DIET, BLOOD CHEMISTRY, BLOOD COAGULATION AND FIBRINOLYSIS IN RELATION TO CORONARY HEART DISEASE: AN INTER-RACIAL STUDY*

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Several genetic and environmental factors predispose towards the development of coronary heart disease. These factors may exert their effects through various mechanisms; of these, the most widely investigated are changes in the blood chemistry (particularly its lipid components) and alterations in the coagulability of the blood or in its fibrinolytic activity. In South Africa, among the White population, the death rate from coronary heart disease is very high, whereas among the Bantu it is extremely low. It was felt, therefore, that some assessment of the importance of the above mechanisms in coronary atherogenesis could be obtained by a comparative study in groups of Bantu men, and in White men with and without overt coronary heart disease. Accordingly, 80 apparently healthy White men, 48 White men with clear evidence of coronary heart disease and 52 apparently healthy rural Bantu men were selected for this study.

The mean age of the 52 Bantu men was 33·8 years. For the purposes of analysing the data, they were compared with an equal number of age-matched White controls (mean age 34·6 years). The mean age of the 48 coronary subjects was 52·3 years; it was not possible to age-match them with Bantu men; they were, therefore, compared with an age-matched group of 52 White subjects of mean age 46·4 years.

RESULTS

A. *Diets*

The average daily food consumption of each subject was recorded and the fat-calorie ratio calculated from food tables. There was no significant difference between the mean daily caloric intake of the 3 groups (control, 2,939 ± 571;† coronary 2,558 ± 517; Bantu, 2,714 ± 506). The fat-calorie ratio was not significantly different in the control (42·7 ± 8·7%) and coronary (41·2 ± 12·5%) groups; in the Bantu group, however, it was very much lower (17·8 ± 6·9%). It was noted that since the onset of their illness, many of the coronary subjects had been tending to restrict their dietary fat intake. Among the Bantu, the dietary fat was derived mainly from maize meal and from soured milk (*amasi*).

B. *Blood Pressure*

No significant differences were noted between the Bantu group and their age-matched controls or between the coronary group and their age-matched controls.

C. *Blood Chemistry*

1. *Serum-cholesterol.* The mean level in the Bantu (147 ± 34 mg. per 100 ml.) was very significantly lower than in their age-matched White controls (243 ± 46 mg. per 100 ml.); this difference was present at all age levels. The mean level in the coronary group (285 ± 44 mg. per 100 ml.) was significantly higher than in their age-matched controls (262 ± 41 mg. per 100 ml.). At the ages of 36-45 years, the difference between the mean level of the controls (251 ± 45 mg. per 100 ml.) and the coronary group (303 ± 50 mg. per 100 ml.) was highly significant; at the ages of 46-55 years and 56-65 years, the mean levels did not differ significantly.

2. *Serum-albumin.* The mean level in the Bantu (4·71 ± 0·3 g. per 100 ml.) was significantly lower than in the controls (4·91 ± 0·5 g. per 100 ml.) but neither of these differed significantly from the coronary group (4·81 ± 0·5 g. per 100 ml.).

3. *Serum-globulin.* The mean level in the Bantu (2·90 ± 0·6 g. per 100 ml.) was significantly greater than in the controls (2·38 ± 0·5 g. per 100 ml.) and in the coronary group (2·38 ± 0·6 g. per 100 ml.).

4. *Thymol-turbidity.* The mean value in the Bantu (1·5 ± 1·7 units) was significantly greater than in the controls (1·2 ± 0·5 units) and in the coronary group (1·2 ± 4 units).

5. *Zinc-turbidity.* This was greatest in the Bantu (11·5 ± 3·8 units) and least in the coronary group (5·3 ± 2·6 units) while the controls were intermediate (6·8 ± 3·0 units); all these values were significantly different.

6. *Serum urea.* The mean level in the Bantu (21·6 ± 6·5 mg. per 100 ml.) did not differ significantly from that of their age-matched controls (25·5 ± 9·2 mg. per 100 ml.). The mean level in the coronary group (28·0 ± 10·2 mg. per 100 ml.) did not differ significantly from their age-matched controls (24·7 ± 8·8 mg. per 100 ml.).

7. *Plasma uric acid.* The mean level in the Bantu (4·22 ± 1·06 mg. per 100 ml.) was very significantly lower than in the controls (5·34 ± 1·02 mg. per 100 ml.). The data for the coronary group are not yet complete.

Comment. The lower serum-cholesterol levels in the Bantu are once more confirmed; the data are consistent with the theory that this is partly determined by the diet of the Bantu, which is low in total fat but relatively rich in unsaturated vegetable fats. The role of genetic, hormonal and other factors in producing the low serum-cholesterol level has not been assessed in this survey. The data are also consistent with the theory that the low serum-cholesterol level is one of the factors which protects the Bantu from coronary heart disease. In the control and coronary groups, the differences in the serum-cholesterol levels are trivial except at the ages of 36-45 years; it will be realized, however, that many of the older 'controls' probably have substantial atherosclerosis and some of them may later develop clinical evidence of coronary heart disease.

