cell suspensions determined in settling experiments agreed with the yield stress determined from shear stress–shear rate information employing Casson's equation.

Theoretical considerations indicate that the shear stress–shear rate curve for blood should approach a straight line. This was found to be true at shear rates above 40 sec^{-1}. The slope of this line was predicted from calculations based on sedimentation experiments and employing a modified Einstein's equation.

The data suggest that the curvature of the shear stress–shear rate plot at low shear-rates is due to aggregates of cells which break down under increasing shear rate resulting finally in individual flocs.

It is suggested that a floc consists of one to four cells with adhering plasma. The aggregate was calculated to have twice as much plasma associated with it as does a floc. However the size of the aggregate could not be determined since the number of flocs associated with an aggregate could not be determined.

No. 158

H. A. COX, Jr. and G.-J. SU: *The influence of electrokinetic charge on the rheological properties of red blood cell suspensions*

University of Rochester, Rochester, U.S.A.

THE relationship between the electrokinetic charge of human red blood cells and the rheological properties of suspensions of these cells have been investigated. The charge was varied as discussed below, and the corresponding effects on suspension flow properties were determined.

Red cells were obtained by venipuncture, washed, and suspended in various isotonic

media. The electrokinetic mobility was determined by microelectrophoresis, while rheological properties were measured with a concentric cylinder viscometer. A range of shear rates was used which roughly corresponds to that found in the body.

The cell charge was altered by changing the pH and the ionic strength of the suspending medium, and by introducing polyvalent cations. In many cases, both cell charge and suspension rheological behaviour were time-dependent. An interpretation of the charge-flow relationship for red cell suspension is given.

No. 159

G. BUGLIARELLO, C. KAPUR and G. HSIAO: *The profile viscosity and other characteristics of blood flow in a non-uniform shear field*

Carnegie Institute of Technology, Pittsburgh, U.S.A.

IN A previous exploratory study of the detailed characteristics of blood flow in small horizontal glass capillaries, viscosity profiles obtained from experimentally determined velocity profiles showed a rapid increase from a low value in the peripheral cell-poor region of the flow to a considerably higher value in the core. Such a trend was frequently accompanied by the occurrence of a peak at an intermediate position between the centerline and the edge of the core.

In the present study the phenomenon is investigated in greater detail. To such a purpose the flow of human blood of varying hematocrits was observed by high speed microcinematography (at 3000 frames/sec and 970 × magnification) in glass capillaries 40–80 μ in diameter, over a range of pressure gradients. Unlike the previous experiments, the capillaries were positioned vertically, so as to eliminate asymmetries in the flow pattern caused by sedimentation, which has been shown to be significant in the horizontal layout. The velocity profiles determined by averaging the observed velocities of erythrocytes at each radial position over the whole duration of the film ($\sim$ 0·3 sec.) were indeed found to be nearly axi-symmetrical in all cases, a result confirmed by the close agreement between flow rates obtained by integration of the profiles and those obtained volumetrically. Almost instantaneous velocity profiles (i.e. profiles corresponding to observation periods of a few milliseconds) were however asymmetric and deviated appreciably from the average profiles.

The axial symmetry of the average flow permitted the more accurate measurement of the peripheral layer characteristics (thickness, standard deviation, power spectrum, etc.), and, from them, the computation of the average concentration in the cell-rich core of the flow. From such concentration and from the results of concentric cylinder viscometric measurements, viscosity profiles were computed for the cross-section of the flow, and compared with experimental viscosity profiles obtained directly by differentiation of the measured average velocity profiles. It was observed that, although the shape of the experimental viscosity profiles—and hence the occurrence and location of viscosity peaks in the core—was influenced by the procedure followed in determining the average velocity profiles, and the presence of a viscosity peak in the core, away from the centerline, was unmistakable in several instances, particularly at high hematocrits. Neither the axial drift responsible for the peripheral layer nor the peak in the viscosity profiles can be predicted from constant-shear

viscometer measurements; they are a characteristic of the non-uniform shear field in the capillaries.

The influence of the various flow parameters on the features of the viscosity profiles is investigated, and several possible mechanisms leading to such features are discussed. In particular, the peaks in the viscosity profiles suggest a stress—and concentration-dependent interplay of multiple causes: axial and centrifugal drift, orientation effects and boundary layer phenomena around the erythrocytes.

No. 160

S. ROWLANDS, A. C. GROOM and H. W. THOMAS: *The difference in circulation times between erythrocytes and plasma* in vivo

St. Mary's Hospital Medical School, London, England

ONE of the figures published by DOW *et al.* [1] indicated that cells and plasma might have different transit times through the lungs of a dog. A possible explanation is the axial streaming of erythrocytes noted by FÅHRAEUS [2].

Quantitative observations have been made on this phenomenon in the anaesthetized cat in two series of experiments. In the first series of experiments the carotid arterial flow on one side was monitored by a scintillation counter and fast recorder (GROOM *et al.* [3]. ^{32}P-labelled red cells and ^{131}I-labelled human serum albumin were injected alternately into a vein and the minimum pulmonary, modal pulmonary and total circulation times of the two substances were measured. The mean ratio of the circulation times of labelled albumin and labelled red cells is greater than unity and the difference from unity is highly significant ($P < 0{\cdot}001$).

In the second series two scintillation counters were used, so designed that one recorded the presence in the blood of ^{32}P only, the other that of ^{131}I only. The outputs were connected to a twin channel fast recorder. Using for injection blood in which both erythrocytes and albumin were labelled it was now possible to measure the circulation times simultaneously. In all of many scores of injections the red cells arrived before the protein.

Examination of the recordings showed that the red cells had got clear ahead of the protein. This suggested that the protein might, in some way, have been held back in the blood stream. An experiment was planned to test whether in fact the protein was being held back by transient absorption at the capillary wall or some similar mechanism. The following four injections were prepared:

(a) red cells labelled with ^{32}P + serum albumin labelled with ^{131}I.
(b) red cells labelled with ^{32}P + sodium iodide labelled with ^{131}I.
(c) sodium phosphate labelled with ^{32}P + serum albumin labelled with ^{131}I.
(d) sodium phosphate labelled with ^{32}P + sodium iodide labelled with ^{131}I.

(a) should show the usual difference in circulation times.
(b) should show a difference if axial streaming was the correct explanation.
(c) should show a difference if protein was delayed.
(d) should show no difference.

(a) and (b) showed a difference and (c) and (d) showed no difference. The protein-delay hypothesis was therefore untenable unless the inorganic ions were also delayed in the circulation. Some observations by TAYLOR [4] on molecular diffusion in fluids flowing slowly in small-bore tubes indicate that a delay in arrival time can occur. Some of our results *in vivo* support this hypothesis but as yet no decisive experiments have been made. Observations *in vitro*, to be presented in the succeeding paper, can be made with better control and greater precision than are possible in an animal. These observations together with the results achieved *in vivo* suggest that molecular diffusion must be taken into account. Further precise measurements are needed before the contributions of axial streaming and molecular diffusion to differential circulation times can be properly assessed.

REFERENCES

[1] DOW, P., HAHN, P. F. and HAMILTON, W. F., *Amer. J. Physiol.* **147**, 493, 1946.
[2] FÅHRAEUS, R., *Physiol. Rev.* **9**, 241, 1929.
[3] GROOM, A. C., MORRIS, W. B. and ROWLANDS, S., *J. Physiol.* **136**, 218, 1957.
[4] TAYLOR, SIR GEOFFREY, *Proc. Roy. Soc.* **A219**, 186, 1953.

No. 161

H. W. THOMAS, ROSEMARY J. FRENCH, A. C. GROOM and S. ROWLANDS: *The flow of red cell suspensions through narrow tubes: the (extracorporeal) determination of the difference in mean velocities of red cells and their suspending phase*

University of Reading, Shinfield, Reading and St. Mary's Hospital Medical School, London, England

WHEN a red cell suspension, or blood, flows through a cylindrical tube, it is believed that the red cells which happen to be flowing along lines of flow near the tube wall are subject to a centripetal force, which is partly mechanical and partly hydrodynamic in origin. As a result they take up positions nearer the axis of the tube, where the fluid velocities are higher. This leads to an increase in the apparent fluidity of the suspension, and to a decrease in the mean concentration of the red cells within the tube; these changes become experimentally significant in tubes with diameters below about 300–400 μ. Parallel changes in apparent fluidity and in red cell concentration are also observed or deduced in *in vivo* studies.

A small but significant difference in the mean circulation time of red cells and plasma flowing through various circulatory beds in experimental animals and in human subjects has been well established. The above-mentioned wall effects could also account for this result, and if this explanation is correct, then the same physical phenomenon should be observed in a physical model of suitable dimensions.

Preliminary work has been confined to an artificial circulatory bed constructed by connecting in parallel sixteen pieces of nylon tubing of about 200 μ bore. The tubes are connected via a system of three-way taps to a reservoir containing a suspension of bovine red cells in albuminized saline. Air pressure applied to the reservoir gives a suitable flow of suspension through the tubes. By means of the tap system, a small volume of a similar suspension labelled with radioactive isotopes can be inserted into the initial sections of the

tubes. On establishing the flow, the arrival of the labelled material at a point 160 cm downstream is detected by means of a twin channel system described previously [1]. When the labelled suspension contains the isotopes ^{32}P and ^{131}I as phosphate and radioiodinated albumin outside the red cell, the clearance curves at the detector are similar for both isotopes. However, if the ^{32}P isotope is contained within the red cell, the clearance curves are markedly different, and there is a significant difference between the mean arrival times of the red cells and of the suspending phase. This difference is of the order of 10 per cent for a suspension of volume concentration about 0·4 and at a wall stress of about 50 dyn cm^{-2}.

