On the Flow of Certain Pathological Human Synovial Effusions through Narrow Tubes

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(*Received* 18 *June* 1953)

Viscosity-concentration relations in both human and bovine synovial fluids have been the subject of considerable attention. (For a recent summary see Frey-Wyssling (1952).) But, although it is generally admitted that most samples are not simple Newtonian liquids, few authors have studied the relationship between rate of shear ($\dot{\gamma}$) and stress (τ). The only notable exceptions are Ogston & Stanier (1950) who, using non-pathological bovine fluids, found an approximate empirical linear relation between $\eta_{\text{rel.}} - \eta_{\text{rel.}\infty}$ and $1/(\dot{\gamma}+a)$, where η_{rel} is relative viscosity, $\eta_{\text{rel.}\infty}$ is relative viscosity at high shear-rates and a is a constant. To substantiate this relationship only a few curves are shown. This equation is very similar to that proposed by Goodeve & Whitfield (1938) for systems which they describe as thixotropic, though some other rheologists disagree with this use of the term. This equation has, in its turn, been shown to be related to the Bingham equation (see Scott Blair, 1949). A similar relation has also very recently been discussed by Prins & Hermans (1953). Since it is established that synovial effusions are in many cases not simple fluids having viscosities independent of rate of shear, it is clearly desirable further to investigate their viscous anomalies, with a view to establishing the number and nature of the parameters needed to describe their behaviour adequately. This is the purpose of the present work.

It has long been known that many colloidal solutions, which, when dilute, obey Newton's law, $\tau/\dot{\gamma} = \eta = \text{const.}$, show, for higher concentrations, a decrease in the ratio $\tau/\dot{\gamma}$ as stress and rate of shear rise; and various empirical functions, such as power laws, have been proposed to fit the facts. The whole subject is admirably summarized by Reiner (1949). Much earlier, however, Ostwald (1925) pointed out that it is not possible that $\tau/\dot{\gamma}$ should continue to decrease indefinitely with increasing shear rate, since the viscosity will presumably never fall below that of the pure solvent (normally water). For this reason he postulated a curve which, at lower stresses, follows a power law but which later inflects and, at higher stresses becomes linear (the 'Laminarast') and is directed towards the origin. Few such curves have appeared in the experimental literature, perhaps because turbulence usually intervenes before the 'Laminarast' is reached, but somewhat elaborate equations have been proposed in order to explain them (see Reiner, 1949).

It is of interest to establish whether such types of behaviour are characteristic of synovial effusions and, if so, under what conditions of flow.

EXPERIMENTAL

The fluids were tested in a viscometer (as originally described by Scott Blair (1941) for work on prenatal mammary secretions), consisting of a horizontal capillary tube attached at each end to relatively wide vertical tubes. Measurements were made in a thermostatically controlled water bath at 38°. The sample is sucked up into one of the side tubes and its rate of fall is then measured on a vertical scale. The initial height of the column above its rest position is $h_0 = 10$ cm. which represents half the head, since the column falls by an equal amount in the other arm of the viscometer. In a few experiments greater heads than this have been used but no extra information appears to be gained by this procedure, which increases the experimental errors. It was shown in the earlier paper (Scott Blair, 1941) that, for true fluids, the viscosity η, is given in terms of the time (t) taken for the head of the column to fall from h_0 to each observed value of h, by the equation

$$\eta = -\rho \frac{gR_c^4}{4LR_w^2} \frac{\mathrm{d}t}{\mathrm{d}(\ln h)}, \tag{1}$$

when R_c and R_w are the radii of the capillary and the wide tubes, respectively, L is the length of the capillary, g is acceleration due to gravity, ρ is the density of the material which, for the present purposes, may be taken as unity.

Defining Δt as the time differences between successive (cm.) readings of h, this may be rewritten

$$\eta = -\rho \frac{gR_c^4}{4LR_w^2} \frac{\Delta t}{\Delta(\ln h)}, \tag{1a}$$

or

$$\eta = -A \frac{\Delta t}{\Delta(\log h)},$$

where A is a constant for each capillary. (The minus sign means that head is falling.) For our standard viscometer, $A = 0{\cdot}000521$.

