The Etiology Of Acute Coronary Thrombosis

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The morphology and pathology of acute coronary thrombosis with or without myocardial infarction is more or less clearly understood but little is known of its etiology. A better understanding of the cause of this disease can be had if one looks back over a period of thirty or more years and compares its frequency then as of today. It would be helpful if we include areas in different parts of the world and a study of the animal kingdom in which it is almost unknown.

The use of anti-coagulant therapy has gained a tremendous following in the treatment of thrombo-embolic disease. As pointed out by Sebrell it is an empirical form of treatment.

It has been established that a normal prothrombin activity varies from eighty-five to one hundred per cent. (Quick) We must conclude that since those cases which develop thrombo-embolic episodes have hypoprothrombinemia a deficiency of prothrombin is responsible. The results of prothrombin deficiency is hemorrhage: either intimal, subintimal or in the atheromatous plaque. (Wartman, Winternitz, Patterson, Boyd, Durlacher) Thus the anticoagulant therapy is the only form of treatment in use today that attempts to convert a normal condition into an abnormal one.

From the private pavilions of The Norfolk General and Leigh Memorial Hospitals.

I wish to thank Dr. Edward Levy, Clinical Pathologist of The Norfolk General Hospital and Mr. A. D. Farmer, Director of The Norfolk City Laboratories. Also the technicians and dieticians of both hospitals for their assistance in this work.

Prothrombin determinations have been routine procedure on all patients either in the hospital or office during the past fifteen years. During this period I have never seen a case of acute coronary thrombosis that was not associated with hypoprothrombinemia. In many instances a temporary rise in the prothrombin activity may reach as high as ninety-five percent following an acute episode, which may be nature's effort to offset the injury but the supply of prothrombin stored is not equal to maintain its activity within the level to prevent further hemorrhage and further thrombosis. Shapiro has attributed this temporary rise to thromboplastin released from the thrombus.

A series of investigations brought out a new fat-soluble vitamin known as Koagulation Factor, later shortened to K Factor and then called Vitamin K. (Dam, Alquist, and Stokstad) Stokstad showed that the product of this vitamin was prothrombin. Dam showed that when chicks were fed on a diet deficient in this vitamin they hemorrhaged and were then controlled by supplying vitamin K. It was found that Vitamin K is absorbed in the small and a portion of the large bowel through the action of bacteria and bile present in the intestines and from there it is carried to the liver through the blood stream where it is synthesized into Prothrombin, an active element in blood clotting.

In determining the prothrombin level the Quick Method still gives the most consistent results as it determines the prothrombin activity by the logarithmic curve. This method shows a lower reading warning of the early danger of hemorrhage.

Primary factors entering into the mechanism of blood clotting:

Platelets plus foreign substance Thromboplastin
Thromboplastin plus Prothrombin plus Calcium Thrombin
Thrombin plus Fibrinogen Fibrin (Clot)

(Alexander)

It is now known that the richest source of Vitamin K is found in pig-liver, fish meal and vegetables such as cabbage, tomatoes, spinach, kale, turnip salad, collards, broccoli, outer leaves of lettuce, all of the pea and bean group, cauliflower. Any two of the above eaten daily will maintain a prothrombin level within safe limits.

Vitamin K is stable to heat but apparently not to extreme cold or freezing. The following chart shows the effect of vegetables frozen and vegetables fresh or canned on the prothrombin activity of one hundred and fifty cases admitted.
to the hospital from June 1, 1952 to June 1, 1955. There were no coronaries in this group.

<table>
<thead>
<tr>
<th>Sex</th>
<th>No. Cases</th>
<th>Admissions</th>
<th>Frozen 4th-6th Day</th>
<th>Frozen 8th Day</th>
<th>Maintained 92%</th>
<th>Canned 94.3%</th>
</tr>
</thead>
<tbody>
<tr>
<td>M</td>
<td>64</td>
<td>77.3%</td>
<td>59.5%</td>
<td>95%</td>
<td>94.3%</td>
<td></td>
</tr>
<tr>
<td>F</td>
<td>86</td>
<td>80.0%</td>
<td>61.5%</td>
<td>96%</td>
<td>96.1%</td>
<td></td>
</tr>
</tbody>
</table>

In this paper we are not referring to the type of heart which is the result of sclerosis of the coronary arteries resulting in lack of blood supply to the heart muscle. The pain is usually associated with excitement, stress or strain and while the patient may die there need be no disturbance in the prothrombin level.

