Fibrinolytic Activity of Whole Blood from South African Bantu and White Subjects

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Mortality from coronary heart disease is believed to be almost unknown among rural South African Bantu; even among urban dwellers, deaths from the disease as proved at necropsy are extremely few.1 2 Confirmation of this belief is being obtained from a collaborative clinical and biochemical study now in progress on Johannesburg Bantu pensioners over sixty years old (some approaching 100 years of age); in 340 subjects thus far examined, only one case of coronary heart disease, judged from clinical and electrocardiograph observations, has been detected.3 In the same number of elderly white people in Western countries, evidence suggests that fifty or more cases would be expected.4 5

This favourable situation among the Bantu is far from explicable. Thus, while severe atherosclerosis of the aorta and, to much lesser extent, of coronary vessels is not common among them, unquestionably on occasion severe lesions do develop.6 11 Hypertension, moreover, is common.6 7 8 9 12 13 Since these conditions, severe atherosclerosis and hypertension, are present in a proportion of adult Bantu, it would seem plausible from current thought14 15 to consider that decreased coagulability and increase fibrinolytic activity of blood may be among the salient factors that prevent the occurrence of acute thrombotic episodes in the coronary vessels of these people. Studies on Cape Town Bantu have revealed a deficiency of some factors in blood coagulation, and a more efficient function with respect to other coagulation mechanisms.16 20 Accordingly, it is at least arguable "that the Bantu should have more thrombotic disease."17 It may be noted that the same difference prevails between Australian whites and New Guinea primitives, the latter apparently evincing "greater blood coagulability."18 Regarding fibrinolysis, however, there is evidence of superiority of activity in Bantu males compared with white males, both in whole blood16 20 and in plasma.21 22 In pursuit of endeavours at this centre to throw light on why the Bantu are virtually free from death from coronary heart disease, it seemed highly desirable to confirm these findings and, in addition, to determine mean values in groups of Bantu of both sexes, primitive and sophisticated, as well as among white control subjects; and to learn, moreover, of the trend of changes in fibrinolytic activity evoked by a fatty meal in comparison with a nonfatty one, and by exercise in comparison with inactivity.

SUBJECTS AND METHODS

Subjects. All subjects were in outward good health and pursuing their usual avocations. Rural Bantu: These included nineteen male and twenty-one female Mocambique Shangaans (Chichumbane region), thirty-nine male and fifty female Bechuanaoland Tswana (Kanye region), and sixty male and sixty female Transvaal Pedi (Jane Furse Hospital region, Sekhukhuniland). From Johannesburg these centres, respectively, are about 500 miles East, 250 miles West, and 200 miles North East; they were chosen deliberately to provide widely separated diverse primitive population groups. The diets consumed in these three...
regions are not identical, but, while probably adequate in calories and possibly in gross protein, they are low in animal protein, fat and cholesterol, and high in carbohydrate and crude fibre. *Urban Bantu males:* These subjects (ninety-three) largely were workers at this Institute; they consumed a partially westernised diet. *Urban Bantu females:* These subjects (fifty-six) were drawn from a variety of sources; they also consumed a partially westernised diet. *Whites:* These subjects (forty-four males and fifty-five females) mainly were workers at this Institute, habituated to a diet common to middle-class white people.

*Ages.* Most Bantu, particularly rural dwellers, are ignorant of their correct age. Hence, the mean ages recorded are approximate.

*Collection of Blood Samples.* In regard to time of collection of samples, there are two alternatives. (1) At first sight it is desirable that in studies of this nature, blood samples be collected under basal conditions, i.e., after a long period of fasting. However, one's past experience in field work on the Bantu has demonstrated the utter hopelessness of attempting to get nonhospitalised subjects to present themselves for blood collection at a specified time in a completely breakfastless state. Hence, if basal conditions are to be aimed at, the investigation is prejudiced from the start. (2) There is, however, a second aspect to consider. Fearnley et al.24 have shown that differences of 100 per cent and even more in blood fibrinolytic activity may occur in specimens taken from the same person very early in the morning and late in the afternoon. The wide extent of this diurnal rhythm has been confirmed by Buckell and Elliott25 in plasma. Limited studies by the former workers have suggested that fibrinolytic activity is roughly steady from just before noon until late afternoon or early evening (subsequent studies at this centre substantially have confirmed this finding). The alternatives, therefore, are either to investigate subjects in early morning at basal state, in which case attempts to study the effect on fibrinolytic activity of a fatty meal or of exercise will be partially masked by the diurnal rhythm; or, to study subjects at the steady state period but under the disadvantage of nonfasting conditions. Bearing in mind that observations at basal state virtually are out of the question, at least for primitive rural Bantu, it was finally decided to collect samples at the beginning of the steady state period, i.e., from 11.30 to 12.30 A.M., four to six hours after breakfast, which in composition was the subjects usual repast.