Experiments are being continued with a view to widening the range of flow condition and improving the accuracy. The results will be described, and an attempt made to correlate them with the results of other authors for the changes of apparent fluidity and red cell concentration under similar flow conditions.

REFERENCE

[1] GROOM, A. C., ROBERTS, P. W., ROWLANDS, S. and THOMAS, H. W., *J. Physiol.* **146**, 17P, 1959.

SYNOPSIS

S. E. CHARM, W. MCCOMIS and G. KURLAND: Rheology and structure of blood suspensions

Professor FÅHRAEUS said that there was good evidence for the existence of a cell-free peripheral layer and an axial core of red cells in blood flowing through glass tubes. He argued that at low shear rates it was highly doubtful that a floc of 4 cells such as postulated by Dr. CHARM actually exists; rather he would expect that there would be much more extensive aggregation.

In answering Dr. CHARM pointed out that he had indeed distinguished between the basic aggregated unit—the 4 cell floc—and loose aggregates of such flocs. It was the loose aggregates which broke down as the shear rate was increased and this gave rise to the curvature observed in the shear stress–shear rate plot at low shear rates. However, he admitted that the manner of aggregation might greatly influence the results obtained in the viscometer.

Dr. MONRO referring to some results which he had recently obtained with the use of the Rabbit ear chamber technique (see session Z5) said that the concept of a floc of 4 to 5 particles would fit in well with his observations. He asked whether Dr. CHARM had observed deformation and break-up of flocs at higher shear rates.

Dr. CHARM replied that there was a slight change in curvature of the shear stress–shear rate plot at higher shear rates and that this could possibly be associated with a break-down of the flocs.

In answer to a question by Dr. RUBINOW on the causes of aggregation Dr. CHARM said that it was not hydrodynamic forces, but rather chemical forces having their origin in the presence of fibrinogen which led to aggregation of red cells.

Dr. MASON said that it was known that some of the behaviour of kaolin suspensions could be explained by the bipolar nature of the suspended particles. In view of this fact would Dr. CHARM venture to comment on the applicability of the kaolin model to the red cell suspensions? Dr. CHARM declined to comment.

H. A. Cox, Jr. and G.-J. Su: The influence of electrokinetic charge on the rheological properties of red blood cell suspensions.

Dr. Tamamushi asked whether the electroviscous effect, treated by von Smoluchowski many years ago and which predicts that the viscosity would increase with increasing charge on the particles, had been taken into account in interpreting the results.

Dr. Cox replied that at a concentration of 40 per cent by volume the Smoluchowski theory would no longer be applicable.

Dr. Goldsmith asked whether the addition of aluminium chloride had brought about changes in cell shape; these could possibly affect the mobility of the red cells.

Dr. Cox said that no significant changes in the shape of the red cells had been observed.

In answer to questions on the magnitude of the shear rates used in the viscometer and their relation to physiological shear rates, Dr. Cox said that the range of shear rates used in his experiments lay between 50 and 100 sec^{-1} The maximum physiological shear rates were thought to lie between 1300 and 1400 sec^{-1}.

Dr. Cox also said that the effect of external electric fields on the viscosity of the suspensions had not been investigated.

George Bugliarello, Chandra Kapur and George Hsiao: The profile viscosity and other characteristics of blood flow in a non-uniform shear field.

Dr. Silberberg asked whether it was possible to perform a count of red cells passing by in different sections of the tubes and thus to obtain a concentration profile which might bear some relation to the viscosity profiles.

Dr. Bugliarello said that with the cine-film obtained in these experiments such a count could not be made. He stressed a point made earlier during the presentation of his paper, viz. that the maximum possible information had already been extracted and that this line of experiments could not usefully be further pursued.

Dr. Rowlands said that M. Taylor had measured the changes in light transmission occuring during the flow of blood in glass capillaries and had found that the results suggested the existence of a marginal cell-free zone and furthermore, that the particles in the axial stream showed increasing orientation with increasing flow rate. Some recent, yet unpublished, work carried out in the laboratory of Professor A. C. Burton in which sections of living blood vessels were subjected to a quick freeze and subsequently microtomed appeared to show that the red cells were preferably oriented in a region close to the vessel centre, whereas in the peripheral region the orientations were random.

Dr. Goldsmith pointed out that in a recent paper by Kuroda and Fujino (*Biorheology* **1**, 167, 1963) the measured changes in light transmission had been interpreted to show preferred orientation of red blood cells with their long axes aligned in the direction of flow.

S. Rowlands, A. C. Groom and H. W. Thomas: The difference in circulation times between erythrocytes and plasma *in vivo*.

H. W. Thomas, Rosemary J. French, A. C. Groom and S. Rowlands: The flow of red cell suspensions through narrow tubes: the (extracorporeal) determination of the difference in mean velocities of red cells and their suspending phase.

Dr. Gregerson asked how the value for the volume concentration of the red cells as calculated from the mean circulation time and the flow rate compared with the measured haematocrit.

Dr. ROWLANDS replied that there was a slight difference between the two values.

Dr. COPLEY asked whether an alternative to the hypothesis of axial flow in order to account for the difference in circulation times could not be found in the adhesion of plasma to the fibrin surface of the endothelium.

Dr. ROWLANDS pointed out that such an explanation was untenable since the work had shown that there was no difference in circulation times between an injection of sodium phosphate labelled with ^{32}P + serum albumin labelled with ^{131}I on the one hand, and an injection of sodium phosphate labelled with ^{32}P + sodium iodide labelled with ^{131}I on the other.

Dr. MASON thought that some very convincing evidence for axial streaming *in vivo* had been reported by Drs. COPLEY and STAPLE (*Biorheology* **1**, 3, 1963) from visual observations of the plasmatic zone in the vessels of the cheek pouch of the hamster.

Dr. GOLDSMITH suggested that the question as to whether the difference in circulation times between red cells and plasma was due to molecular diffusion or axial streaming could be solved by injecting into the suspension particles of the order of $1/2\,\mu$ (e.g. polystyrene latex particles labelled with a radioactive element) which would not be subject to molecular diffusion but which would acts as tracer particles giving an outflow curve for the plasma.

Dr. THOMAS thought that such an experiment would still not be conclusive since although the tracers would not be subject to molecular diffusion they would still be subject to convective diffusion.

Dr. WHITMORE asked whether Dr. THOMAS had calculated the width of the cell free plasmatic zone at the wall of the tube corresponding to the observed differences in mean circulation times.

Dr. THOMAS replied that at a flow rate corresponding to a wall stress of about 50 dyn cm^{-2} the ratio of mean circulation times of 1·076 gave a cell free zone of $3\,\mu$ width, the calculations being based on the Whitmore model.

SESSION III (Y8)

Thursday, 29 August, 1963

Medical Biorheology

Chairmen: Professor H. HARTERT, University of Heidelberg, Heidelberg and Municipal Hospital, Kaiserslautern, Germany
Professor R. E. WELLS, Jr., Harvard Medical School and Peter Bent Brigham Hospital, Boston, U.S.A.

No. 162

S. E. CHARM, G. E. KURLAND, C. TEJADA and W. MCCOMIS: *The effect of a fatty meal on whole blood and plasma*

Massachusetts Institute of Technology, Cambridge, Beth Israel Hospital and Harvard Medical School, Boston and Institute of Nutrition of Central America and Panama, U.S.A.

AN EXAMINATION of the blood viscosity of 40 medical students with a cone and plate viscometer before and after a fatty meal showed no change in blood viscosity although the serum lipids increased.

In a separate experiment, it was found that no change occurred in plasma viscosity as determined by the capillary tube technique although the plasma lipids increased.

From theoretical considerations, it was suggested that in order to detect changes in plasma and whole blood viscosities after a fatty meal, it would be necessary to employ methods of determining viscosity within a 2 per cent error.

Employing the GDM narrow gap viscometer which determines viscosity within a 2 per cent error, no differences were observed in either plasma or whole blood viscosities even though the plasma lipids increased.

In certain cases it was observed with both the Brookfield cone and plate as well as the GDM viscometers that whole blood viscosities *decreased* with an increase in plasma lipids. The plasma viscosities were unchanged. It was suggested that the decrease in whole blood viscosities was caused by the effect of the plasma lipids on the cell aggregate forces.

No. 163

B. ZEDERFELDT: *Rheological disturbances and their treatment in clinical surgery*

University of Gothenburg, Gothenburg, Sweden

IN HIS communication at this Symposium, Gelin shows that the viscosity of red cell suspensions is dependent on the rate of flow, the hematocrit and the vehicle viscosity and also on a "viscosity plus factor" which is dynamically dependent on the other factors. This means that in normal conditions blood streaming in venules and veins has a higher

viscosity than the same blood streaming in arteries and arterioles. Following tissue injury, changes occur in the blood and plasma with aggregation of formed elements and increase of large and asymmetrical protein molecules in the plasma. These changes will markedly influence the viscosity of whole blood and plasma at all rates of flow but are most marked at slow flow rates. A vicious circle will occur with increased suspension viscosity, decreased rate of flow and thereby further increase of the viscosity. This will result in stagnation of cells in postcapillary venules and in a decreased venous return to the heart, all leading to an impairment of the nutritional blood flow through the tissues.

These changes call for an effective counter action of the increase in whole blood viscosity which follows tissue injury. Experimental and clinical studies have shown that this can occur following infusion of low viscous dextran, with consequent restoration of the balance between small and large molecules in the plasma.

The indication for such treatment is shortly to increase the perfusion of tissues with blood when this perfusion is decreased by rheological disturbances. Such rheological disturbances do occur in shock following burns, crush injury and influence of toxic agents either exogenously or endogenously after major surgery and after perfusion procedures.