Certain drugs have a decided effect on producing hypoprothrombinemia. The entire mycin group, penicillin and sulfaguanadine lower the prothrombin level as the result of sterilization of the intestinal tract. Mineral oil and its derivatives inhibit the action of Vitamin K because K is a fat soluble vitamin. Although the barbiturates and salicylates lower the prothrombin level the action is not known. When these drugs are prescribed a daily check on the prothrombin activity should be carried out and when the level begins to drop Vitamin K should be given intramuscularly or intravenously.

Hypoprothrombinemia is a common finding in patients with edema.

I should like to give the findings from the report from The Committee of The American Heart Association in cooperation with The Society For The Study of Arterio-sclerosis. The fact is that the basic problem is not lipemia, hypercholesteremia or hepatic lipid excess, but it is atheromatosis and in particular myocardial infarction. Atheromas have not been described or associated clinically or experimentally with fatty acid deficiency. With the exception of Hartcroft and Thomas' recent production of myocardial infarction in animals on certain dietary regimens high in fat: myocardial infarction has not been precipitated in animals by excessive intake of any particular fat or of cholesterol or by a deficiency of pyridoxine or any unsaturated fatty acid.

Considering the production of myocardial infarction in animals fed a high fat diet this would have no meaning if the animals were restricted on foods containing Vitamin K or if they were penned up and not allowed to supply themselves naturally.

The ratio of acute coronary thrombosis with myocardial infarction is approximately six to one in favor of the white male over the negro male. Let us give some thought to the Southern section of The United States where we have a lower income bracket and a vast population of negroes, which means that they live as cheaply as possible, a large number having their own vegetable gardens in back yards. We find them for about eighty years relying chiefly on a diet of salt pork and fresh green vegetables. Why then did they not outstrip the white male in coronary thrombosis?

Elliott¹⁴ quotes J. C. Gilroy, V. H. Wilson, A. B. Gillanders and I. J. Grek as agreeing that all forms of arterio-sclerosis, atherosclerosis and Monckeberg's Sclerosis are common in the Bantu tribe of Africa yet he comments that it may be safely stated that coronary disease is extremely rare. In East Africa, Davies (1948) reports that one of the most puzzling features of atheroma in Negroes is the rarity of coronary thrombosis. Edington (1954) confirms the low incidence of myocardial infarction in the West African Negro. These people rely heavily on a diet of vegetables, as shown by Dr. Frederick Stare, Department of Nutrition, Harvard Medical School.

If one takes the mortality rate from acute coronary thrombosis as shown by the American Heart Association throughout the world (1953) and then refers to the book by M. K. Bennett, Director, Food Research Institute, Stanford University, on food consumption per dollar value there will be little difficulty in determining which countries have a high or low rate of coronary thrombosis.

Acute coronary thrombosis is practically unknown in cattle, dogs or rabbits although thrombosis occurs in the superficial vessels as the result of trauma or infection. The prothrombin activity is far greater in animals than it is in the human yet when six rabbits were put on a diet of frozen vegetables and given antibiotics the prothrombin time became prolonged just as it does in the human.

In six rabbits using a thirteen second prothrombin activity as normal they showed an average of 3.5 to 4 seconds. They were then divided using two for controls which were put
coronary thrombosis showed 113 white males and 13 negro males. In 1956 the mortality rate had risen to 2,614 white males and 1,122 white females; 448 negro males and 270 negro females.

It is of great interest to note the rural areas after 1950 pulling up and surpassing the urban areas in coronary thrombosis. In 1930 the urban areas showed 65 deaths and the rural 61 deaths. In 1950 the urban areas showed 1,621 deaths and in the rural areas 1,975 deaths while the year 1955 showed 1,929 deaths while the rural areas showed 2,306 deaths. 14

In 1947 the deep freeze ice boxes were installed in the rural areas and most of the people are making use of them for the storing of vegetables through the winter months rather than the old canning procedure.

I should like to conclude this paper by saying that in a case of coronary thrombosis with or without myocardial infarction, keeping the prothrombin level at what may be considered a low safe by the use of anti-coagulants, is not the answer to the problem of hemorrhage. Vitamin K should be given at the time of the initial attack to restore the prothrombin level to normal thereby reducing further danger of hemorrhage and thrombosis.

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