*Method of Assay.* The method of Fearnley et al.24 using whole blood was employed, mainly because it is far easier to undertake under field conditions compared with methods using plasma, but also because of certain criticisms that have been made about the reliability of values obtained on plasma by Billimoria et al.26 All glassware was washed with acid and sterilized with heat immediately prior to use. Apparatus was used at or near 0°C, as were all reagents, which were freshly prepared for each run. Determinations were carried out in triplicate, sometimes quadruplicate. Briefly, 5 ml. or more venous blood was withdrawn without stasis, and immediately 0.2 ml. was added to 1.7 ml. phosphate buffer (pH. 7.25)* and just previously added 0.1 ml. thrombin solution (Parke Davis & Co., Thrombin* topical, 50 units per ml. in sterile normal saline) contained in tubes (9 by 1.5 cm.) surrounded by ice water in a beaker. After thorough mixing, tubes were refrigerated for a half to one hour, and then incubated at 37°C. in a water bath fitted with glass windows. Lysis time (taken to the nearest quarter hour) was that taken by clots from start of incubation to time of disappearance, tubes being inspected every ten to fifteen minutes. The recorded figure was the mean of the values for the tubes used for each determination. When individual tube values differed from the mean by more than 10 per cent (which happened in 10 per cent of cases), results were rejected, and tests repeated on fresh blood samples.

It will be understood that the shorter the

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* The buffer mixture specified by Fearnly et al. and Billimoria et al. has a pH value of about 7.25, not 7.4 as stated.
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lysis time, the greater is the fibrinolytic activity in blood and vice versa.

RESPONSE TO FAT-FREE AND TO FATTY MEALS

The purpose of investigating the effect of the fat-free meal merely is to establish a base line against which the effect of the fatty meal may be judged. In seeking to determine the effect of the latter on fibrinolytic activity, there are two alternatives: (1) A very large intake of fat may be desirable in order to exaggerate the inhibitory or other effect produced in activity levels. (2) Notwithstanding, there is much to be said for limiting intake to amounts which are physiologic, i.e., not excessively divorced from everyday intake of the particular type of fat partaken of at a single meal. In the Bantu, this amount necessarily will be low, certainly much lower than white people are accustomed to. A compromise must therefore be reached. Before discussing the amount, it should be remarked that the feeding of butter fat, at least in the first instance, is desirable, partly on account of its place in everyday regimens, partly because other workers have used it in analogous tests, and not least because it is considered by many to be the most noxious of fats in relation to the disease process under investigation.

The feeding of butter fat as butter under South African conditions of temperature presents difficulties. The unit of intake ultimately decided upon was the 5 \( \frac{1}{2} \) tin (can) of Nestlé's Cream, containing 31 to 34 gm. (1 \( \frac{1}{4} \) ounces) butter fat. In the performance of the tests, series of subjects (Bantu and white) consumed either a meal of canned fruit and bread rolls (the fat-free meal), or a meal of canned fruit, rolls and the tin of cream, blood being sampled before (about noon) and three hours afterwards, and the clot lysis times determined.

Unfortunately, it was seldom possible to persuade the same group of subjects to participate in both fat-free and fatty meal tests.

RESPONSE TO EXERCISE

In seeking to determine the part played by exercise in its effect on fibrinolytic activity, again there are two alternative courses: (1) Exercise, if vigorous, will demonstrate its role in an exaggerated manner in influencing fibrinolytic activity;\(^{(28-29)}\) it has seemed to me much more desirable to learn of the role of exercise under conditions relevant to everyday life. It was therefore decided firstly to carry out a comparative test on groups of subjects, working at, or relaxing from their usual tasks; and secondly, in the case of subjects studied at this Institute, to determine whether an inverse correlation obtains between clot-lysis time and degree of habitual physical exercise, both for individuals and for groups of persons. In the carrying out of the comparative test a series of male and female Bantu adults at Kanye were divided into two groups, each consuming the fat-free meal at noon. One group “loafed” for three hours; the other group pursued their usual tasks (washing, cleaning and gardening). Blood was sampled at the appropriate times, and the clot lysis times determined.