The effect of rheological treatment with low viscous dextran will be illustrated with case reports.

No. 164

C.-M. RUDENSTAM: *Rheological disturbances and tumor spread*

University of Gothenburg, Gothenburg, Sweden

SURGERY, still the most effective therapy for malignant tumors, runs the risk of tumor spread increases. This spread can be explained by increased liberation of tumor cells into the blood stream because of the manipulation of the tumor during operation. The surgical trauma as such may in itself increase the risk of development of metastases. Earlier experimental investigations have shown an increased take of subcutaneously injected tumor cells in relation to trauma. This increased take has been thought to depend on hormonal effects in connection with the stress reaction induced by the trauma.

Injury is followed by changes in the flow properties of blood with increased blood viscosity and aggregation of the formed elements leading to stagnation of cells in post-capillary venules. After trauma, there is also an increased tendency to thrombus formation and during the first 2–3 hr after a tissue injury, a consumption of coagulation factor occurs in the blood, indicating an intravital coagulation process.

If tumor cells are circulating in the blood, it is probable that the post-traumatic changes in the rheology of blood will influence the distribution of tumor cells and the formation of metastases.

The purpose of this study was to investigate whether changes in the microcirculation influence the frequency of take and the number of metastases in the lungs after intravenous injection of tumor cells. Three different tumor-host systems have been used (1) 20-methyl-cholantrene induced sarcoma in rats, (2) Rous-rat sarcoma, and (3) spontaneous mammary carcinoma in C_3H-mice.

It was found that changes in the microcirculation induced by injury or by injection of high viscosity dextran increases the take frequency, especially when a comparatively small number of tumor cells are given, and the number of metastases in the animals with take. The effect of disturbed microcirculation on these two factors is different for different tumors.

SYNOPSIS

THIS session consists of three papers, one dealing with the effects of a fatty meal upon plasma and blood viscosity and the other two upon the effects of low molecular weight dextran in clinical surgery and in tumor spread.

The first paper presented by Dr. KURLAND revealed no significant changes in viscosity following fat. The discussion following noted the positive results found by others and raised the question as to whether the time of sampling might not be a factor. The present study was made 3 hr after fat ingestion in normal volunteers.

The paper on dextran by Dr. ZEDERFELDT reported on the clinical improvement and viscosity lowering effects when this material was employed following burns or injury. It was suggested that low molecular weight dextran infused at the beginning of major surgery might have a protective action in the rheology of blood in the microcirculation.

The paper by RUDENSTAM also from the laboratories of Dr. Gelin, considered the effects of tumor spread as a function of changes in blood flow. Using high viscosity dextran or injuring tissue increased the frequency of tumor spread or metastases. The type of tumor cells used also influenced the results.

SESSION I (Z5)

Friday, 30 August, 1963

Chairmen: Dr. E. DAVIS, Hadassah Medical Organization, Jerusalem, Israel
Professor S. ROWLANDS, St. Mary's Hospital Medical School, London, England

No. 165

H. HARDERS: *Hemorheological investigations in the "arterial spider" of the human skin*

University of Hamburg, Hamburg, Germany

THE arterial spider of the human skin is a unique object for hemorheological studies in man.

This arises from the following circumstances:

(1) Immediate accessibility (by the use of Cantharide blisters) of an arterial vascular tree with an inner diameter of the central artery of several hundred μ in its connection with arterial branches, capillary network and venous net.

(2) The possibility of direct microscopical observation under high resolution of flow characteristics and of the behavior of single cells; the possibility of micromanipulation and pressure recordings.

(3) The possibility of using different methods successively or simultaneously for the study of the same vessel, which provides detailed information about the value and limitations of the methods used.

(4) Unusually high pressure values in a peripherally localized terminal vascular area.

Similar conditions exist elsewhere in man only in the retinal arterial circulation, but there is no immediate accessibility under normal circumstances. Furthermore additional dynamic influences result from the intra-ocular pressure.

Morphology of the vascular spiders is described in detail with special emphasis on unusual vascular formations (spiral arteries) and abrupt changes of inner vascular diameter.

The peculiar functional and rheological findings are described and pressure recordings discussed, which show systolic arterial pressures exceeding 100 mm Hg dropping abruptly within the course of some millimeters to values just above 10 mm Hg. Under clinical conditions the arterial spiders are observed in apparently healthy persons, in small children, in puberty, pregnancy, and above all in chronic liver disease. They do not constitute a localized vascular abnormality, but are part of a wide-spread structural and functional transformation of the whole peripheral vascular bed, such as palmar erythema, changes in the terminal vascular bed of mucous membranes, skin and finger tips, which are described in detail.

The origin and the purpose of this universal micro-vascular transformation is unknown, but a relation to the fact that cirrhotic patients almost never develop arterial hypertension will be discussed.

Detailed hemorheological investigations are adequate to show the influence on, or the role in, general circulation of the described changes.

No. 166

J. W. IRWIN and DOLORES C. ALCAIDE: *Biological reactions interfering with flow through the microcirculation*

Massachusetts Eye and Ear Infirmary, Boston, U.S.A.

BLOOD, a mixture of complex materials, flows through multiple channels which are capable of changing diameters individually or collectively. The study of rheology of blood, therefore, is most difficult. To date it has not been possible to formulate adequate mathematical equations which are truly significant. Fortunately, mathematicians, physicists, engineers, and biologists realize that they must unite their efforts to achieve desired progress. Since the biologists have studied blood and its flow for many years, perhaps they can define some of the problems. Certain biological reactions can result in marked impedance or increase of the flow of blood through the small vessels of the micro-circulation.

Because the circulatory system is one of the fundemental integrative systems of the body, sudden, severe changes in this system may well be fatal. In anaphylaxis, both active and passive, hyaline emboli have been observed plugging small arterioles, capillaries, and venules so as to obstruct blood flow. Such obstruction has usually been followed by death within minutes. Immunochemical studies indicate that the probability of death increases as the amount of circulating antibody increases. That all animals do not die of anaphylactic shock, especially those at low antibody titers, indicates that other factors are involved. Antigen–antibody interaction, therefore, does not appear to explain this phenomenon in entirety.

Chemicals can either inhibit or increase the amount of blood in a microcirculatory area. Intravenous injection of histamine or serotonin into living, non-sensitized animals has also led to the formation of plugging, hyaline emboli in small arterioles, capillaries and venules. Sympathomimetics such as epinephrine have been observed to increase the number of open, functioning capillaries within certain organs. Furthermore, epinephrine usually increases the rate of blood flow through the microcirculation. Thus, some chemicals can increase the activity of the microcirculation, whereas others can impede blood flow in similar areas.

Observations will be demonstrated with a 16 mm motion picture film.

No. 167

R. E. WELLS, Jr.: *Rheology of blood in the microcirculation of man*

Harvard Medical School and Peter Bent Brigham Hospital, Boston, U.S.A.

THE shear rate dependence of the viscosity of blood is of greatest significance in the microcirculation i.e., in vessels whose diameter is 100 μ or less. Rate of shear appears to be least in the post capillary venules and it is in these vessels where intravascular cell aggregation can be observed in normal man. It has been demonstrated that at low rates of shear (0·5 sec^{-1} and less) blood develops a fluid structure which appears related to the presence and concentration of the plasma protein, fibrinogen. This clotting protein with its fibrillar structure (axial ratio 15:1) and high molecular weight (330,000) is well established

as the agent responsible for erythrocyte aggregation and settling. Studies were conducted in order to compare the aggregation characteristics and viscosity of blood *in vitro* in those changes observed *in vitro*. Freshly drawn whole blood was analyzed in a Couette type viscometer over a shear range from 20 to 0·1 sec^{-1}. The sample was analyzed for its content of total protein, and fractions of albumin, globulin and fibrinogen. The packed volume of red cells and osmolality was also measured. Suspension stability was observed through standardized vertical glass tubes by timing the onset and rate of cell mass descent. Photomicrographs were made of the cell formations in the tubes. *In vivo* studies were made by photomicroscopy of the conjunctival vessels of the eye simultaneous with the *in vitro* studies of blood from the same subject. *In vitro* cell aggregation correlated well with that observed *in vivo*. Fibrinogen levels had the most direct correlation with both *in vitro* and *in vivo* aggregation. Elevated levels of fibrinogen both *in vitro* and *in vivo* led to larger cell aggregates which were more resistant to the dispersing forces of higher shear stress. *In vivo* observations revealed the aggregates to be in the larger venules and in the arterioles—the latter leading to blockage of capillary flow and opening of arteriole-venous shunts. The high molecular weight globulins had a similar effect both *in vitro* and *in vivo*.

No. 168

P. A. G. MONRO: *Visual particle velocity measurement in fluid streams*

University of Cambridge, Cambridge, England

VISUAL measurement of the velocity of an object is quick and convenient and an optical aid such as a microscope or telescope may be used to form a visible image of adequate size. If this image moves through an arc greater than approximately 100° per second, it can no longer be followed by the eye and the image is seen as a streak. It is impossible to gain any idea of the velocity of such a streak and often not even of its direction. If the image is displaced by optical means in a plane at right angles to its original movement, the streak will be seen inclined at an angle. If the relative velocity of the moving image is the same as that of the displacement produced by the rotation of a glass block (or a mirror) the angle of the streak will be 45°. This angle gives the greatest accuracy since the eye can easily match this against a graticule line pre-set in the eyepiece. If the magnification of the image is known and if the speed of rotation of the glass block can be adjusted to a value which fulfils these conditions, and this value be known, the velocity of the object can be calculated or read off directly from a scale.