For a Newtonian fluid, since $\tau = h\rho g R_c/L$, and, by definition, $\dot{\gamma} = \tau/\eta$, we have

$$\dot{\gamma} = -\frac{4R_w^2}{R_c^3} h \frac{\Delta (\ln h)}{\Delta t}.$$

The side tubes are sufficiently wide for their resistance to be ignored.

Methods of expressing results in relation to experimental method

Provided that η is effectively constant, as was the case with the prenatal mammary secretions, equation (1) may be integrated (Scott Blair, 1941) to give:

$$\eta/\rho = \frac{t}{\ln (h_0/h)} \frac{gR_c^4}{4LR_w^2}. \quad (2)$$

Curves for any single capillary may therefore be plotted as $t/\log (h_0/h)$ against some suitable function of h, or as t against $\log (h_0/h)$, as was done in the earlier paper using equation (2) which applies to a Newtonian fluid. When the anomalies are considerable, however, this is not a sound method, since, unless h_0 can be chosen to mark some well-defined, constant viscosity, such as the beginning of the 'Laminarast', its value is entirely arbitrary. Moreover, any function of h which is linear with $t/\log (h_0/h)$ for one arbitrary value of h_0 will not, in general, be strictly linear for other selected values, even though in practice the curvature may not be very noticeable.

Moreover, the use of the integrated form of the equation implies that the value of the 'viscosity' ($\tau/\dot{\gamma}$) for any given value of h is calculated for the range between the arbitrarily chosen h_0 and h and the actual values for 'viscosities' so calculated are therefore highly dependent on the choice of h_0.

For these reasons it is better to use the differentiated form of the equation (i.e. equation 1*a*) rather than equation (2), even though the use of the integrated form generally gives smoother curves having less scattered points.

Selection and preparation of samples

The samples of synovial fluid were all obtained from knee joints by aspiration with a wide-bore needle. The fluid was kept in a screw-capped bottle in a refrigerator. Shortly after aspiration most fluids form a fine clot. Before any measurements were made the fluid was centrifuged in order to separate this clot and any fibrin flakes or cellular debris which might obstruct the capillary.

The fluids tested were unselected, being from the knees of any patient in whom fluid was clinically demonstrable. Of the 63 samples tested, 34 were from 17 patients who suffered from rheumatoid arthritis, 13 samples from 4 patients with ankylosing spondylitis, 5 from osteoarthritis, 1 from Reiter's disease, and 10 from 3 patients with undiagnosed effusions.

RESULTS

The results of our experiments are best classified under two headings.

Anomalies of flow within a single capillary. For a Newtonian fluid, η is independent of τ and this is found to be nearly the case for the thinner synovial fluids (see lowest curve to Fig. 1). For thicker samples, however, this law does not hold.

Using a single standard capillary, we find that, for such samples, a plot of $\Delta t/\Delta (\log h)$ against $\log h$ gives excellent straight lines for effusions covering a very wide range of consistency.* The great majority of such curves drawn for more than sixty samples, show no sign of curvature. Among those that do show slight upward or downward curvature, of which there are about equal numbers, there is no relation observed between the direction of curvature and the consistency. Since for a single capillary, $h \propto \tau$, this plot may be expressed by the equation

$$\tau/\dot{\gamma} = \eta = \eta_0 + \alpha \log \tau, \quad (3)$$

where α is the slope of the straight line. A few typical examples are shown in Fig. 1. The original data are given in Table 1.

A plot of $\log \dot{\gamma}$ in place of $\log \tau$ against η (where η is defined as $-A\Delta t/\Delta (\log h)$) also gives good straight lines for both sets of results. The equations represented by these two plots cannot both be strictly true. Apart from all else, if both were valid, then the values of $\log \dot{\gamma}$ should be linear with those of $\log \tau$ and this is not the case. Experimentally, we cannot decide which equation fits the data more closely, nor is there any obvious statistical procedure for doing so. Our preference for the $\log \tau$ plot is largely arbitrary.

Many biological fluids show some type of thixotropy (see Frey-Wyssling (1952)). Repeated shearing of the synovial fluids, however, leads to a slight increase in consistency. Thus, for example, the readings for a typical sample for the final value of $h = 2$ are shown in Table 2. On still further shearing a stage is reached at which the consistency does not change any further.