OTHER STUDIES

Various biochemical, haematologic and other tests were undertaken on whole blood (also plasma and serum) from subjects. Although data on serum protein fractionation and on thymol turbidity are mentioned later, they will be discussed in detail in subsequent publications. A point worth mentioning at this juncture concerns the commonness of abnormally high erythrocyte sedimentation rates in the Bantu subjects.\(^{(29)}\)

### Table 1

<table>
<thead>
<tr>
<th>Population Group</th>
<th>Age (yr.), Mean and Range</th>
<th>No. of Subjects</th>
<th>Lysis Time (hr.), Mean and Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Combined rural Bantu</td>
<td>35 (19-75)</td>
<td>118</td>
<td>3.17 (1.5 -8.0)</td>
</tr>
<tr>
<td>Johannesburg Bantu</td>
<td>35 (20-62)</td>
<td>93</td>
<td>3.81 (1.75-9.5)</td>
</tr>
<tr>
<td>White subjects</td>
<td>33 (15-66)</td>
<td>44</td>
<td>4.42 (2.0-11.5)</td>
</tr>
</tbody>
</table>

\(^{(28-29)}\)
The results of these experiments are summarized in Tables I through IV.

Since the mean clot-lysis times for each sex in the three rural groups of Bantu studied (Shangaans, Pedi and Tswana) were found to be closely similar, results have been combined into a single group for each sex. Table I: Mean fibrinolytic activity of blood from rural Bantu males is significantly higher than that from urban Bantu males (P<0.002); mean activities for rural and urban Bantu male groups are significantly higher than for white males (P<0.0005 and P<0.05, respectively). Table II: Mean activities of blood from Bantu females, rural and urban, are significantly lower than that of white females (P<0.05 and P<0.02, respectively). In the Bantu, the sex bias of activity in favour of males prevails significantly in both rural and urban groups (P<0.00001 and P<0.001, respectively). There is no significant difference in mean activities between white males and females (P<0.20). Table III: Mean fibrinolytic activity determined in Bantu and white subjects (males and females) at noon, followed by a fat-free or fatty meal (31 to 34 gm. butter fat) reveals inconsistent and not significant changes; the majority of Bantu males and females tend to show acceleration of activity following the fatty meal; White females tend to show slight inhibition of activity after both fatty and nonfatty meals. (For the maximum change, i.e., increase in fibrinolytic activity in Bantu females on the fatty meal, P = 0.20.) Table IV: No significant difference in mean blood fibrinolytic activity is apparent between Bantu groups active and nonactive under the experimental conditions employed.

COMMENTS ON RESULTS

It is imperative to bear in mind the uncertainty over the relevance of fibrinolytic measurements carried out in vitro to conditions in vivo. It must be stressed that all subsequent comments and discussion refer exclusively to the results of the test tube studies.

Regarding repeatability of observations, findings in general are in agreement with those of Billimoria et al.26 who found that activity...
levels in blood do not usually vary grossly when sampled at the same time on different days. With fifteen of twenty subjects examined at the same time of day on six or more occasions, examples of sequences of lysis times (in hours) are as follows: (1) six and one half, seven and one quarter, seven and one quarter, six and three quarters, six and one half, seven; (2) three, two and three quarters, three and one half, three and one quarter, three, three and one quarter. On the other hand, in the other five subjects, examples of sequences of lysis times (in hours) are: (1) six, two and one half, five and one half, four and three quarters, six and one half, four; (2) three and three quarters, seven and one quarter, four, six and one half, five, six.

Briefly then, it would seem that whereas fibrinolytic activity at noon is fairly constant with the majority of subjects, it is irregular with the minority. In the latter subjects, the etiological significance of these gross changes is doubtful in view of such fluctuations being found to be as common among Bantu as among white subjects. With plasma, in contrast to blood, Buckell and Elliott have reported considerable irregularity in fibrinolytic activity in subjects examined on different occasions.