An instrument is described which can be used to measure a wide range of velocities of blood cells in living tissue or in a glass tube. The image of the blood vessel is first aligned in the optical slit by rotation of the K-mirror system. The blood flow in small veins is slow, not ordinarily exceeding 1 mm/sec, and can be measured by rotating the lower glass cube about its vertical axis so that the image of an illuminated spot is traversed to match the moving blood cells as seen in the lower eyepiece.

For the measurement of fast blood flow (in practice up to 5 mm/sec in arterioles of 12 μ bore) the image seen in the upper eyepiece is displaced by rotation of the upper glass cube about its horizontal axis so that the streaks are aligned with the streak image of the illuminated spot which is always inclined at 45°. The two glass cubes are coupled by 1:1

helical gearing driven by an infinitely variable ball and plate gear whose speed is known.

For the measurement of much faster flows of whole blood in glass cubes up to 100 μ bore a simpler eyepiece instrument can be used in which the glass block is driven by a small geared electric motor. This will measure particle velocities up to $10^5 \times$ their diameter/second and probably much faster speeds are possible under conditions of good optical contrast.

The appearance of the profile velocities across the diameter of blood streams in arterioles and fine tubes will be discussed.

No. 169

S. WITTE: *Flow pattern pertaining to vascular permeability as observed by fluorescence vital microscopy*

University of Erlangen, Erlangen, Germany

THE permeability of the blood vessels allows an exchange of substances and fluids between blood and surrounding tissues. The intravascular blood flow forms the basis of an undisturbed vascular permeability. Of special interest is the behavior of macromolecular material especially of the plasma proteins. Visibility of these proteins *in vivo* may be achieved by fluorescence labelling and observation by fluorescence microscopy (Rat mesentery). Various rheological phenomena may be observed there. Firstly the spreading of the labelled material after passing the wall of the terminal vessels will be demonstrated. Two different forms of spreading in the perivascular tissues may be distinguished. Normally tiny capilliform fluorescent streaks arranged in a network will develop. This phenomenon would be compatible with a flow along a preformed system. If permeability will be increased, pathologically, the extravascular fluid will spread in a diffuse cloudy manner. The velocity of spreading of fluorescent material was determined. It is increased in cases of disturbed permeability. Relations to the formation of lymphatic fluid may be observed. These investigations of the streaming interstitial fluid will give access to a new field of biorheology.

No. 170

P-I. BRÅNEMARK: *Intracapillary rheological phenomena as studied by direct microscopic observation in living animals and man*

University of Gothenburg, Gothenburg, Sweden

THE behavior of the corpuscular elements of the blood, including erythrocytes, granulocytes and platelets, as well as plasma constituents, such as chylomicrons, will be described and different types and degrees of corpuscular deformation analysed.

Special attention will be paid to the interaction between the blood corpuscles and the endothelial wall and its components, including a structural unit consisting of the endo-endothelial plasma layer, the nuclear region of the endothelial cell and periendothelial cells, e.g. so called mast cells.

These biological phenomena will be presented and illustrated in a film, showing blood capillary events in animals and man, as studied by vital microscopy at high resolution, thereby forming a basis and material for consideration of biorheological phenomena as they really occur in the living, intact organism.

SYNOPSIS

Zu Vortrag No. 165, HARDERS.

Auf die Frage nach der Methode der Blutdruckmessung an den Spider-Gefässen wurde geantwortet, dass bisher keine direkten Messungen durch Punktion möglich waren sondern nur mit Hilfe einer Mikrokapsel, wie sie von Ophthalmologen in Gebrauch ist. Die erhaltenen Werte sind ungenau. Vor allem sind die systolischen Blutruckserte zu hoch Über die Entstehungsbedingungen der Spider herrscht Unklarheit. Sie scheinen kein Beziehungen zu Serumglobulinveränderungen zu haben. Das Überwiegen des männlichen Geschlechts erklärt HARDERS mit dem bei Männern bevorzugten Auftreten einer alkoholischen Lebercirrhose. Dagegen besteht eine Beziehung zur Gravidität. Durch den Reiz des Cantharidenpflasters lassen sich bei Fällen mit Lebercirrhose Gefässveränderungen im Sinne von Mikrospider provozieren, nicht dagegen bei Gesunden. COPLEY weist auf die rete mirabilia hin, welche als arterielle kapilläre gefässnetze in Waalfischen vorkommen. Er fragt, ob etwa die Spider-gefässe bei den Patienten irgendwelche Ähnlichkeiten mit den rete mirabilia, deren Funktion unbekannt ist, haben.

Zu Vortrag No. 166, IRWIN and ALCAIDE.

Die Diskussion beschäftigte sich vor allem mit der Zusammensetzung der demonstrierten hyalinen weissen Emboli. Die von COPLEY und KNISELY vermutete Bildung aus Plättchen wurde von HARDERS aus Volumen-Gründen abgelehnt. BRÅNEMARK hält sie für eine Mischung aus verschiedenen Blutbestandteilen. COPLEY wies auf alte Befund von NOLF hin, wonach die Emboli aus Fibrin und Plättchen bestehen. Dabei Könnte es sich nach seiner Meinung um ein durch Fibrinolyse modifiziertes Fibrin handeln. Versuche mit Injektion von Fibrinolytica oder Serotonin-Antagonisten, nach denen gefragt wurde, hat IRWIN nicht angestellt.

Zu Vortrag No. 168, MONRO.

Im Anschluss an seinen Vortrag demonstrierte der Autor einen Film, der besonders das Strömungsverhalten in arteriovenösen Anastomosen demonstrierte.

Diskussionsbemerkungen waren hier ebenfalls nicht notiert. Auch hier könnte man den Autor nach seinen entsprechenden Aufzeichungen hierüber fragen.

Zu Vortrag No. 169, WITTE.

Zweifach fragte nach dem bevorzugten Ort der Gefässpermeabilität, der entsprechend den Literaturbefunden an den Venolen lokalisiert wird, sowie nach dem Verhalten der Fluoreszenz bei Stase. Witte antwortete, dass die Permeabilität für das fluoreszenzmarkierte Plasmamaterial ausser an Venolen auch an echten Capillaren gross ist. Die Ausbreitung im perivasalen Gewebe ist in der Umgebung der Capillaren unter normalen Bedingungen

signifikant schneller als an Venolen. Bei einer Stase tritt die Fluoreszenz nicht aus den betroffenen Gefässen aus. Man beobachtet vielmehr eine besonders starke intravasale Fluoreszenz, was mit einer Plasmaproteinkonzentration infolge eines perivasalen Verlustes von nicht-markiertem Blutwasser erklärt wird. Auf die Frage von ROWLANDS nach der Möglichkeit des Lymphstudiums mit der demonstrierten Versuchsanordnung erwiderte WITTE, dass man die Passage der markierten Flüssigkeit durch das Interstitium zu den Lymphbahnen, ihre Aufnahme in der Lymphe und den Abtransport durch die Lymphgefässe gut beobachten kann. COPLEY regte an, nach Korrelationen zwischen dem Permeabilitätsverhalten und der elektrophoretischen Zusammensetzung der markierten Flüssigkeiten zu suchen.

Zu Vortrag No. 170, BRÅNEMARK.

Die von Whitmore gestellte Frage, ob die demonstrierte Gefässströmung als turbulent oder laminar aufgefasst wird, blieb offen. Die Anheftung der Erythrocyten an der Gefässwand ist ein leicht pathologisches Symptom, erklärte der Autor auf eine Frage von Rowlands. Monro hielt sie für das erste sichtbare Zeichen einer Gefässwandschädigung. COPLEY korreliert das Phänomen mit der Gefässpermeabilität. Nach ZWEIFACH bleiben die Erythrocyten zwischen zwei benachbarten Endothelzellen stecken. DAVIS machte auf die merkwürdige Tatsache aufmerksam, dass Erythrocyten durch ein Loch in der Capillarwand treten können, das den wesentlich kleineren Plättchen offenbar verschlossen bleibt. Schliesslich wurde auf die Beobachtung hingewiesen, dass Erythrocyten eine Deformierung, die sie im Verlauf der Passage enger Gefässstellen erlitten haben, länger beibehalten als Leukocyten.

SESSION II (Z6)

Friday, 30 August, 1963

Biorheology of Tissue Materials

Chairmen: Professor G. VEJLENS, University of Gothenburg and Vasa Sjukhus, Gothenburg. Sweden
Dr. R. D. HARKNESS, University College, London, England

No. 171

MARGARET L. R. HARKNESS and R. D. HARKNESS: *Some mechanical properties of collagenous frameworks and their functional significance*

University College, London, England

THE soft tissues of vertebrates are built upon a framework of collagen, which provides tensile strength, and a limit to deformation under tension of short duration. Measurements of the limiting size of collagenous frameworks have been made from tension-length curves carried to the point of rupture in a number of tissues, in particular those of the reproductive tract of the rat under different physiological conditions. More prolonged tension leads to plastic extension in many collagenous frameworks which may progress to the point of rupture.

Measurements of this property of "extensibility", standardized to constant tension per unit cross sectional area of collagen to allow comparisons between different tissues, have also been made. Both size and plasticity of collagenous frameworks have been found to alter under different physiological conditions and these alterations appear to be of considerable functional importance. Changes in these properties were found also to take place unexpectedly rapidly. For example, in the female mammal the collagenous framework of the lower part of the reproductive tract is normally too small and rigid to allow the passage of an object as large as the mature foetus. During pregnancy two changes take place, first an anticipatory increase in the circumference of the collagenous framework of the birth canal and, second, an increase in its extensibility [1, 2]. Both these changes show rapid reversal towards normal after parturition [3]. Extensibility falls to normal values in 24 hr and circumference is reduced to about a third.