It was at first thought that this effect might be caused by some structure set up by the shearing which does not relax when the sample is left in the viscometer between the shears. However, when the sample was taken out of the viscometer and fairly thoroughly mixed before re-testing, a similar increase in consistency was found to have taken place. It does not seem likely that this change can have been due to evaporation and the mechanism of the process is obscure. Centrifuging for 20 min. instead of the usual 5 min. has no effect on the consistency.

Data from a few samples, when τ was plotted against $\dot{\gamma}$, show some tendency to inflect and to give a 'Laminarast', but this is only really clearly defined by the first two or three readings from the falling column. Using the differential form of the equation (equation 1*a*), the effect is much less marked than it is when the integrated form (equation 2) is used. This is to be expected, since in

* Consistency is defined as 'that property of a material by which it resists permanent change of shape' and is described by the complete flow-force relation.

Table 1. *Values of t (sec.) corresponding to readings of h (= half-head) for a number of synovial effusions*

($h_0 = 10$.)

h (cm.)		8	7	6	5	4	3	2
Sample no.	4	78	130	194	277	393	559	836
	25	27·0	44·9	68·7	98·7	141·5	203	304·8
	35	18·3	30·4	45·1	64·2	87·5	122·9	178·3
	39	35	58	88	127	180	260	388
	42	12	20	29	41	56	78	110
	44	7	11	17	23	31	41	57
	105	—	111	168	242	340	—	710

the former plot each point represents the viscosity of the sample covering a small region of stress (Δh) of which the plotted value of h forms the centre. In the latter plot, viscosity is interpreted over the whole range from h_0 to h; hence changes in viscosity are not so clearly shown.

Through the kindness of Dr A. G. Ogston and Dr J. E. Stanier, it has been possible to examine data obtained by them on six samples of bovine synovial fluid from the slaughter house, using a concentric cylinder viscometer. Except at the lowest rates of shear, where the points are somewhat irregular, equation (3) gives very satisfactory straight lines. However, the plots of two experiments on equine slaughter-house samples, tested by us in the capillary instrument showed marked curvature.

Effects of varying capillary radius and length. A number of rheologists, specifically Schofield & Scott Blair (1930) have shown that anomalies in flow in capillary tubes may be classified as of two kinds: (*a*) deviation from the Newtonian law that $\tau/\dot{\gamma} = \eta =$ const. although certain basic conditions are maintained. These are that each particle of the material flows in a straight line parallel to the wall of the tube, that there is a monotonic relation between τ and $\dot{\gamma}$ and that there is no slippage or sticking to the walls. (*b*) Conditions under which one or more of these three postulates do not hold.

Anomalies of type (*a*) lead to non-linear relations between τ and $\dot{\gamma}$; but, if data from different capillaries are plotted τ versus $\dot{\gamma}$, the curves should be unique. Schofield & Scott Blair, and later many others, have studied so-called 'sigma-effects' in which the curves are not unique and where the Poiseuille-Hagen fourth-power-radius law is not obeyed. Zamboni (1943) showed that mucins from many sources, as well as some unspecified synovial fluid, failed to obey the linear-length law, flow being relatively slowed down in longer tubes. Similar effects, both positive and negative, have been recorded for other materials (see Scott Blair, 1949).

Experiments using a number of capillaries differing in radius and length have shown that the fourth-power-radius law holds for our materials within the rather wide limits of experimental error. There is some evidence that the length law does not