The superiority of fibrinolytic activity found in Bantu males compared with white males (Table I) was as expected, and confirms the conclusion reached locally, both for blood and for plasma. Our mean value for white males bled at noon, namely, 4.42 hours (Table I), may be compared with the mean for the ten men examined at 2 P.M. by Fearnley et al., namely, 4.6 hours. Our mean value for white males over thirty years of age, namely, 4.65 hours, is similar to that given by Nestel for thirty elderly Australian white males, namely, 4.9 hours, although the time of collection of blood was not stated.

The superiority in mean blood fibrinolytic activity of white females over Bantu females was entirely unexpected. No explanation can be offered. Our mean value for young white females under thirty years of age bled at 3 P.M. and without respect to diet consumed (whether fat-free or fatty) was 3.85 hours. This figure may be compared with the value, namely, 3.7 hours, reported for the group of fifteen nurses (presumably in the younger age group) bled at 4 P.M. by Fearnley et al.

Combining information given in Tables I and II, two comments may be made. (1) Merskey et al., in their comparison of Bantu and white males, have entertained the possibility that fear among the former regarding venipuncture, might augment their fibrinolytic activity. That possibility was also considered at this centre, but was discarded for the following reasons. Firstly, of the Bantu (both rural and urban) who were bled on several occasions for lysis time determination, their becoming accustomed to the taking of blood samples had no obvious influence on the values obtained. Secondly, mean fibrinolytic activity of Bantu females is lower than that of white females (Table II.) (2) Gillman, referring to the commonness of liver dysfunction and disease in the Bantu, considers that such conditions almost certainly have a bearing on the rarity of mortality from coronary heart disease among them. More apposite, Gillman et al. have confirmed in Bantu the observation of Kwaan et al. that higher fibrinolytic activity in plasma is usual in those who suffer from cirrhosis, compared with control subjects,

The present study using whole blood from both Shangaan and Pedi Bantu ambulant patients with cirrhosis (mean lysis time, 2.85 hours for ten male patients bled at noon). Moreover, Merskey et al. have noted liver dysfunction, as reflected by certain biochemical tests, to be more prevalent in Cape Town Bantu males compared with white males (as also is cirrhosis), and have wondered whether the more rapid lysis times of Bantu may not be a manifestation of such dysfunction. At this centre, numerous investigations have testified to the commonness of liver dysfunction and disease among Johannesburg Bantu. There is certainly no intention of excluding the possible role of such stigmata in influencing fibrinolytic activity: nevertheless, it may be pointed out that although certain of our Bantu groups (male and female) who
were investigated to shed light on this aspect, had higher mean serum gamma globulin and thymol turbidity levels and lower serum albumin levels compared with white subjects; no correlation was apparent in individuals between such data and fibrinolytic activity. In addition, although mean values among the Bantu for the serum components mentioned were similar for both sexes, there was a significant sex difference in mean fibrinolytic activity.

Among both races and sexes, and in every run of determinations, lysis times were accelerated in some subjects, whereas they became prolonged in others following the fatty meal. But broadly, Bantu males and females evince a tendency toward acceleration of fibrinolytic activity, acceleration occurring in roughly half of the subjects, little or no change in a quarter, the remainder showing inhibition. On the other hand, there is a tendency for slight inhibition of activity to occur with white females consuming either type of diet (fat-free or fatty), about half showing inhibition, a quarter little or no change, and a quarter showing acceleration. Mean changes, however, are not large (Table III) and it would seem prudent not to lay stress upon them, but simply to emphasize the inconsistency of the response. Nitzberg et al.42 using the same method of determination, investigated the response to a meal containing 85 gm. animal fat by groups of normal, hyperlipemic, hypercholesterolaemic and coronary patients; after three hours a "definite postprandial shortening of fibrinolysis time" was observed in twenty-six of twenty-nine subjects. Whether such acceleration of activity was statistically significant or otherwise was not stated. Employing a modification of the Fearnley method on whole blood, Billimoria et al.43 reported a general decrease in fibrinolytic activity following consumption of 42 gm. butter fat, this change being apparent in fourteen of twenty-one subjects after a two-hour interval (statistically significant) and in ten of fifteen subjects after an interval of four hours (not statistically significant).