Changes of this type in the size of the collagenous framework of the horns of the uterus (independently of the contents) have also been found [4], but there is little or no alteration in extensibility which is much lower than that of the birth canal at the end of pregnancy. This fits with the function of horns which is to contain, and later expel, the foetuses by contraction, stretching the birth canal rather than its own tissue. The inextensibility of the collagenous framework of the horn could be of practical importance since its connection with the birth canal is close and any extension of this type of framework into the latter would be expected to cause difficulty in parturition.

Investigation of the same nature as above has been extended to the collagenous framework of the skin [5]. Extensibility was found to diminish greatly with age in the rat, and was correlated approximately with rate of growth [6].

The object of this communication will be to draw attention to the functional importance of these mechanical properties of tissues and briefly to discuss the mechanism by which they might be brought about.

REFERENCES

[1] HARKNESS, MARGARET L. R. and HARKNESS, R. D., *J. Physiol.* **148**, 524, 1959.
[2] HARKNESS, R. D., and NIGHTINGALE, MARGARET A., *J. Physiol.* **160**, 214, 1962.
[3] HARKNESS, MARGARET L. R., and HARKNESS, R. D., *J. Physiol.* **156**, 112, 1961.
[4] HARKNESS, MARGARET L. R., and HARKNESS, R. D. (Unpublished).
[5] FRY, PHYLLIS, HARKNESS, MARGARET L. R., HARKNESS, R. D., and NIGHTINGALE, MARGARET, A. *J. Physiol.* **164**, 77, 1962.
[6] HARKNESS, MARGARET L. R. and HARKNESS, R. D. (Unpublished).

No. 172

L. DINTENFASS: *Rheology of synovial fluid and its role in joint lubrication*

University of Sydney, Sydney, Australia

A STUDY of rheology of synovial fluid was carried out by means of a cone-in-cone rotational viscometer. Samples of synovial fluid were obtained from traumatic arthritis and rheumatoid arthritis cases. An attempt was made to explain friction and lubrication in normal and abnormal joints using the available data.

The theories of lubrication were reviewed and it was concluded that neither the hydrodynamic theory nor boundary theory permits an adequate description and explanation of lubrication in synovial joints.

It is suggested that joint lubrication depends on the existence of a thixotropic and elastic fluid between the articular surfaces, that the area of the load-carrying film depends on the elasticity of cartilage, and that the velocity gradient existing in the gap between articular surfaces depends also on the lateral movements of these surfaces.

Synovial fluid is characterized by thixotropic and elastic properties. Its viscosity decreases with an increase in the rate of movement, but it is pressure-resistant under sudden impact. Due to its visco-elastic properties (i.e., normal stress effect) and due to its affinity to the surfaces, it cannot be squeezed out from the area between the opposing surfaces. If, however, synovial fluid undergoes any chemical or physical changes resulting in its acquiring Newtonian properties, it may be squeezed out and it is no longer capable of carrying a constant load at all rates of movement. Such changes will result in a damage to the articular cartilage since the elasticity, resilience and the slippery characteristics of the cartilage would not be sufficient to prevent an increased friction. Also, there exists a possibility that the elastic properties of the cartilage undergo simultaneous changes, as part of the free volume within the porous cartilage is made up of the synovial fluid.

On the other hand, synovial fluid *per se* is not sufficient to maintain an efficient lubrication in the presence of rigid or damaged cartilage. When the cartilage degenerates or disappears, the synovial fluid may be expected to undergo mechano-chemical degradation, analogous to mechanical degradation of polymers at high rates of shear. Degraded fluid will not show

any more proper lubricating and shock-absorbing properties. This, in turn, might cause further wear and tear on articular surfaces.

The proposed outline explains the interdependence of synovial fluid and articular surfaces in joint lubrication.

No. 173

W. PIGMAN, G. MATSUMURA, M. DE SALEGUI and A. HERP: *Factors affecting the viscosity of hyaluronic acid.*

New York Medical College, New York, U.S.A.

HYALURONIC acid exists in connective tissue as a linear polymer with a molecular weight of about 8 million. In solution its viscosity is dependent upon the rate of shear, probably because of its tendency to form weak gels at physiological concentrations. It occurs in the "ground substance" or matrix between the cells of connective tissue and presumably provides a gel structure through which substances required by the cells must diffuse from the blood capillaries. Waste products move in reverse order from cells to the capillaries. The hyaluronic acid gel provides a barrier which may control the movement of metabolites through the tissue. The mechanical "pore" effect may be modified by the degree of polymerization of the hyaluronic acid any by the presence of carboxyl groups (on the glucuronic acid constituent) at distance of 10–15 A throughout the gel structure.

Evidence will be given that hyaluronic acid can form loose "complexes" with serum proteins, especially serum albumin. This was shown by the increased electrophoretic mobility of serum proteins in the presence of hyaluronic acid and by the formation of a new electrophoretic component, called the Pi component. Depolymerization of hyaluronic acid reduced its ability to bind proteins.

Evidence will also be given that the state of polymerization of hyaluronic acid may be controlled by an auto-oxidation process through an oxidative chain probably involving metallic ions and "reducing substances" such as ascorbic acid. This reaction called the ORD reaction (oxidative-reductive depolymerization) seems to be a free radical reaction.

Another mode of depolymerization of hyaluronic acid will be described. Serum proteins at pH 3 rapidly degrade the viscosity of hyaluronic acid. This reaction could be enzymatic or could be a variation of the ORD reaction with proteins acting as carriers in auto-oxidation.

No. 174

B. J. RIGBY: *Thermal transitions in native collagen and their physiological significance.*

Commonwealth Scientific and Industrial Research Organization, Ryde, Australia

NATIVE collagen under conditions resembling the *in vivo* state exhibits structural transitions when heated. The best known of these is the shrinkage temperature, Ts, which for mammalian samples occurs around 60°C. Other transitions occur, however, and interest is directed here particularly at transitions occurring in the neighborhood of normal blood temperature (38°C). Thus in the unstrained material there is a glass→ rubber type transition

temperature close to 40°C manifested by an abrupt increase in the thermal expansion coefficient. Moreover, when the sample is under strain, the mechanical properties show irreversible behavior if the temperature rises above 40°C; for example, a specimen of tendon under tension is permanently deformed.

From a study of the collagen of other species it is known that some, if not all, of these transitions are correlated with the same amount of proline and hydroxyproline in the sample, a lowering of these two amino acids being associated with a lowering of the transition.

A reduction in the amount of proline and hydroxyproline in collagen and/or an increase in body temperature to above normal could allow the lower structural transition to take place *in vivo*.

It is suggested that these transitions might be considered as possible causative factors in collagenous disease such as, for example, rheumatoid arthritis.

No. 175

H. COREY: *The subsidence of muscle fiber dispersions*

T. J. Lipton Inc., Hoboken, U.S.A.

THE settling behaviour of meat dispersions was investigated as a possible objective method for the evaluation of texture.

Samples of cooked, freeze-dried chicken meat were dispersed in a Waring blendor with deionized water and the resulting slurries deaerated and "aged" before experiments were begun. Prior to the onset of settling, these dispersions form large flocculated structures which apparently undergo syneresis. The distance-time data give curves that are invariably S-shaped and can also in part be fitted to the La Mer subsidence expression $t/(h_0 - h_t) = \alpha + \beta t$ whereby the expected linearity is observed.

The several variables of the system including particle size, percentage solids, salt (NaCl) concentration, "aging" time, shearing time in blendor and vessel geometry were examined for their effect on the linear region of the La Mer plot. Of particular interest is the observation that under conditions where floc formation is the dominant initial phase, the magnitude and relative displacement of the slopes are hyperbolic functions of the initial height and the percentage solids in the dispersion. For any given percentage solids the slopes *increase* in magnitude with *decreasing* column height. When the height is kept constant the slopes *decrease* in magnitude with *increasing* percentage solids.

The subsidence velocity of these muscle fiber dispersions exhibits a marked dependence on the starting height of the system. This remarkable phenomenon leads to the conclusion that the mechanism of settling can be considered an overdamped elastic recoil. On this basis a modified form of the well known vibration equation was derived:

$$h = C_1 e^{-u_1 t} + C_2 e^{-u_2 t} + f(t).$$

This proves adequate to describe completely the general form of all the settling curves obtained. In a particular case, with proper choice of spring constant and damping factor, the calculated time-distance curve closely matches that drawn from experimental data. Since the major exponential terms diminish rapidly with time, the vibration equation also

predicts a linear decay of velocity as does the La Mer expression. Thus the physical picture of homogeneous density during compression required by the La Mer treatment may very well represent the limiting mode of behaviour for the elastic recoil model.