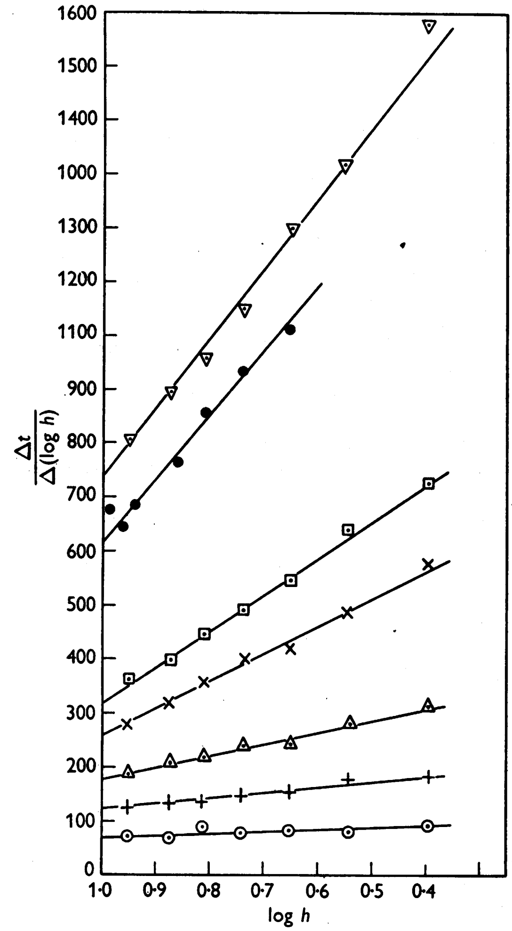

Fig. 1. Viscosity of synovial effusions (differential definition) plotted against logarithm of stress (t in sec, h in cm.). The seven types of points refer to seven different samples: ▽, no. 4; ⊡, no. 39; ×, no. 25; △, no. 35; +, no. 42; ⊙, no. 44; ●, no. 105.

Table 2. *Effect of repeated shearing on consistency of a synovial effusion*

(t_2 is time taken for column to fall from $h_0 = 10$ to $h = 2$.)

No. of shear	1	2	3	4	5	6
t_2 (sec.)	285	291	292	295	297	299

hold perfectly, flow being relatively slower in the longer tubes. This effect, though marked only in the case of samples of high consistency, may well be similar in character to the flow-hardening phenomena reported by Zamboni (1943).

DISCUSSION

The use of the differential form of the equation (equation 1a) eliminates the explicit arbitrary length h_0, but there still remains the problem of how to describe curves plotted in accordance with equation (3). Being straight lines, these curves require two parameters: the slope α, and a second parameter which we have defined as η_0, being the viscosity at an arbitrary stress corresponding to $h = 10$ cm.

From purely algebraic considerations, we should probably choose that value of log h (and hence h) corresponding to zero viscosity when the curve is extrapolated. But it is clear that equation (3) will certainly not hold to this limiting condition, since the viscosity will never fall below that of water.

Thus, for want of any well-marked stress or shear rate clearly characterizing the material, the arbitrary choice of $h = 10$ cm. for a point at which to quote viscosity measured in this way can hardly be improved upon.

The results given in the last section show that, except in the case of effusions of very high consistency, the effects of radius, thixotropy and even length can be ignored for many purposes. Each sample may thus be designated by the two constants from equation (3). Of these two properties, η_0 represents the viscosity at comparatively high shear rates and α, which has also the dimensions of a viscosity ($ml^{-1}t^{-1}$), defines the rate at which viscosity changes with changing stress, i.e. the viscous anomaly. It is not surprising that the magnitude of the viscous anomaly should be a function of η_0, especially since viscosity is itself defined as $\tau/\dot{\gamma}$; but it is, perhaps, remarkable how close is the relationship. Fig. 2 shows a scatter curve for fifty-four samples. The correlation coefficient is 0·958. It is seen that, statistically, the anomaly only appears when η has reached a certain well-defined value. Using the standard viscometer, $\eta_0^* = 50$ corresponds to $\eta_0 = 0{\cdot}052 \times 50 = 2{\cdot}60$ centipoise. (Starred symbols represent values for a single capillary, not converted into absolute units.)

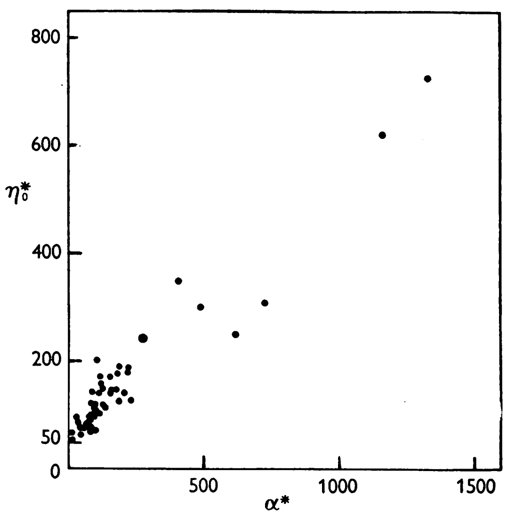

Fig. 2. Scatter diagram relating viscosity at high stress to viscous anomaly. (Rise in viscosity with falling stress.) η_0^* and α^* in arbitrary units.