It is not known whether the peculiarities of the serum-protein pattern and the flocculation tests in the Bantu are of genetic or environmental origin, and their significance in relation to the development of coronary heart disease cannot be defined at present. There is a known association between high serum-urate levels and coronary heart disease; furthermore, gout, like coronary heart disease, is rare in the Bantu; hence, the relatively low serum-urate levels in the Bantu may be relevant to the problem of atherogenesis.

D. *Blood Coagulation*

(*a*) Comparison of the coronary group with their age-matched

* Abstract of papers presented at meetings of the Research Forum, University of Cape Town, held at Groote Schuur Hospital, Cape Town, on 4 and 17 June 1958.

† Standard deviation.

controls showed no significant difference with respect to the following tests of coagulation:

1. Coagulation time in glass or in silicone-treated tubes.
2. Prothrombin consumption during coagulation of blood in glass or in silicone-treated tubes.
3. Factor V and anti-haemophilic globulin content of plasma.
4. Plasma prothrombin as measured by Quick's (one stage) method, the P. and P. method of Owren, the Russell viper venom (R.V.V.) method, the R.V.V.-cephalin method, or the Biggs method.
5. Factor VII measured on serum.

(*b*) When the Bantu group was compared with the age-matched controls, no significant difference was found in the following tests of coagulation function:

1. Coagulation time in glass or in silicone-treated tubes.
2. Prothrombin consumption during coagulation of blood in glass tubes.
3. Factor V in plasma.
4. Plasma prothrombin when measured by Quick's method, R.V.V. method or R.V.V.-cephalin method.

The following significant differences between the Bantu and their age-matched controls were noted:

1. The Bantu consumed more prothrombin than the controls during coagulation of blood in silicone-treated tubes.
2. The Bantu had greater amounts of antihaemophilic globulin in the plasma.

In these 2 respects the Bantu blood might be considered potentially more coagulable. On the other hand:

1. The Bantu had less Factor VII in their serum than the controls.
2. There was less prothrombin in the plasma of the Bantu group when measured by Owren's P. and P. method which is sensitive to the presence or absence of Factor VII). There was also less prothrombin when it was measured by Biggs' method, which is said not to be sensitive to a deficiency of Factor VII.

In these 2 latter respects, the Bantu blood might be considered less coagulable than the White controls.

Blood thromboplastin generation was measured in the 3 groups. The coronary patients generated a little more thromboplastin than the controls; in the Bantu group this difference from control was more clear-cut than in the coronary group. There was no significant difference between the amount of thromboplastin generated by the Bantu and the coronary groups.

Comment. This phase of the investigation did not provide any clear evidence of a greater tendency to coagulation in the blood of patients with coronary heart disease than in apparently healthy controls; nor did it explain the relative immunity of the Bantu from thrombotic disease. In fact, the results of these investigations might suggest that the blood of Bantu men has a greater tendency to clot than that of White men.

E. *Fibrinolysis*

Fibrinolytic activity was estimated as the clot-lysis time of a 1 : 10 diluted blood clot. It was found that clot-lysis in the Bantu (mean: 5·59 ± 5·7 hours) was almost twice as fast as in their age-matched controls (mean: 10·44 ± 10·1 hours); this difference was significant at the 1% level. There was no significant difference between the mean lysis time of the coronary group (12·31 ± 13·4 hours) and their age-matched controls (11·03 ± 22·5 hours).

Whereas in the Bantu 8 clots lysed in less than 2 hours, in none of the control or coronary subjects was a lysis time of under 2 hours recorded. Only 1 Bantu clot took longer than 16 hours to lyse but 17·6% of the coronary and control subjects had lysis times of over 16 hours and in 12·8% it was over 20 hours. Studies on the day-to-day variation of fibrinolytic activity in the same subjects under standard conditions indicated that apparently spontaneous fluctuations of up to 300% may occur.

Although the Bantu have faster lysis times and lower serum-cholesterol levels than the controls, these factors do not seem to be closely related. Changes in the serum-cholesterol level induced by feeding 2 Bantu subjects in the metabolism ward with saturated and unsaturated fats, failed to show any correlation with fibrinolytic activity.

Comment. It appears that phases of slow fibrinolysis are characteristic of the White race, but the role that this may play in atherogenesis remains purely speculative. The Bantu is characterized by a greater fibrinolytic activity but whether this is the result of hepatic dysfunction, dietary custom or any other inherent or environmental factors is at present unknown.

Acknowledgment is made to the South African Council for Scientific and Industrial Research and to the following additional sources of financial aid in these studies: the National Heart Institute of the United States Public Health Service, the Cape Town City Council, the South African Mutual Life Assurance Society, the Cape Fishing Industry, the A. R. Richardson Research Fund and the Staff Research Fund of the University of Cape Town.