Turning now to plasma, using a modification of the clot lysis technique of Bidwell43 as described by Biggs and MacFarlane,44 Greig48 found an inhibition of fibrinolytic activity in all subjects studied (twenty-six males and females) three hours after the consumption of a fatty meal made up of everyday foods, when judged over a twenty-four-hour incubation period. In addition, Greig and Runde49 reported that inhibition was greater with butter fat and eggs, compared with the vegetable oils tested (corn, coconut, sunflower and arachis). Using these technics, Buckell and Elliott46 studied the response (three hours later) to 50 gm. butter fat by twenty normal men; they found a decrease in activity only in eight subjects when determined after a six-hour incubation period, and in five of twenty when determined after a twenty-four-hour incubation period. Bradlow et al.53 using the same method on plasma, studied a series of twenty-three Bantu and eighteen white subjects after an overnight fast, and four hours after ingestion of a fatty meal; no significant change in fibrinolytic activity was found. Hougie and Ayers,47 working with their own modification of the method on plasma, were unable to confirm that lipaemia inhibits "fibrinolysis potentiality." Their research indicated that the ingestion of butter, cream and eggs had no significant effect on "fibrinolysis potentiality" determined between three and one half and four hours after the meal. The foregoing, and other studies that could be cited, thus reveal complete disagreement (both for whole blood and plasma) over the effect of a fatty meal on fibrinolytic activity, in which increase, little change and decrease in activity all have been reported. It would not be appropriate at this juncture to seek to elucidate the reasons for disagreement, but in judging the lack of concordance in observations, the following must be remembered: (1) the existence of the diurnal rhythm of fibrinolytic activity and the different times of collection of blood samples; and (2) the differences in methods of determination, and also the fact that some studies were undertaken on blood and others on plasma.

Before considering the effect of exercise on fibrinolytic activity, attention must be drawn to the inexplicably high level of motor fitness of the Bantu (children, young men and older men) as assessed by the Harvard step test,48
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a superiority out of proportion to the admittedly higher level of habitual physical activity common to these people. Attention is also drawn to the fact that in rural areas, the harder physical work (housework, fetching water, "stamping" or grinding of maize and weeding) is normally carried out by the Bantu women. Yet, fibrinolytic activity in Bantu females has been found to be lower than that of Bantu males, and lower too than that of the white women studied (Tables I and II). Table IV reveals that the two rural Bantu groups investigated under different conditions of bodily activity showed no difference in mean fibrinolytic activity, i.e., it would seem that the relatively leisurely physical activity of the "active" Bantu studied was insufficient to accelerate their blood clot lysis times. Furthermore, examination of individual fibrinolysin values for Bantu and white subjects investigated at this Institute has shown no correlation with level of individual habitual physical activity.

There is no doubt, of course, that under conditions of physical activity divorced from that experienced habitually, there is enhancement of fibrinolytic activity. This has been demonstrated in plasma of subjects after running up and down stairs, although the level returned rapidly to normal soon after cessation of exercise. Enhancement of activity in plasma was also noted by Greig, and in whole blood by Billimoria et al. following periods of brisk walking; the latter group also demonstrated the evanescent character of the stimulated fibrinolytic activity. The somewhat negative findings reported in this section do not imply that the higher motor fitness of the Bantu is of little relevance to their freedom from death from coronary heart disease. Observations merely indicate that within the limits of the sensitivity and specificity of the test employed, marked differences in fibrinolytic activity associated with differences in habitual exercise have not been demonstrable.

Not apparent from the tables are a number of interesting points. (1) Among both Bantu and white subjects, lysis times of as long as six to eight hours were encountered occasionally in young persons; on the other hand lysis times of two to two and one half hours were noted not infrequently among very elderly subjects. (2) As already state, most subjects have similar lysis times when examined on several occasions at the same time of day. Furthermore, activities measured in groups of subjects have shown higher activity early in the morning and a roughly steady state from noon until late afternoon. Nevertheless, both time of peak activity and amplitude of diurnal rhythm have been found to vary from subject to subject.