No. 176

HANS H. PFEIFFER: *Polarization optics of spinning threads drawn from the vitreous humor of animal eyes as expression of their biorheological behavior*

Laboratorium für Polarisations-Mikroskopie, Bremen, Germany

THE vitreous humor of eyes of *mus musculus* and other mammalia shows the phenomenon of fibrogenesis (in German: Fadenziehen, Spinnvermögen). Such a deformation of the substance must be associated with an orientation of the leptones. Thus, polarization optics can lead to some notable contributions to our knowledge of the structure of the threads. Polarization methods may be qualitative, merely to detect the presence of orientated structure, but more valuable information can be obtained by quantitative application (see Hans H. Pfeiffer, *Das Polarisationsmikroskop als Messinstrument in Biologie und Medizin* Braunschweig 1949, Friedr. Vieweg & Sohn). With the threads drawn from the vitreous humor, one observes flow birefringence, and this effect may be measured by the angle of isocline (Auslöschwinkel) χ, which indicates the position of the index ellipsoid. By means of an adjustable precision split, one must darken an area outside of the axis of the thread. Then the result is, depending on the viscosity and yield stress, a value of $\chi = 65$ to $72°$. In the diagonal position of the nicols one then determines, by means of little plates of plaster, Red 1st order, or a quartz-wedge, the positive character of the anisotropy. By means of a variable azimuth compensator of fixed retardations, according to Köhler and Brace, together with a half-shadow plate, according to J. Macé de Lepinay, one measures the intensity of flow birefringence. This value is reduced to unity of thickness of threads, yield stress and viscosity. It is remarkable that the intensity of anisotropy, determined in this way, shows a minimum at central places of the thread which can be interpreted as due to a weaker orientation within central parts as a result of different strain rates. From experiments in stretch-hardening with a spinning balance, according to Nitschmann and Schrade, a considerable increase of birefringence was observed. It increases, in general, at first linearly, then more slowly with the strain rate until saturation. The leptones of the vitreous humor, in this manner, cannot be compared with colloid associates which fall herewith in less anisotropic or quasi-isotropic micro-leptones. At a rapid pressure stop a certain inverse flowing occurs. This flow elasticity can be found together with higher and lower values of flow birefringence (PFEIFFER, *Biorheology* **1**, 111, 1963). At increasing temperature, the optimal anisotropy of the thread decreases because of compensation of orientating effects by a growing liveliness of the Brownian movement. In some experiments, a turbidity of the vitreous humor was observed, perhaps called into being by a *synchisis scintillans*, and in connection with that, a higher viscosity and a lower flow birefringence occurs. As the optical anisotropy of flowing substances can manifest itself also in anisotropic absorption or dichroism, experiments and measurements of this phenomenon have likewise been done with the same material. From our findings, it may be concluded that a corroboration of the interpretation of spinning of threads is implied as an effect of orientation of the leptones.

SYNOPSIS

Paper 171. MARGARET L. R. HARKNESS: and R. D. HARKNESS Some physical properties of collagenous frameworks and their functional significance.

The author was asked if the layer of keratin over the skin of the rat could affect the physical properties. He replied that this layer is very thin. Such evidence as had been obtained (for example by stripping it off with Scotch tape, by the use of collagenase and heat) indicated that it was not important in the tests used.

Paper 172. LEOPOLD DINTENFASS: Rheology of synovial fluid and its role in joint lubrication.

This paper was read, in the absence of the author, and there was no discussion.

Paper 173. WARD PIGMAN, GO MATSUMURA, M. DE SALEGUI and A. HERP: Factors affecting the viscosity of hyaluronic acid.

Dr. HARKNESS asked if he had any more to say about the function of hyaluronidase as a lubricant in connective tissues as he thought this was an important subject which had been much neglected. He said that he had used it in an attempt to sort out the nature of interfibrillous material and found that it had little effect on the rate of creep under constant load, reducing it if anything, suggesting that either a substrate, or conceivably hyaluronic acid, had a lubricating function.

Paper 174. B. J. RIGBY: Thermal transitions in native collagen and their physiological significance.

Someone inquired if the collagen molecule was still considered to be a triple helix and the reply was "yes".

There was a technical discussion on the results shown in one of the slides which it is impossible to describe without the original data.

Paper 175. H. COREY: The subsidence of muscle fiber dispersions.

The author was asked if his heat dispersions were analogous to a spring system. The answer was "no, but if you put collagen gels into an ultra-centrifuge, you do see signs of a spring system."

He was also asked if particles settling in the air can be treated in the same way and replied that he did not know since his work had been restricted to a flocculated solid in a liquid.

He was also questioned about the method of standardizing the size of the particles, and said it was merely to treat them in a Waring blendor for a constant time. He said that when he divided his suspension into two, and put one half through a colloid mill he got very small particles which took much longer to aggregate.

Dr. HARKNESS pointed out that tender meat in a Waring blendor for a standard time would probably end up as different particles from tough meat, and this might be the true cause of the difference in settling behaviour. The author agreed that this was largely the basis of the effect.

Paper 176. HANS H. PFEIFFER: Polarization optics of spinning threads drawn from the vitreous humor of animal eyes as expression of their biorheological behavior.

Dr. HARKNESS asked if Dr. PFEIFFER had observed any position difference in the properties of the vitreous humor described in his paper and he said he had not.

SESSION III (Z7)

Friday, 30th August, 1963

Blood Clotting and Low Shear Hemorheology

Chairmen: Dr. M. JOLY, Institut Pasteur, Paris, France
Professor K. M. BRINKHOUS, University of North Carolina, Chapel Hill, U.S.A.

No. 177

M. E. LEROUX: *Les propriétés hémorhéologiques du caillot et la fonction thrombodynamique des plaquettes*

Université d'Orléans, Orléans, France

L'AUTEUR a montré en 1957 que la propriété physique des caillots explorée par le thrombélastographe de HARTERT n'est pas convenablement réductible à l'élasticité. Elle est très complexe mais spécifique et représente l'aptitude des caillots à effectuer un travail mecanique. Pour cette raison, le terme de *thrombodynamographie* doit etre préféré à celui de thrombélastographie et il convient de désigner la propriété spécifique explorée sous le nom de *propriété thrombodynamique*. L'expérimentation et la clinique démontrent que sa normalité témoigne d'une aptitude physiologique des caillots à l'hémostase.

Des plaquettes participent à l'élaboration et à la structuration du caillot, dès le stade le plus précoce de la fibrino-formation. L'auteur appelle cette fonction des plaquettes la fonction *thrombodynamique*. Il s'agit d'une fonction vitale à laquelle participe l'élément figuré tout entier, sous sa forme spiculaire apte aux activités vitales, pourvue d'une atmosphère plasmatique péri-plaquettaire bio-active, capable d'entrer en métamorphose visqueuse. La fonction thrombodynamique des plaquettes représente l'archétype des activités plaquettaires de l'hémostase. Elle se distingue fondamentalement de la fonction prothromboplastique et des autres activités plaquettaires de la coagulation.

L'auteur a démontré que la thrombodynamographie permet d'étudier et de mesurer la rétraction du caillot, qui est liée à l'activité évolutive, dans le caillot, des plaquettes thrombodynamiques. Deux forces antagonistes d'arrangement interne gouvernent à tout moment la structuration et l'évolution dynamique du caillot: une force de synérèse, liée aux structures de fibrine et une force de rétraction, liée aux plaquettes. Dans le caillot normal, les forces de rétraction finissent par l'emporter. Au contraire, certains caillots pathologiques évoluent indéfiniment vers la synérèse.

L'enregistrement thrombodynamographique simultané de la coagulation du plasma riche en plaquettes (PRP) et du plasma déplaquetté (PDP) permet d'explorer le comportement respectif des divers facteurs qui participent à la structuration du caillot. L'amplitude maxima des diagrammes de PDP (Am PDP) dépend de la masse de fibrine (donc du fibrinogène), du facteur de stabilisation de la fibrine de LORAND et LAKI (fibrinase de LOEWI) et de certains facteurs sériques accessoires. L'amplitude maxima des diagrammes de PRP (Am PRP) dépend en outre des plaquettes thrombodynamiques.

La différence Am (PRP)—Am (PDP) est une constante spécifique de la fonction thrombodynamique des plaquettes. Sur ce principe, il est possible d'explorer l'activité thrombodynamique des plaquettes. Sur ce principe, il est possible d'explorer l'activité thrombodynamique globale ou individuelle des plaquettes présentes.

Une adynamie du caillot est réalisée au cours des thrombopénies et des thrombopathies de la fonction thrombodynamique. Une hyper-thrombodynamie est au contraire présente dans tous les cas d'hyperplaquettose numérique ou fonctionnelle. Il en résulte diverses images graphiques d'hyper-rétractilité. Leur analyse permet de comprendre pourquoi l'hyper-rétractilité est à la fois la cause de thromboses et d'hémorragies.

No. 178

H. HARTERT: *Clot retraction. Kinetics and correlation with the clotting process*

University of Heidelberg, Heidelberg and Municipal Hospital, Kaiserslautern, Germany

CLOT retraction is usually understood as a behaviour of the blood clot occurring some time after the termination of clotting. On this supposition, various explanations for the retraction of the blood clot have been given: namely, it seems to approach the rims of a wound, or it may play its part in the recanalization of thrombosed vessels. As could be shown in our experiments, retraction originated simultaneously and with clot formation.

A clot in the test tube must usually counteract several resistances before it is able to bring about or to complete retraction. One of these resistances is the clot's adherence to the wall of the container. It is paralleled by the surface skin of clots suspended in oil (e.g. as in the Hirschboeck method), which has to be torn before the volume of the clot is allowed to shrink. The other category of resistance is the relatively very high viscosity of the serum creeping through the narrow meshes of the clot, which become more and more narrow, as the clot contracts.

If by special methods both the resistances mentioned are reduced to a minimum value, retraction will start immediately with the clotting process; in this way retraction may indicate clotting as well as any other continuously recorded measurement of the clotting process, provided that there are viable blood platelets in the clotting substrate.

Experiments to explain the nature of the retraction process revealed, that the fibrin strands are stretched exclusively during the clotting process, first of all in an isometric way. This strain, comparable to that of a spring in a wound-up clock, may operate at any time after its winding when the pendulum is set free. Yet the time of operating ability is restricted by a gradual relaxation of the strain in the course of several hours. On the average it is reduced to two thirds of the starting value, four hours after the clotting has been completed.

If the early clotting process is interrupted by cold treatment shortly after the beginning of contraction activity, the retraction will stop as well. If the substrate is warmed up again, both processes of clotting and retraction continue.

After completion of the clotting process, cooling does not have any effect on the retraction activity. This means that the clot structure is stretched for contraction activity only during the phase of chemical activity of the clotting process. As has been proved by several authors

in different kinds of experiments, a strong relation seems to exist between the ATP activity of the platelets involved and the retraction activity of the clot. These findings are an explanation for the impaired retraction in defective platelets.