Below this viscosity, given by the extrapolated intercept of the scatter curve, samples are, to all intents and purposes, Newtonian fluids, since $\alpha = 0$. For higher viscosities, and presumably when the concentration of mucin reaches a value large enough to produce marked intermicellar interference, there is a clear linear (statistical) relation between η_0 and α, the anomaly increasing progressively with increasing viscosity. This does not mean, however, that the individual samples can be described by a single parameter. Thus the ratio of $\eta_0^* - 50$ to α^* varies quite widely between individual samples, corresponding to their individual positions on the scatter curve. The extreme values are 1·48 and 0·25. This ratio may even eventually prove to be of clinical significance. Even with its two parameters, however, equation (3) represents a very simple law of flow for such complex materials which, as far as we are aware, has not been used previously by rheologists for any material.

Clinical value of results. Previous observations on the viscosity of pathological synovial fluids have taken no account of its non-Newtonian properties. As a consequence, normal values in various diseases have been expressed in terms of relative viscosity alone. Ropes, Robertson, Rossmeisl, Peabody & Bauer (1947) give the relative viscosities of synovial fluid for a number of diseases. We are now able to give true figures for the stress anomaly (α) and a viscosity (η_0) at a chosen stress. This gives a more complete picture of the behaviour of these fluids.

Since the samples were mostly from cases of rheumatoid arthritis, an idea of the range of viscosity in this condition is obtained. These are all fairly low, ranging from 2·9 to 10·3 centipoise.

That these results are not of specific diagnostic importance is shown, however, by the similarity of viscosities and stress anomalies shown by fluids from other conditions. Many more readings will have to be made before these results can be compared with the ranges given by Ropes *et al.* (1947).

An interesting observation is that when a joint is repeatedly emptied, neither the viscosity nor the quantity of effusion remains constant. It appears that the larger the amount of the effusion from any given joint, the lower is the viscosity. The emptying of the joint thus alters both the quantities and the quality of the effusion. These findings show that in any *in vivo* experiment, account must first be taken of the variations resulting from the process of aspiration itself.

However, taking the whole group of patients with rheumatoid arthritis on whom these studies have been made, without repeated aspiration, no correlation could be found between the size of the effusion and its viscosity; nor did the acuteness of the effusion, the erythrocyte sedimentation rate, sex, age, nor duration of the disease show any relationship to the viscosity.

The importance of these rheological properties of synovial fluid is likely to be more in their relationship to the biochemical changes occurring in the formation of effusions than as direct clinical diagnostic tests.

SUMMARY

1. An examination of over sixty samples of human synovial effusions in a capillary viscometer has demonstrated relatively simple rheological behaviour. While thinner samples are almost true fluids, for the thicker samples, especially at high stresses, an anomalous viscosity appears. The anomalous viscosity may be described in terms of a parameter also having the dimensions of viscosity, equal increments of which correspond to progressive halvings of the remaining stress.

2. Although individual samples thus require two parameters for their specification, these are very highly correlated statistically. Anomalous viscosity starts when a certain basic viscosity ($\sim 2{\cdot}6$ centipoise) is reached and is thereafter closely proportional to the normal viscosity term.

3. Synovial fluids show no serious divergence from the Poiseuille-Hagen fourth-power law in relation to capillary radius and only a slight increase in viscosity with increasing capillary length, except in the case of effusions of very high consistency, which seem to flow less readily in the longer tubes. Repeated shearing or stirring causes a small but definite increase in viscosity, the cause of which is not known.

4. Since no obvious relation has been found between the viscosities, normal and anomalous, and acuteness of effusion, erythrocyte sedimentation rate, sex, age, or duration of disease, it is probable that their importance will be found to lie more in their connexion with biochemical changes occurring during the formation of the effusions, than in their use as diagnostic criteria.

We are indebted to Mr C. P. Cox for helpful discussions and useful suggestions, and Dr H. A. B. Simons for technical advice. Prof. J. McCunn of the Royal Veterinary College provided us with samples of equine synovial fluid. Facilities and assistance were made available by the Endowment Fund Subcommittee and the Board of Governors of The Royal Free Hospital.

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