COMMENTS

All that I wish to conclude and discuss from the experimental observations reported is the superiority of fibrinolytic activity in Bantu men, the inferiority (or at least lack of superiority) in Bantu women, and the inconsistent response to a fatty meal and to exercise. In discussing the relevance of these findings to the wider subject of ischaemic heart disease, it is useful to consider the aspects of blood coagulation and fibrinolysis together.49

The conception of decreased coagulability and of increased fibrinolytic activity operating to obviate serious ischaemic episodes in a population such as the Bantu is plausible, and numerous schema have been advanced which imply the possibly important role of these two factors in the pathogenesis of arterial thrombosis.14,21,50,51 However, the evidence bearing on the subject is far from conclusive. It should be noted that Poole has emphasized that "It is still too often assumed that factors which influence clotting must necessarily influence thrombosis and conversely that factors which do not affect clotting cannot be concerned in thrombus formation. Such assumptions are not justified. Later work may well show that factors which are important in coagulation are unimportant in thrombosis and vice versa." Merskey also has pointed out that "it is still unproved that there is any relationship between blood coagulation and coronary artery disease." Others have averred that "There is no clear evidence that fibrinolysis plays any part in the normal working of the body."
The Bantu may be regarded as a critical population because they are characteristically free from mortality from coronary heart disease. What information then have they to contribute? In regard to blood coagulation, the studies of Merskey and co-workers have failed to reveal that the Bantu are at an unequivocal advantage in comparison with the white population. The observations on fibrinolysis described in this paper certainly have confirmed that Bantu males have a superior capacity to lyse blood clots, but any intention of attaching etiologic significance to this observation is precluded by not finding similar superiority of activity in blood from Bantu females. The existence of this significant sex bias (not present in white subjects) is puzzling: in any case it is the reverse of what one would conjecture. There appears to be no sex bias of lesions in the aorta and coronary vessels of the Bantu, nor apparently of deaths from coronary heart disease, few in number though they be. If the foregoing be the confused position in regard to blood coagulation and fibrinolysis with a population not prone to die from coronary heart disease, is the corresponding picture at the other extreme, i.e., among those who have had a coronary episode, any more definite?

On the basis of their careful investigations on animals and studies on human autopsy patients, Thomas et al. have postulated "that two factors are involved in arterial thrombosis: (1) a local factor (arteriosclerosis), and (2) a haematological factor (either antifibrinolytic or procoagulative or both)." Now some workers, for example, McDonald and Edgi have reported increased coagulability of blood in patients with ischaemic heart disease; but with other workers, this phenomenon has not been apparent, or only to a limited extent. Although significantly decreased fibrinolytic activity of whole blood has been reported in elderly subjects with intermittent claudication, a decrease in plasma fibrinolytic activity was noted in a series of patients with coronary disease only for a few days immediately after infarction. Furthermore, Merskey et al. have found no difference in mean blood fibrinolytic activity between normal white control subjects and patients who undoubtedly had ischaemic heart disease. In addition, no correlation was found between the level of fibrinolytic activity in patients with coronary disease and the clinical severity of infarction. Briefly then, it will be apparent that in the sequence of Bantu, "normal" white subjects and white subjects with coronary disease, there is no nicely graded series with blood coagulation and with fibrinolytic activity, such as obtains with levels of biochemical components such as serum cholesterol.

The information on the influence of a fatty meal on blood coagulation and fibrinolysis is discordant. Significant alterations in certain blood coagulation criteria evoked by the ingestion of a fatty meal have been reported by some workers, but not by others, except in the case of the "Stypven" time. As already referred to, an increase in fibrinolytic activity following consumption of a fatty meal has been reported by some workers, yet a measure of inhibition by others. In the assessment of such controversial evidence, different conclusions are being drawn. Thus some authorities, such as Jolliffe, consider that "the increased blood coagulability and decreased fibrinolytic activity of certain fats seem established." Others, however, seem driven to conclude that the effect of hyperlipaemia on coagulation and fibrinolysis may not be of major importance in the development of ischaemic heart disease.

The subject of physical exercise and blood coagulation seems to have been insufficiently studied. Billimoria et al. found no change in "Stypven" times. There is no doubt, however, that vigorous exercise and brisk walking temporarily do accelerate fibrinolysis. Nevertheless, the observations reported herein indicate that differences in fibrinolytic activity, whether between groups or among individuals, do not appear to parallel differences in habitual physical activity.

The observations on the Bantu provided herein do little to clarify why these people do not die from coronary thrombosis; indeed, they bring to the fore a number of questions.

(1) A segment of the Bantu population have
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relatively high serum cholesterol levels, long clot-lysis times, severe arterial lesions, also hypertension: why do not more of the elderly people in this particular group die from coronary thrombosis?