It appears from these mentioned basic physical phenomena that the progress of retraction in containers of great diameters is very slow. There the retraction strain may have come to an end before the retraction has reached its smallest possible volume.

No. 179

S.-E. BERGENTZ: *Fat embolism: A hemorheological disturbance*

University of Gothenburg, Gothenburg, Sweden

FAT does not occur normally in plasma in free form, but bound as lipoprotein of various density. The term "fat embolism" indicates a pathological condition which occurs when fat appears in the vascular bed as free droplets, which can be visualized by fat stains.

For almost 100 years the explanation for the genesis of fat embolism has been that fat droplets enter the blood stream from the bone marrow after bone fracture and are transported to the lungs. Even if this explanation may have some bearing on post-traumatic fat embolism, it cannot definitely explain the fat embolism seen after various kinds of infection, intoxication, and metabolic disturbances, nor after cardiopulmonary by-pass. In addition it cannot explain the clinical picture of fat embolism, since it has been demonstrated that the amount of bone marrow fat, tolerated intravenously, is very high and possibly higher than the fat content in the bone marrow of a whole femur.

We have found that fat embolism can be produced by initiation of an intravascular coagulation process, caused by injection of thromboplastic substances or by the disruption of platelets which occurs in extracorporeal circulation. A major trauma, such as fracture or massive soft tissue injury, also initiates a generalized coagulation process. This is indicated by the fact that ligation of the femoral vein in the rabbit, which does not cause a thrombus in the normal animal, does so within a few hours after soft tissue injury even in the contralateral limb. It is also indicated by the formation of platelet aggregates after trauma; by a decrease in the number of platelets; by a consumption of the various coagulation factors; and by a tendency to shortening of the coagulation time. The relationship between the initial part of the coagulation process and formation of fat droplets has been established microscopically. This was shown in dark field illumination and with a special staining technique of the white part of a freshly formed thrombus, where an accumulation of large amounts of chylomicra, aggregates of chylomicra, and fat droplets of various sizes were found.

From these and other experimental studies it is concluded that injury causes such physical changes in blood that fat droplets are formed from the fat contained in blood. These changes represent the first sign of alteration of the rheological properties of blood, induced by trauma, and probably are closely related to the initial step of the coagulation process.

No. 180

L. DINTENFASS: *A study of the rheology of blood clotting in human subjects*

University of Sydney, Sydney, Australia

A STUDY of viscosity and clotting of human blood was carried out by means of a cone-in-cone viscometer. Blood samples were obtained from normal donors and from patients suffering from coronary occlusion, venous thrombosis, polycythaemia, haemophilia and anaemia.

Clotting was followed in each sample at one particular rate of shear and the results plotted as viscosity against the time which had elapsed from the moment of extraction of blood. At least two samples were used in each case in order to study behaviour at low and at high rates of shear. Viscosity of blood was also measured in its unclotted state, but in the absence of anti-coagulants.

It was observed that clotting takes place after various time periods, depending not only on the intrinsic properties of the particular blood sample, but also on the temperature and on the velocity gradient.

The effect of the latter is most significant. In many cases, a consistently more rapid clotting takes place at higher rates of shear, at temperature 37°C. At lower temperatures this pattern may be reversed, and clotting might take place more rapidly at lower rates of shear. An application of a cone-in-cone viscometer allows one to distinguish between various patterns of blood clotting.

It appears that the molecular and the colloidal mechanisms of clotting move along different pathways depending on the velocity gradient. Relevance of these observations to thrombosis and anti-coagulant therapy is indicated.

No. 181

E. W. MERRILL, W. MARGETTS, G. R. COKELET, A. BRITTEN and E. SALZMAN: *Importance of fibrinogen in the low shear rheology of human blood*

Massachusetts Institute of Technology, Cambridge and Massachusetts General Hospital, Boston, U.S.A
Columbia University, New York, U.S.A.

BY MEANS of a Couette viscometer (GDM) described in *Trans. Soc. Rheology*, 7 by GILINSON, DAUWALTER and MERRILL, and in continuation of experimental procedures and correlation methods described by COKELET, MERRILL *et al.* described in *Trans. Soc. Rheology* 7, further studies were made on the role of fibrinogen in the rheology of blood measured near and at zero shear.

These studies include (a) correlation of the rheological parameters (including yield stress) with the measured fibrinogen content of numerous samples of normal human blood, (b) unique properties of blood from a patient with afibrinogenemia, (c) comparison of the rheological properties of suspensions of red cells in the Cohn fractions (courtesy Protein Foundation, Boston) and (d) the effects produced by increasing albumin concentration in the presence of fibrinogen.

No. 182

M. I. GREGERSEN, B. PERIC, S. CHIEN, D. SINCLAIR, C. CHANG and H. TAYLOR: *The influence of erythrocyte size on the viscosity of blood at low shear rates*

Columbia University, New York, U.S.A.

FRESHLY drawn blood from several species of mammals including elephant, man, dog, sheep and goat was used for the investigation of the effect of red cell size on the relation between viscosity and volume concentration of cells. The mean corpuscular volume of erythrocytes in these species ranged from 20 μ^3 (goat) to 114 μ^3 (elephant). Viscosity was determined at 37°C with the G.D.M. air-bearing Couette viscometer (P. J. GILINSON, Jr., C. R. DAUWALTER and E. W. MERRILL, *Trans. Soc. Rheol.* 7, 1963) at shear rates ranging from 100 sec^{-1} down to 0·05 sec^{-1}. The studies were made simultaneously on heparinized blood, defibrinated blood and on washed cells suspended in Ringer-Locke solution. In each instance a series of samples was prepared in which the hematocrit value ranged from about 10 to 70 or 80 per cent. The exact volume per cent cells (H) was ascertained by conventional hematocrit determinations corrected for "plasma trapping" in the red cell column.

On a semi-log plot (log of viscosity versus volume per cent erythrocytes) the results of the tests consistently showed a straight line relationship, (i.e. $\log \eta = aH + b$, where a and b depend not only on shear rate and suspending medium but also on the mean corpuscular volume of erythrocytes).

The results reveal that cell size has a marked effect upon viscosity. For example, if the viscosity of heparinized blood in the goat and the elephant is compared at a given shear rate and at a given hematocrit (corrected for plasma trapping) the viscosity of elephant blood is several times higher than that of goat blood. Similar differences are also observed using defibrinated blood and red cells suspended in Ringer-Locke solution. The most convincing evidence appears from the experiments on washed cells suspended in Ringer-Locke solution where the possible effects of differences in the suspending medium are eliminated.

Shear stress-shear rate plots of the data indicate the existence of a yield stress in heparinized blood as well as in defibrinated blood and in washed cell suspensions. These yield values appear to increase with cell size and also to vary with the suspending medium.

SYNOPSIS

(1) Dans son exposé sur les propriétés hémorhéologiques du caillot et la fonction thrombodynamique des plaquettes M. E. LEROUX montre que l'emploi du thrombo-élastographe de Hartert renseigne sur des propriétés des caillots autres que l'élasticité et il introduit la notion de propriété thrombodynamique et de fonction thrombodynamique des plaquettes. Le rôle fondamental de celles-ci est mis en évidence ainsi que les multiples interférences avec les fonctions du fibrinogène, du calcium, et de nombreux autres facteurs. Leur intervention dans la lyse des caillots ou dans la synérèse est précisée. L'auteur tente de définir les diverses forces plus ou moins antagonistes qui interviennent dans la structuration et dans l'évolution normale ou pathologique des caillots.

K. M. BRINKHOUS demande des précisions numériques sur l'effet du nombre de plaquettes présentes.

H. HARTERT conteste le point de vue de M. E. LEROUX et considère que le thrombo-élastographe ne mesure que l'élasticité du caillot et non la fonction thrombo-dynamique.

Je pense que cette divergence d'opinion ne fait que refléter un malentendu. Il y a d'une part la grandeur mesurée, qui est en fait la rotation d'un plongeur dans des conditions particulières déterminées et qui peut, en première approximation, être relié à une élasticité apparente: celle d'un système homogène continu purement élastique dont la déformation, dans les mêmes conditions cinématiques, provoquerait le même déplacement du plongeur que celui observé en présence du système hétérogène complexe qu'est un caillot en cours d'évolution. Il y a d'autre part la signification de la grandeur "fictive" ainsi arbitrairement choisie, c'est-à-dire son interprétation en termes de structure, d'interaction, d'organisation et éventuellement d'évolution du caillot. H. HARTERT met l'accent sur le premier aspect de la thrombodynamographie tandis que M. LEROUX s'attache surtout à dégager les éléments du second aspect, même si cela l'oblige à introduire un plus grand nombre d'hypothèses.

(2) H. HARTERT, dans son exposé sur la cinétique de rétraction du caillot et sa corrélation avec le processus de coagulation, s'efforce d'analyser les différents facteurs qui interviennent dans ce phénomène complexe, et insiste sur le fait que la rétraction du caillot et sa formation sont des processus simultanés. L'importance des surfaces solides et des variations de tension interfaciale est mise en évidence ainsi que le rôle du sérum qui accroît la rétraction. Un point particulièrement important est la possibilité de "mise en réserve" de la déformation de rétraction, ainsi que l'effet très marqué de la température. De même, le rôle très net joué par l'ATP produit par les plaquettes montre que le phénomène de rétraction comprend une partie chimique et une partie physique

M JOLY demande quelques précisions sur la tension interfaciale que l'auteur fait intervenir et sur la façon dont elle est déterminée

(3) Dans sa présentation du travail de S. E. BERGENTZ sur l'embolie graisseuse, L. E. GELIN insiste sur la relation étroite qu'il y a entre l'apparition des gouttelettes de lipides dans le sang et le processus de coagulation provoqué par les traumatismes. Il semble bien que ce soit la thrombose qui entraîne l'agrégation des chylomicrons et des gouttelettes lipidiques dont la formation est d'ailleurs très précoce. De nombreuses expériences montrent que les lipides de ces gouttelettes n'ont pas une origine extra sanguine contrairement à ce qui a été cru pendant longtemps.