(2) Why do the antithrombogenic factors which presumably protect the Bantu from acute occlusive lesions in the coronary vessels fail to prevent them from serious disease or death from thromboembolic lesions occurring in other parts in their arterial system? Hartroft et al.51 have discussed the hypothesis that thrombotic phenomena elsewhere in the body would be expected to be correspondingly low in populations in which coronary heart disease is rare. They adduce that among Uganda Africans the hypothesis is valid. The situation, however, with the South African Bantu would seem to be out of harmony, for cerebral vascular disease (including cerebral artery thrombosis) is an important cause of death.2,9,19,70,71 Indeed, for the forty-five to sixty-four year old age group, mortality rate from this cause among Johannesburg Bantu appears to be one of the highest in the world.5 It must be admitted, however, that the precise moiety of deaths due to cerebral thrombosis is not known; furthermore, as Brock and Gordon72 have pointed out, there is no adequate data on these people to assess the incidence of cerebral accidents due to atherosclerosis per se.

(3) Directly linked with the foregoing is the question of the rationale of seeking, under certain circumstances, to increase fibrinolytic activity on a long-term basis. The need for means to accomplish this has been indicated by a number of authorities.73,74 Yet the anomalies revealed by the data on the Bantu render the position confused. Thus, the mean fibrinolytic activity in elderly Bantu men is much the same as that for young white females, yet elderly Bantu men, while not dying from coronary thrombosis, die readily from cerebral vascular disease. Again, the mean activity of elderly Bantu women is lower than that of elderly white women, yet the former, while not dying from coronary thrombosis, die readily (more so than men) from cerebral vascular disease; elderly white women die readily from both causes. In seeking, therefore, to raise fibrinolytic activity, whether therapeutically76 or by means of restriction of diet and increase in exercise as indicated by Elliott,74 what order of clot-lysis times are to be aimed at? In trying to answer this question, on the one extreme, ignorance of fibrinolytic activity in subjects just prior to an acute thrombotic episode provides a handicap which will not be easy to surmount; on the other extreme, the data on the Bantu, at least in respect to females, afford no guidance.

(4) If atherosclerosis stems primarily from successive thrombotic episodes, as the hypothesis of Duguid75,76 suggests, one wonders why the progression of events in the Bantu almost invariably stops short of coronary occlusion?

It must be made abundantly clear that all that has been adduced and discussed herein does not imply that the in vivo processes of blood coagulation and of fibrinolysis, or the metabolic ramifications of fatty meals or of habitual activity, are of limited importance in regulating the development of ischaemic heart disease. It is entirely possible, as numerous others have stated, that present experimental technics fail to bring out all the differences that prevail between populations prone and not prone to die from coronary heart disease. But on the other hand, again quoting Merskey,17 the possibility cannot be ignored that in such contrasting populations we are looking for differences in certain specific criteria which in actuality do not exist, or exist only to a limited extent.

SUMMARY

Fibrinolytic activity in whole blood has been determined in groups of rural Bantu, urban Bantu and white subjects. It has been found that: (1) Mean activity in rural Bantu males is significantly greater than in urban Bantu males; both groups are significantly superior in activity to the white males studied. (2) Rural and urban Bantu females have significantly lower activities than the white females studied. (3) Fibrinolytic activity determined in groups of Bantu and white
subjects at noon, followed by a fat-free or a fatty meal (31 to 34 gm. butter fat), shows no significant change when determined three hours later; in Bantu males and females there is a tendency toward acceleration of activity following ingestion of the fatty meal, whereas white females tend to show a slight inhibition of activity following both fat-free and fatty meals. (4) A group of rural Bantu pursuing active occupations did not have greater mean fibrinolytic activity compared with another group doing no active work during the experimental period, nor was a correlation apparent in the numerous individual Bantu and white subjects investigated.

It is imperative to take account not only of the limitations of current methods of determining fibrinolysin activity, but also of our ignorance over the applicability of the results obtained to in vivo conditions. Nevertheless, the experimental in vitro observations reported herein, indicating superiority in fibrinolytic activity of Bantu males over white males, but not of Bantu females over white females, demonstrate that higher fibrinolytic activity is not characteristic of the Bantu population. Caution must therefore be exercised against assigning undue importance to fibrinolytic activity (as assessed by the test used) in retarding the occurrence of acute thrombotic episodes in the coronary vessels of these people.

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