Sur une question le présentateur précise qu'après les traumatismes on observe un changement très notable de la distribution des lipides du sérum, en particulier un accroissement important du taux de triglycérides.

(4) Le travail de L. DINTENFASS sur la rhéologie de la coagulation du sang humain est présenté par R. B. WHITTINGTON. Après avoir décrit le viscosimètre utilisé, le présentateur insiste sur l'influence du mode de prélèvement du sang et montre des courbes représentant la variation de la viscosité apparente en fonction du temps pour diverses valeurs de la vitesse de cisaillement. Celle-ci, ainsi que la température, agit grandement sur la vitesse de coagulation. Cette action du gradient de vitesse est particulièrement importante pour l'étude de la thrombose. Les comportements des divers sangs normaux et pathologiques étudiés peuvent être classés suivant un certain nombre de types caractéristiques. L'attention est attirée sur le rôle éventuel des globules sanguins dans le processus de coagulation.

H. HARTERT fait des réserves sur l'état du sang dans le viscosimètre à cônes utilisé, mais R. B. WHITTINGTON en justifie l'emploi.

L'influence de la vitesse de cisaillement sur la vitesse de coagulation peut vraisemblablement être rapprochée de l'action de la vitesse de cisaillement sur les processus de prégélification que l'on observe fréquemment, même avec des systèmes aussi simples que des solutions aqueuses de gélatine ou de copolymères de l'acide acrylique et de l'acrylonitrile. Il serait intéressant de rechercher si, pour la coagulation sanguine, on peut, comme pour ces gélifications, trouver, dans des conditions données, une vitesse de cisaillement pour laquelle la vitesse de ces processus passe par un maximum.

(5) W. G. MARGETTS présente un travail collectif de E. W. MERRILL, W. G. MARGETTS, G. R. COKELET, A. BRITTEN, E. W. SALZMAN, R. B. PENNELL et M. MELIN sur l'importance du fibrinogène et l'influence des protéines du plasma sur la rhéologie du sang humain aux faibles forces de cisaillement.

Après avoir indiqué les avantages de l'emploi de l'équation de Casson dans l'étude rhéologique du sang il met en évidence l'intervention de l'orientation des rouleaux. La linéarité de la racine carrée de la tension de cisaillement seuil en fonction de la concentration en fibrinogène est démontrée pour diverses valeurs de l'hématocrite supérieures à une valeur critique au-dessous de laquelle l'écoulement est purement visqueux. Les résultats sont comparés avec ceux que l'on obtient par adjonction de protéines plasmatiques autres que le fibrinogène. Dans leur tentative d'interprétation des faits observés les auteurs envisagent des modifications de la surface des globules. Des mesures de comparaison ont été effectuées avec des suspensions aqueuses de globules.

(6) M. I. GREGERSEN expose le travail qu'il a fait en collaboration avec B. PERIC, S. CHIEN, D. SINCLAIR, C. CHANG et H. TAYLOR sur l'influence de la taille des erythrocytes sur la viscosité du sang à faible vitesse de cisaillement.

L'étude au moyen du viscosimètre de précision G.D.M. permet de mettre en évidence, pour une même valeur de l'hématocrite, une influence des dimensions des globules sur les propriétés rhéologiques du sang, en particulier sur la tension seuil d'écoulement pour diverses valeurs de la vitesse de cisaillement. Les divers paramètres sont déterminés par l'emploi convergent de différentes techniques. En particulier des rapprochements sont faits entre les résultats de la viscosité et ceux de l'électrophorèse.

Les sangs de diverses espèces de mammifères sont comparés, en fonction de l'hématocrite, et aussi par rapport à la composition du sérum. De même est examinée l'influence de l'héparine et des milieux de suspension artificiels.

L'emploi de la représentation de Casson permet de dégager une relation entre la tension seuil et le volume des cellules. La question se pose de la signification physiologique des propriétés rhéologiques et, d'une façon générale, de leurs conséquences en ce qui concerne les divers problèmes posés par la circulation sanguine.

Au cours de la discussion on signale l'intérêt qu'il y aurait à étudier aussi des globules nucléés tels que ceux d'oiseau. Il serait également important d'arriver à préciser l'éventuelle influence de la plus ou moins grande déformabilité des globules en fonction de la vitesse de cisaillement.

BIORHEOLOGICAL TOPICS OF INVITED PAPERS BEFORE THE ENTIRE CONGRESS

Thursday, 29 August, 1963

A. KATCHALSKY: *Mechanochemistry*

Weizmann Institute of Science, Rehovot, Israel

MECHANOCHEMISTRY is the study of the conversion of chemical energy into mechanical work and of vice versa, mechanical work into chemical energy in cyclic processes. The natural mechanochemical conversions take place, as a rule, in contractile macromolecular systems endowed with the property that extent of reaction determines molecular shape and conversely molecular shape determines extent of reaction. This coupling of contraction and degree of reaction is generally found in polyelectrolytes or in polymers at phase transition. It is a simple case of cybernetics in which the mechanochemical properties of the contractile macromolecules provide the feed-back mechanism.

For reversible mechanochemical systems, the classical thermodynamic treatment is readily applicable to provide the conditions of conversion of chemical into mechanical energy in cyclic processes. A mechanochemical equivalent of Kelvin's principle is derived and the differential characterization of a mechanochemical field is given.

The MAXWELL relations obtained from the general thermodynamic expressions were used to test the reversibility of mechanochemical performance in various real systems, both natural and synthetic. The systems considered were polyelectrolytes under neutralization or ion exchange, the redox systems of KUHN *et al.*, contractile collagen fibers and muscle.

The last part of the paper is devoted to the analysis of mechanochemical rate processes by the methods of the thermodynamics of irreversible processes. The coupling of the rate of chemical reaction in the fibers with their rate of contraction is described by phenomenological equations and some general relations between the kinetic parameters derived. It was possible to derive in a general thermodynamic manner the celebrated equation of A. V. HILL for the rate of muscular contraction without applying any specific model.

Friday, 30 August, 1963

Chairman: Professor E. H. MÜLLER, Marburg University, Marburg/Lahn, Germany

No. 184

R. L. WHITMORE: *Some flow properties of blood*

University of Nottingham, England

THE paper considers in non-biological terms, some of the reasons why the rheological properties of blood may have physiological and pathological significance. Present-day

knowledge of the rheology of blood is then summarised and the dynamics of its flow in living bodies and in capillary tubes is examined. The various anomalies and conflicting opinions on its flow behaviour are considered and an attempt made to resolve them in terms of particle mechanics and hydrodynamics. It is concluded that existing theory is insufficiently advanced to be applied with confidence to the problem but that further clarification of its observed flow behaviour is also essential.

Friday, 30 August, 1963

Chairman: Professor H. KOLSKY, Brown University, Providence, R.I., U.S.A.

No. 21

N. KAMIYA: *Rheology of cytoplasmic streaming*

Osaka University, Osaka, Japan and Princeton University, Princeton, U.S.A.

The cytoplasm of living cells often exhibits vigorous streaming. One of the most striking examples of this is found in plasmodial masses commonly known as slime molds. Of many species of these slime molds, or myxomycetes, *Physarum polycephalum* is especially favorable for experimental work, since it is easily cultivated in the laboratory. Unlike cells of most plants, slime molds have no cell walls during their vegetative or growth stage.

Among the motions of which these slime molds are capable are (1) rapid flow of cytoplasm which shuttles back and forth every minute or so, (2) regular contractions and expansions of the contour which are synchronized with the streaming inside, and (3) a twisting of the strands in which the streaming occurs.

The velocity distribution of the endoplasmic flow along the plasmodial capillary takes the form of a revolution of a flat-headed parabola. It is inferred from this fact that the endoplasm is non-Newtonian and its flow is caused by a local difference in the internal pressure of a plasmodium.

Through the development of a double-chamber method, it is possible to counteract by gas pressure the force which moves the endoplasm. Two blobs of a dumbbell-shaped plasmodium are placed in a divided chamber connected by a strand, so that normally cytoplasm shuttles back and forth between the blobs through a channel in the strand. When gas pressure is applied to one chamber, flow can be either accelerated or reversed at will. If, by this means, endoplasm in the strand connecting the two blobs of protoplasm is held still, the counter-pressure applied is a measure of the motive force responsible for streaming.

The balance-pressure which is just sufficient to keep the endoplasm immobile changes rhythmically. The range of this pressure, and therefore, the range of the strength of the streaming force, is between ± 20 cm of water. Consecutive values of the balance-pressure plotted against time yield undulating curves ("dynamoplasmogram") which portray all the characteristics of the spontaneous rhythm of the slime mold, such as frequency, amplitude and wave form. This rhythm has been shown to be sinusoidal in the simplest cases, but polyrhythmic tendencies have also been noted. The double-chamber method gives us a

unique opportunity to test the effect of various physical and chemical agents on the production of the motive force.

Another aspect of the behavior of the slime mold protoplasm which is of special interest and is closely related with the protoplasmic streaming is a tendency of the slime mold to twist itself. If a strand is hung in the air with one end free to rotate, it twists back and forth, but always more in one direction than in the other. The result is that it twists itself indefinitely in one direction as long as the strand is alive. For this to occur there must be a shifting within the gel structure of the strand, hence this too is a special case of cytoplasmic flow.